Journal of the University of Malaya Medical Centre

JUMMEC

Volume 8 **2003–2005**

Correspondence

All manuscripts, general correspondence and enquiries should be addressed to:

The Editor
c/o Dean's Office, University of Malaya Medical Centre
50603 Kuala Lumpur, Malaysia
Tel: (03) 7950-2077 Fax: (03) 7956-8841
E-mail: ZAKIIAH@ummc.edu.my

Publisher

JUMMEC is published twice a year by the University of Malaya Medical Centre, 50603 Kuala Lumpur, Malaysia

Cover

L pneumophila viewed by immunofluorescence staining
(Courtesy of Professor Ngeow YF, Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Kuala Lumpur)

Printed by

Millennia Comms, Petaling Jaya, Selangor Darul Ehsan, Malaysia

Journal of the University of Malaya Medical Centre
JUMMEC

Instructions to Authors

JUMMEC welcomes manuscripts on all aspects of medicine in the form of original articles, case reports, review articles, clinico-pathological conference abstracts and letters to the Editor. Manuscripts should be submitted to:

The Editor
JUMMEC
c/o The Dean's Office
University of Malaya Medical Centre
50603 Kuala Lumpur
Malaysia

Manuscripts: All manuscripts should be submitted in duplicate, typed on one side of A4 size paper and double-spaced with at least 2.5 cm margin. A computer diskette (3.5 in) containing the manuscript in MS Word 6.0 or Word Perfect and a covering letter, stating that the work has not been published or under consideration for publication elsewhere, should be submitted to the Editor. Presentations at meetings do not class as prior publication. The text of the manuscript should be in the following form:

Title page: The title page should contain a concise title of the article. It should identify all the authors, the name(s) of the institution(s) and their full addresses where the work was carried out. The initial and address of the corresponding author should also be indicated.

Abstract and Keywords: The second page should contain an abstract of about 150-200 words. It should state the purpose of the study, a brief description of the procedures employed, main findings and principal conclusions. Three to ten keywords should also be listed below the Abstract.

Text: Wherever possible, the text should consist of an introduction, materials and method, results, discussion and references.

References: Number references consecutively in the order in which they are first mentioned in the text. References in the text should be indicated by a figure within parenthesis ( ). The titles of journals in the list should be abbreviated according to the Index Medicus. Authors are responsible for the accuracy of all references. Examples of correct forms of references are given as follows:

i) Journal reference:
Roberts CW, Alexander J and Bossi L. Studies on a murine model of congenital toxoplasmosis. Parasitol 1992; 104:19-23.

ii) Personal author(s) of book:
Osler AG. Complement: mechanisms and functions. Englewood Cliffs: Prentice-Hall, 1976.

iii) Chapter in book:
Weinstein L., Swartz MM. Pathogenic properties of invading microorganisms. In: Sodeman WA Jr, Sodeman WA, Eds. Pathologic physiology: mechanisms of disease. Philadelphia: WB Saunders; 1974; 457-72.

Tables: Type each table on a separate sheet and number in arabic numerals. The tables should be as few and as simple as possible, with the title above and any notes or description below. Explain all abbreviations.

Figures: Graphs, drawings and photographs should be submitted as clear, glossy prints measuring 12 cm by 17 cm. Figures should be identified on the back with the title of the article and figure number (in light pencil) and an arrow to indicate the top. Legends to the figures should be submitted on a separate sheet. Explain all abbreviations and symbols used.

Letter of Consent: Submissions must be accompanied by a letter of consent, signed by ***all*** authors, containing the following text:

"The manuscript represents original, exclusive and unpublished material. It is not under consideration for publication elsewhere. Further, it will not be submitted for publication elsewhere, until a decision is conveyed regarding its acceptability for publication in the JUMMEC. If accepted for publication, I agree that it will not be published elsewhere, in whole or in part without the consent of the Journal of the University of Malaya Medical Centre. The undersigned author(s) hereby transfer/ assign or otherwise convey all copyright ownership of the manuscript entitled (*the title of article*) to the Journal of the University of Malaya Medical Centre."

REBIRTH OF JUMMEC

The year 2005 has been magnificent. We celebrated the centennial anniversary of our university – a remarkable milestone in our history. And, after a hiatus of two years, JUMMEC is now making its long awaited comeback. We aim to make a definite presence in the University of Malaya Medical Centre. Through the publication of JUMMEC, we will be able to disseminate information and learn of each other's work and highlight studies that are particularly relevant in our local context.

As the new Editor of JUMMEC, I see this opportunity as a challenge to revive this journal and share with you all the knowledge, ideas and thoughts presented by those published. There are no limits or boundaries in Medical Science, and in this issue, there is a mix of original and review articles as well as a case report. Wong and Mohd Amin in their paper on "Malaysian Society and Health: Issues and challenges in the 21st century" highlight the health transition from communicable diseases to chronic illnesses – the price we pay for our rapid advancement and development. There are emerging and re-emerging health problems that Malaysia, an aspiring developing country, will have to grapple with. In "Cardiopulmonary Exercise Testing: Utility in research and patient care", Elina *et al* in their review note that cardiopulmonary exercise test, a non-invasive physiological test, is also a valuable tool for assessing therapeutic interventions in heart failure. The use of cardiopulmonary exercise testing in research has led to its extensive clinical usage, particularly in respiratory and cardiovascular medicine, sports medicine, surgery and occupational and rehabilitative medicine. Wan Azman and Haizal then provide an "Overview of peripartum cardiomyopathy" and discuss the challenges that lie in diagnosing and managing this disease.

Original articles in this issue include Chin *et al*'s paper on the "Isolation of *Legionnella* from cooling towers and potable water systems in hospital and non-medical buildings in a university campus". Four water samples yielded *Legionnella*-like organisms, out of 17 water samples collected, and areas that harbour *Legionnella* in a hospital are pinpointed as the authors discuss how serious the implications could be. Monitoring of water supplies and chemical disinfection with oxidizing agents or thermal disinfection should be carried out as preventive measures. Fathihah *et al* in their animal study on the "Antiulcer and cytoprotective effect of *Ageratum conyzoides*-honey combination in rats", demonstrate that honey in combination with plant extracts might be beneficial in the treatment of gastric mucosal injury.

Lifestyle disease is prevalent in today's society, brought about by rapid industrialisation and urbanisation. Moy and Atiya carried out a cross-sectional study of 136 respondents, and uncover a high prevalence of obesity, co-morbidities (diabetes mellitus and cardiovascular diseases), as well as unhealthy lifestyle practices such as smoking, along with the low prevalence rate of adequate exercise. There is certainly a need for health promotion and education targeted towards increasing awareness of healthy lifestyles. Meanwhile, Noor Azmi and Aniza undertook a retrospective study of 217 term breech infants and consequences on practice, and report a noticeable trend towards Caesarean sections. The authors note that neonatal outcomes of babies born abdominally were statistically better than those born vaginally, but there was little clinical impact.

In the past two decades, cost containment of anaesthesia and surgery as well as changes in surgical practices have led to changes in anaesthetic practice. Chiu *et al* did a "Prospective audit of Desflurane anaesthesia in the University of Malaya Day Surgery Unit" of fifty ASA I-II patients, and found that Desflurane provides controllable anaesthesia and is haemodynamically similar to other commonly used inhalational anaesthetics. Desflurane may be a suitable agent for daycare anaesthesia. Omar did a restropective study of 102 hands with Carpal Tunnel Syndrome, comparing conservative treatment to surgery. Hands that failed conservative treatment and later underwent surgery tended to have longer duration of symptoms prior to treatment. Surgery offered faster relief from pain and numbness. The author recommends that conservative treatment be abandoned after a trial period of at least three to five months in favour of surgery for speedier recovery. In Loo and Razif's randomised prospective study on "Skin closure using simple interrupted and continuous subcuticular nylon sutures: A comparison of results", eighty patients with closed fracture of radius-ulna or femur were roped in, and the simple interrupted technique was shown to be slower than the subcuticular technique, with higher early post-operative wound complication rate. The authors conclude that the choice of technique did not affect the final outcome of the wound, up to the sixth month post-surgery.

As we dash into the second half of this new decade, the Editorial team welcomes everyone's contribution to fill these pages with fundamental discoveries and innovations and findings that pique us all towards further advancements and greater challenges. The success of a journal depends on our enthusiasm to impart our knowledge, so please, "write away" for JUMMEC. We, the Editorial team will continue to seek exclusive material. You, in turn, are our avid readers, eager submitters, and venerable reviewers. This is your Journal. JUMMEC is now reborn!

Rosmawati Mohamed ***(MBBS, MRCP, M.Med, MD)***
Editor, JUMMEC
Dean's Office, Faculty of Medicine, University of Malaya

MALAYSIAN SOCIETY AND HEALTH: ISSUES AND CHALLENGES IN THE 21ST CENTURY

Wong YL[1] and Mohd Amin J[2]
[1] Health Research Development Unit (HeRDU), University of Malaya Medical Centre, 50603 Kuala Lumpur
[2] Dean's Office, University of Malaya Medical Centre, 50603 Kuala Lumpur

ABSTRACT: Malaysia, like many aspiring developing countries, is undergoing a health transition that has seen the concomitant decrease in communicable diseases and increase in chronic diseases due to urbanization, modernization and ageing population. Health in the Malaysian society will thus increasingly focus on emerging problems that are both chronic and infectious in nature, such as, heart disease, diabetes, cancer, mental health, hepatitis and HIV/AIDS. Re-emerging diseases previously well-controlled, such as, tuberculosis for instance is another addition to these immediate health issues facing Malaysian society today.

Despite the tremendous health gains and above average health status that Malaysians now enjoy, we are compelled to take stock of these urgent issues as well as to anticipate and handle serious challenges to our health in the 21st century. In this paper, we review the changing trends and discuss related challenges in disease pattern, environmental health, demographic impacts on health, migration influxes and health, effects of globalization on health, mental health and wellness as well as fundamental access and equality in health care.

Being proactive, resilient and innovative, Malaysian society would forge ahead towards our Vision for Health in this new era. ***(JUMMEC 2003-2005; 8: 2-8)***

KEYWORDS: Society and health, health trends and issues, Vision for Health, Malaysia

Introduction

Health is complete physical, mental, social well-being
and not only the absence of illness of an individual.
– WHO/Allopathic Practitioner –

Health is not simply a physical or a mental state.
Health is a state of balance in the body,
the family, the village, the country,
and the world.
– Sri Lankan Ayurvedic Practitioner –

In the new era, Malaysia may well be on the road towards achieving developed nation status. To some extent and in comparison to neighbouring countries, Malaysian society today enjoys relatively high standards of living, above average health status, political and economic stability. Yet, we must not become complacent. With the dawning of the new millennium, there are also numerous challenges to our society, not least of which is ensuring the availability of sustained quality health care and services. The recent economic and financial climate pose serious challenges to the Malaysian health care system and our above average health status. There is also the need to continually improve the management of our health care system to cope with changing demography, rapid social change due to modernization/urbanization, newly emerging as well as re-emerging diseases that were previously well-controlled.

Correspondence:
Wong Yut Lin
Associate Professor
Health Research Development Unit (HeRDU)
University of Malaya Medical Centre
50603 Kuala Lumpur
Tel: 603-7967 5739/5728
Fax: 603-7967 5769
Email: wongyl@um.edu.my

Health Status

Access

Malaysians today enjoy greater accessibility to health services as indicated by the proportion of doctors per 10,000 population that had trebled from 2.6 in 1980 to 6.8 in 2000. 88% of the urban poor and 77% of the rural population are within nine km of either a Government or private clinic. It is important to point out that these milestones towards achieving good health status had been gained with relatively low health expenditure. The 1996 National Household Health Expenditure Survey (NHHES) found that although private health care costs were higher, private facilities were the most frequently utilized sources of care for acute conditions. However, for inpatient care, the low-income group tended to utilize services provided by the public or government health sector (1). The Second National Health and Morbidity Survey 1996 reported that only 26% of women had gone for pap smear screening despite availability of pap smear screening since the 1960s, indicating that sociocultural and gender factors impact on access to health services (2).

Mortality

It is an undeniable fact that Malaysians enjoy a relatively good health status as reflected in our selected health indicators (Table 1). Increasing life expectancy and the sustained decline in infant (IMR) and maternal mortality rates (MMR) are significant indicators of the above average health status of Malaysian society. Male life expectancy increased from 66.7 years in 1980 to 70.2 years in 2000, while Malaysian women today are expected to live up to 75 years. As shown in Table 1, the sharp decline in the Malaysian infant mortality from 19.7 per 1,000 livebirths in 1980 to 7.9 per 1,000 livebirths in 2000 is an impressive achievement, comparable to that for middle-income and high-income countries. However, IMR rates for Sabah and Sarawak are not comparable to that in the Peninsular because of under-reporting, lower level of development, and higher proportion of births delivered by untrained birth attendants (3).

Over the 20 years from 1980 to 2000, maternal deaths have not only been significantly reduced, from a MMR of 0.6 per 1,000 livebirths to 0.2 per 1,000 livebirths, respectively, but the latter has been sustained since 1995. Once again, we need to take note of the regional and social class differences. For instance, while the rate of decline seems more rapid for Peninsular Malaysia, it appeared to have stabilized in the 80s due to the lag in development in Sabah (0.4 per 1,000 livebirths in 1998). In Sabah, the implications of migrants from poorer neighbouring countries have to be considered, that is, their lower socio-economic status impacting upon infant and maternal mortality (4).

Morbidity

As mentioned earlier, Malaysian society experience both infectious and chronic diseases due to the health or epidemiologic transition that we find ourselves in today.

Communicable/Infectious diseases

Malaysia has been successful in controlling communicable diseases through child immunization programmes, provision of safe water supply, proper sanitation and waste disposal, and food quality control. For example, the immunization programme in 1999 achieved 100% coverage for BCG, 94.1% for the triple antigen vaccine (diptheria, pertussis and tetanus),

Table 1. Selected indicators of health status

Health Status Indicator	1980	1985	1990	1995	1997	2000*p*
Life Expectancy						
Male	66.7	67.9	68.9	69.3	69.6	70.2
Female	71.6	73.0	73.5	74.0	74.5	75.0
Infant mortality rate (per 1,000 livebirths)	19.7	17.0	13.5	10.5	9.5	7.9
Toddler mortality rate (per 1,000 livebirths)	1.8	1.4	1.3	0.8	0.7	0.6
Maternal mortality rate (per 1,000 livebirths)	0.6	0.4	0.3	0.2	0.2	0.2
Crude birth rate (per 1,000)	30.9	31.7	28.4	28.0	25.5	24.5
Crude death rate (per 1,000)	5.3	5.0	4.7	4.4	4.6	4.4
Doctors per 10,000 population	2.6	3.2	3.8	4.5	6.6	6.8
Dentist per 10,000 population	0.5	0.7	0.7	0.9	0.9	0.8

Source: References (8), (12) and (13)
Note: p – preliminary figures

86.2% for measles, and 93.4% for poliomyelitis. Indeed, Malaysia was declared a polio-free area in October 2000. The incidence rate for malaria declined from 286.1 per 100,000 population in 1995 to 60.8 in 1999 (1). Outbreaks of dengue haemorrhagic fever occur periodically, more so in urban areas. A seasonal variation in dengue outbreaks has been identified, with increased rates during the dry season (May to September) (5). Malaysian society was recently shaken by the emergence of the Nipah Virus outbreak. Learning from this experience, efforts to establish the Infectious Disease Centre were started in 1999; and rapid response and greater collaboration efforts were established through the inter-ministerial committee and networking with international bodies, such as the WHO and the CDC in Atlanta (1). Full coverage of piped water supply was achieved for urban areas and 84% for rural areas in 2000. These efforts contributed to a reduction in the incidence of water-borne disease from 3,500 in 1995 to 2,100 in 2000. The rural sanitation programme covered 99% or 1.7 million households in the same year (1).

Malaysian society ought to wake up to the HIV/AIDS epidemic in our midst impacting on everyone – men, women, adults and adolescents, and not confined only to intravenous drug users. The data point to a dramatically increasing trend since the first cases were identified in 1986. The HIV/AIDS incidence rate increased steadily over the 10 years, from 0.01 per 100,000 population in 1987 to 2.43 per 100,000 population in 1997. Whilst the mortality rate of AIDS followed a similar increasing trend from 0.02 per 100,000 population in 1988 to 1.88 per 100,000 in 1997 (6). From three HIV cases in 1986, the number escalated to 4,692 cases in 1999, with a cumulative total amounting to 33,233. The cumulative total for AIDS cases was 3,554 in 1999. 94% of these were men and 6% were women. The upward trend for women is noticeable since 1995 and this is worrisome. 42% of the HIV+ cases were below 29 years of age and 30% of AIDS cases were found within this cohort. Although a relatively small proportion (4%) of known AIDS cases were adolescents (13-19 years), 22% of them were between 20-29 years. This latter group may have first contracted HIV during their teens, given the possibly lengthy period between viral infection and appearance of disease symptoms. Indeed, data showed that the Heterosexual category had the second highest proportion of HIV+ and AIDS cases, following after the intravenous drug user category (7).

In terms of programmes, the Ministry of Health Malaysia began monitoring and surveillance since 1985 of the numbers afflicted by instituting mandatory reporting under the Prevention and Control of Infectious Diseases Act (1988). In 1995, a Malaysian AIDS Charter was launched by the Minister of Health, a document formulated by nearly 80 government and NGO agencies involved in AIDS-related activities, in consultation with people with HIV/AIDS, representatives from various groups, including religious leaders and sex workers. This Charter explicitly states the rights and responsibilities of individuals, organizations and government bodies pertaining to AIDS, and addresses significant issues such as testing, confidentiality and access to information and education (3).

Among the principal causes of hospitalization at government hospitals in 1998 in Malaysia, excluding normal birth deliveries and pregnancy complications, injury and poisoning and infectious and parasitic diseases were prominent causes (Table 2).

Data on deaths by medically certified and inspected cause in Table 3 show that septicaemia, pneumonia and tuberculosis were the most common fatal infections in 1998, accounting for 6.7%, 4.3% and 1.3% of total deaths (43,514), respectively. Moreover, there was an increasing trend for all three diseases for the period 1994 to 1998 (8).

Chronic diseases

Chronic diseases have become more prominent in our country with time. Part of the increase in chronic ailments is due to improved longevity among Malaysians as mentioned earlier. At the same time, economic progress and increased affluence accompanied by changes in lifestyle, including diet, have also contributed to this change in disease pattern.

The Second National Health Morbidity Survey showed increasing incidences of non-communicable or chronic diseases amongst the Malaysian population, such as, hypertension, diabetes, and obesity as well as mental disorders (1). A review of hospital deaths also revealed the relative importance of adult non-infectious diseases related to lifestyle, occupation and environmental risks such as cardiovascular diseases, cancers, injuries, and accidents. While deaths due to communicable/ infectious diseases and fevers have seen marked reductions in all age-specific groups, deaths from accidents, cardiovascular-related diseases, and cancers have increased in almost all age-specific groups between 1982 and 1996 (6).

Table 3 shows the increasing prominence of non-communicable illnesses with regards to causes of medically certified deaths, such as heart disease and cerebrovascular disease, compared to infectious diseases such as pneumonia over the period 1994-1998. The most common certified cause of death continues to be cardiovascular, particularly, acute

myocardial infarction, and cerebrovascular disease. As a group (hypertensive disease, myocardial infarction, ischaemic heart disease, cerebrovascular disease, atherosclerosis and other diseases of the circulatory system), these conditions constitute about 27.8% of total deaths in 1998 (8).

Malignant neoplasms have increased as a contributor to total deaths in this country, particularly, malignant neoplasms of trachea, brochus and lung (Table 3). In 1999, the annual prevalence of cancer in Malaysia was estimated to be 230 per 100,000, and the annual incidence was estimated to be 30,000. The incidence of cancer is expected to rise with an increasingly ageing population. A regional cancer registry has shown that the ten leading cancers among men were lung, nasopharynx, stomach, urinary bladder, rectum, non-Hodgkin's lymphoma, larynx, liver, colon, and the oesophagus. While the ten leading cancers among women were cervix, breast, ovary, lung, nasopharynx, oesophagus, thyroid, colon, rectum, non-Hodgkin's lymphoma (8-9). It is important to note here that cancer of the lung is the most common killer amongst malignancies.

Mental health

Until very recently, relatively little attention has been paid to mental health issues in this country despite the growing manifestations. Hence, it is timely to take note of this problem here. Mental health problems tend to bear the stigma of shame and embarrassment for family members, and hence, are kept concealed. Skilled manpower resources, such as psychiatrists, psychologists, counsellors and behavioural scientists, capable of dealing with mental health issues are very much lacking in Malaysia at this stage of its development. It is alleged that traditions, religious beliefs, and social behaviours have important influences on suicides in every country, as illustrated in the consistently low rates in Islamic countries and rising trends in societies experiencing rapid social change (9).

As an indicator of mental health, the number of deaths due to suicides and self-inflicted injuries had increased from 36 or 0.1% in 1994 to 200 or 0.4% of total deaths in 1998 (Table 3). The data collected from the Ministry of Health hospitals from all states showed that there was 2,931 suicide cases in 1996 and 2,738 cases in 1997. In Malaysia, the suicide rate is 3 per 100,000 population which is relatively low as compared to a rate of 20% in France (1990). The suicide rate prevalent in a society is said to be one of the important indicators of its socio-economic structure and status and is determined by various psychological, socio-economic and cultural factors. There seemed to be a gender difference in suicide rate, as shown in data on suicide and parasuicide from public hospitals in the country whereby the rate among women was higher than that among men for the years 1995, 1996 and 1997 at 59.9%, 63.3%, and 60.8% respectively (9). Data on attempted suicides admitted to a major public hospital in the capital city showed that the majority were women of lower income, low education, Indian ethnicity, and younger age (< 39 years) (10). There were twice as many women as men among the cases. Depression caused by maladjustment to psychosocial stressors, particularly, financial problems and interpersonal conflicts with spouses, friends and family members, was the main predisposing factor involved in the suicide attempt.

Table 2. Principal causes of hospitalization in government hospitals, Malaysia, 1998

Principal Causes	Number of Discharges
Total	1,552,845
Normal delivery	305,380
Complications of pregnancy	186,994
Injury and poisoning	162,170
Diseases of the circulatory system	103,512
Certain conditions originating in the perinatal period	83,022
Diseases of the respiratory system	101,123
Diseases of the digestive system	72,006
Signs, symptoms and ill-defined conditions	63,120
Infectious and parasitic diseases	116,703
Diseases of the urinary system	68,590
Diseases of the blood and blood-forming organ	10,749
Others	279,476

Health Issues and Challenges

Despite the tremendous health gains and above-average health status that Malaysians now enjoy as described above, we are compelled to take stock of the emerging health issues as well as to handle serious challenges to our health in the 21st century. These include changing trends in diseases due to demographic and health transitions, environmental health, migration influxes and health, effects of globalization on health, mental health and wellness as well as fundamental access and equality in health care.

Demographic and health transitions – Impact on morbidity patterns

The changes in the Malaysian demographic profile that will warrant attention from the health sector are our gradually ageing population, urbanization/modernization, the nuclear family structure, and a population that is increasingly health conscious (6). In the foregoing discussion on diseases, some of the recorded changes in the pattern of morbidity have been due to changes in the age composition of the population. At the same time, modernization has also influenced society's values and behaviour with an impact on both communicable and non-communicable diseases. For example, demographic changes have led to an increase in the number of adolescents and young adults being exposed to the related rise in the risk and prevalence of sexually transmitted diseases. Moreover, changing attitudes towards sexuality might also influence sexual behaviour and the transmission of diseases. Thus, how sex education can impact positively on sexual behaviour in the future and how to prevent or diminish the incidence of disease will be one of the future challenges. Although generally Malaysia has been successful in controlling communicable diseases, some of these, such as, HIV/AIDS, dengue, and tuberculosis will continue to be a challenge together with non-communicable diseases such as cardiovascular-related diseases, cancers, and accidents. Thus, we would need to be vigilant in sustaining the health successes and gains and not be lulled into complacency.

Environmental degradation and health

The Ministry of Health (MOH) has identified environmental factors to be the major contributors to the health problems of Malaysian society in the future. Environmental degradation is becoming a great concern for the country because it will undermine the sustainability of social and economic development and health. The three areas pertinent to environmental consideration and public health are water pollution, air pollution, and the management of solid waste. The MOH alleged that the observed rise in cardiovascular diseases, cancer, and accidents should not be attributed entirely to individual lifestyle changes or viral infections. Instead, environmental and occupational hazards such as industrial conditions, crowded roads and pollution are major causes of

Table 3. Deaths by medically certified and inspected cause, Malaysia, 1994-1998

Cause of Death	1994	1995	1996	1997	1998
Total deaths	38,223	41,395	41,694	44,154	43,514
Pneumonia	1,245	1,492	1,433	1,670	1,865
Tuberculosis	525	524	573	569	573
Septicaemia	1,980	2,399	2,641	2,741	2,923
Malignant neoplasm of tranchea, bronchus and lung	832	884	821	909	941
Malignant neoplasm of female breast	260	320	297	339	339
Malignant neoplasm of cervix uteri	165	142	146	129	177
Diabetes mellitus	720	734	677	807	729
Hypertensive disease	275	285	362	530	450
Acute myocardial infarction	3,166	3,383	3,306	3,426	3,328
Other ischaemic heart disease	899	931	932	1,039	1,062
Cerebrovascular disease	3,136	3,349	3,271	3,355	3,367
Atherosclerosis	5	5	2	1	1
Other diseases of circulatory system	3,274	3,664	3,621	3,830	3,902
Motor vehicle traffic accidents	2,039	2,289	2,693	2,985	2,577
Suicide and self-inflicted injury	36	52	92	177	200
Homicide and injury purposely inflicted by other persons	47	44	74	117	141
Other violence	2,303	2,534	2,429	2,300	2,115

Source: Reference (8)

injuries, respiratory disease linked to cardiovascular disease, and cancer. The impact is more marked in males in the 30-63-years age group, particularly in relation to accidents, cancers, and heart attack rates. It is important to note the MOH views seriously the effects of urbanization on the environment and health. The urban areas, with the 'built environment', are now faced with a host of new problems arising out of atmospheric and water pollution, accidents, urban housing, town planning as they relate to mental, social, and physical health (3,6).

Migration and health

Here we are concerned in particular with the issue of foreign migrant workers. As Malaysia's relatively favourable socioe-conomic conditions have drawn a large pool of foreign workers, it has also created a whole set of health and social issues and problems, especially in the introduction and transmission of diseases and different value systems that need to be addressed. In 1994, foreign workers represented 35.4% (118 cases) of the total reported cases of leprosy nationwide. With regards to tuberculosis, they constituted 10.5% (1,230 cases) of the total, and they made up 12.6% (7,421 cases) of new cases of malaria. Foreign workers constitute a large proportion of the urban poor living in unhealthy and crowded squatter/ slum conditions, leading to problems of violence and disease infection (6).

Globalization

The fervour of globalization raging around us has been increasingly acknowledged as a force that is changing our lives, including our health, far beyond financial markets and international trade. Changes in trade and markets, the movement of people, goods and services including trade in legal and illegal substances, contaminated foodstuffs, inappropriate medical technology and military arms are being facilitated by the globalization process. It is, thus, a concern that continuing globalization reduces the control that governments have over a growing number of health determinants that derive from the international transfer of health risks (6).

Mental health and wellness

As mentioned earlier, mental disorders are one of the chronic diseases on the rise. However, the issues of early recognition and detection in the form of depression and anxiety illnesses are taken seriously only recently. Another issue is the failure to link the relationship between mental health and physical illness, and hence the inadequate as well as ineffective treatment being given to mental health patients. For instance, while millions of dollars are spent on reduction of cigarette smoking, there are few attempts to relate smoking behaviour to mental health factors in the smoker. Similarly, in health promotion efforts to reduce obesity so as to decrease incidence of non-insulin dependent diabetes and cardiovascular diseases, mental factors are seldom, if ever, taken into account in looking into the causes of diet, eating habits and obesity (11).

Although as discussed earlier that the suicide rate in Malaysia is relatively low compared to other countries, it is doubtful that this low trend will continue as our society is undergoing rapid and unprecedented social changes mentioned previously. It is pertinent to stress here, that studies have indicated that approximately 80% of parasuicide cases have no underlying psychiatric disorders, thus emphasising the need for more awareness of general public and health care practitioners on the association between risks of suicide and mental health (9). Thus, for the immediate and now, specific services to promote mental health and to help people cope with such traumatic social and structural changes are greatly needed. Whilst, for the long run, preventive approaches such as wellness programmes are also equally important. The fundamental concept of wellness or healthy lifestyle dates back to the concepts of 'holistic health'. Wellness refers to a lifestyle that one chooses and designs to maximize one's potential for well-being through a balanced life that gives a sense of purpose, inner peace, and satisfaction. Wellness involves eight dimensions, each an important facet of life – the social, physical, spiritual, emotional, nutritional, intellectual, occupational and the environment. It is also a framework that can be used in many ways to help in organising, understanding, and balancing human growth and development towards a more proactive, responsible, and healthier existence. The Eighth Malaysia Plan has specifically stated that the expansion of the wellness programme will be one of the strategies for the country's health sector development (1).

Equity health care

The Ministry of Health has acknowledged that although progress in the health status of the general Malaysian society is evident, the number of people living in poverty and poor conditions of nutrition and health is significant. Indeed, it has been alleged that the issue of equity in health care will be the most challenging of all. Equity in health care refers to equal access to available care for equal needs, equal utilisation for equal need and equal quality of care for all, regardless of class, ethnicity, and gender. Closely associated with equity health care is the appropriateness of care, gender-sensitivity, availability of affordable care and quality of care. The MOH has stressed that

any future health system should ensure the delivery of dependable and high quality care which is based on need and not on the ability to pay. Fundamental and complex issues of health costing and health financing, thus, arise and many are still in the process of being debated – health reform, privatization, national health insurance, public-private mix and so forth. In essence, the debate has revolved around whether health financing is a social responsibility or a private matter to be left to market forces. It has been argued that usually the pursuit of free price setting and consumer choice (market forces) is in conflict with concerns for equity, efficiency and budgetary constrains (6).

Future Prospects

In view of the above health issues and challenges facing Malaysian society today, the mounting pressure for health care reforms and transformational changes are taking place. It has been alleged that this can only occur if the MOH is successful in its mission of building partnerships in health and the creation of health as an asset. It is hoped that Malaysia will continue its emphasis in upholding and conforming to the principles of Primary Health Care. At the same time, both the Vision for Health and the Health for All strategy should remain on Malaysia's health agenda in the new millennium. As pressures on resources increase, health care decisions have to be made explicitly and publicly, warranting a basic scientific approach to health care management (6).

Thus, the strategies for health sector development during the Eighth Malaysia Plan period will include the following:

- Improving accessibility to affordable and quality health care;
- Expanding the wellness programme;
- Promoting coordination and collaboration between public and private sector providers of health care;
- Increasing the supply of various categories of health manpower;
- Strengthening the telehealth system to promote Malaysia as a regional centre for health services;
- Enhancing research capacity and capability of the health sector;
- Developing and instituting a health care financing scheme; and
- Strengthening the regulatory and enforcement functions to administer the health sector, including traditional practitioners and medical products.

Conclusion

Being proactive, resilient and innovative, the Malaysian society would forge ahead towards the Ministry of Health's Vision for Health in this new era. That is, to be a nation of healthy individuals, families, and communities, through a health system that is equitable, affordable, efficient, technologically appropriate, and environmentally adaptable, with emphasis on quality, innovation, health promotion and respect for human dignity, and which promotes individual responsibility and community participation towards an enhanced quality of life.

References

1. Government of Malaysia. Eighth Malaysia Plan 2001-2005. Kuala Lumpur National Printing office, April 2001.
2. Ministry of Health. The National Health and Morbidity Survey II (1996). Ministry of Health, Malaysia, 1996.
3. Low WY, Zulkifli SN, Wong YL, *et al.* Dawn of a new millennium: Issues and Challenges of Public Health in Malaysia. In: Yusof K, Low WY, Zulkifli SN, *et al.* Issues and Challenges of Public Health in the 21st century. Faculty of Medicine, University of Malaya, University of Malaya Press, 1996; 191-232.
4. Ministry of Health. Health For All Indicators. Ministry of Health, Malaysia, May 2000.
5. Sekhar CK, Ong LH. Epidemiology of dengue/dengue haemorrhagic fever in Malaysia – a retrospective epidemiological study 1973-1987. Asia Pac J Public Health 1992/1993; 2:15-25.
6. Abu Bakar Suleiman, Jegathesan M (eds). Health in Malaysia: Achievements and Challenges. Ministry of Health, Malaysia, Kuala Lumpur, undated.
7. Data sourced from Resource Centre, Malaysian AIDS Council, 2000.
8. Department of Statistics. Social Statistics Bulletin 2000. Kuala Lumpur Department of Statistics, Malaysia, November 2000.
9. Ministry of Health. Malaysia's Health 1999: Technical Report of the Director-General of Health. Ministry of Health, Malaysia, 1999.
10. Mohd. Hussain H, Ganesvaran T, Agnes LS. Attempted Suicide in Kuala Lumpur. Asia Pac J Public Health 1992/1993; 2:5-7.
11. Deva MP. Mental Health in the Developing Countries of the Asia Pacific Region. Asia Pac J Public Health 1999; 11(2):57-59.
12. Government of Malaysia. Seventh Malaysia Plan 1996-2000. Kuala Lumpur National Printing office, 1999.
13. Department of Statistics. Vital Statistics Malaysia 1997. Kuala Lumpur Department of Statistics, Malaysia, 1997.

CARDIOPULMONARY EXERCISE TESTING: UTILITY IN RESEARCH AND PATIENT CARE

Elina RA[1], Husain R[1] and Lang CC[2]
[1] *Department of Physiology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia*
[2] *Department of Cardiology, Ninewells Hospital and Medical School, Dundee, United Kingdom*

ABSTRACT: Cardiopulmonary exercise testing is a non-invasive physiological test which incorporates the conventional method of exercise stress test with a more advanced breath-to-breath ventilatory analysis. The physiological parameters obtained from the test help to illustrate the cardiovascular, respiratory and metabolic responses to physical exertion. Individual's functional capacity and aerobic fitness is reflected by the value of maximal oxygen consumption (VO_2 max) obtained from the cardiopulmonary exercise test. This non-invasive and sophisticated test is regarded as a valuable assessment tool in research and clinical practice. Cardiopulmonary exercise test has been extensively utilized to define the mechanisms of exercise intolerance in various clinical disorders, to evaluate responses to therapy and indicate disease prognosis. Emerging data obtained from the use of the cardiopulmonary exercise testing in the research field, has led to its extensive clinical usage. It is now utilized as an integral part of the patients' clinical evaluation in the field of respiratory and cardiovascular medicine, sports medicine, surgery as well as occupational and rehabilitative medicine. It has a clinical role in assessing patient's functional capacity, monitoring disease progression and response to therapy, predicting prognosis, and perioperative morbidity and mortality, as well as constructing and monitoring training and rehabilitative programs. This article aims to give an overview of the physiological profiles obtained from cardiopulmonary exercise testing, its methodological aspects, as well as its utility in research and clinical practice. *(JUMMEC 2003-2005; 8: 9-22)*

KEYWORDS: Cardiopulmonary, exercise, physiology, respiratory medicine, oxygen consumption

Introduction

Exercise is the most common form of physiological stress encountered by the body. It requires a coordinated interaction of virtually all body systems to effectively adapt to the physiological and metabolic demands incurred. The cardiopulmonary system is one of the crucial systems in the body which copes with the major demands of exercise, ensuring adequate oxygen delivery to the working muscles. Exercise test has traditionally been regarded as a valuable tool to evaluate cardiac perfusion and function under controlled conditions, due to its ability to detect cardiac dysfunction under stress, which may not necessarily be present at rest. Recently, the incorporation of ventilatory gas analysis into the conventional method of exercise testing has further expanded its utility in research and clinical field. Formal cardiopulmonary exercise testing is a non-invasive and sophisticated physiologic testing technique, which includes the recording of the exercise ECG, heart rate and blood pressure responses to exercise, minute ventilation, and allows calculation of the subject's maximal oxygen consumption. It provides a comprehensive functional assessment, that helps to define the relative contribution of various human physiological systems (cardiovascular, pulmonary and muscle metabolism) in determining exercise performance.

At the early phase of exercise, there is a gradual increase in oxidation of substrate such as carbohydrate and fat for regeneration of high energy in the form of

Correspondence:
Dr Raja Elina Afzan binti Raja Ahmad
Department of Physiology
Faculty of Medicine, University of Malaya
50603 Kuala Lumpur.
Tel: 603-7967 4742
Fax: 603-7967 4775
Email: rajaelinaafzan@um.edu.my

Adenosine Triphosphate (ATP), to sustain muscular contractions. The increasing metabolic requirements of the cells under stress can essentially be met by effective adaptations of the central (cardiopulmonary) and peripheral systems (skeletal muscle cellular and metabolic responses) in the body. The respiratory system provides enhanced ventilation and gas exchange during exercise. The cardiovascular system adapts by increasing the cardiac output to ensure effective systemic oxygen transportation. In addition, there is an increase in oxygen extraction by the working muscles, reflecting adaptation of the peripheral system to this state of physiological stress. Disturbance in any one of these systems will cause considerable changes in the adaptations to an acute episode of exercise, and this can be quantified during cardiopulmonary exercise test. Hence, the cardiopulmonary exercise test allows for an integrated assessment of the cardiovascular response, respiratory mechanics, gas exchange process and metabolic responses to the stress of physical exertion.

Physiological basis of cardiopulmonary exercise testing

During exercise, both oxygen delivery and tissues oxygen extraction rise. The increase in oxygen delivery during exercise is primarily achieved by increasing the cardiac output (four to five folds) (1). There is a linear increase in both oxygen consumption and cardiac output with increasing workload, until an individual maximum value is reached. This oxygen consumption plateau, termed maximal oxygen consumption (VO_2max), is the hallmark of cardiopulmonary exercise testing, representing a marker of exercise capacity or cardiopulmonary fitness. VO_2max is defined as the maximum amount of oxygen a person can take in the form of inspired air while performing dynamic exercise involving a large muscle group (2). It represents the amount of oxygen transported and utilized in the cellular metabolism, as reflected by the Fick principle*: (VO_2max = maximal cardiac output (CO)) x maximal arteriovenous oxygen difference (a-vO_2 diff)*. Because the arterial-venous oxygen difference is generally considered to widen by a relatively fixed amount during exercise, and VO_2max is typically achieved by exercise that involves at least half of the total body musculature (that is, not limited to a focal area), it is generally believed that VO_2max is primarily limited by cardiac output rather than the peripheral oxygen extraction (3). Hence, VO_2max defines the upper limit of cardiac function during aerobic exercise, and is therefore, utilized as an objective measure of cardiorespiratory fitness during cardiopulmonary exercise testing. Apart from differences in cardiopulmonary responses to exercise, factors which are known to influence the individual variation of VO_2max include age, gender, individual fitness or conditioning status, type of exercise being performed, the presence of various diseases, medications, genetic factor, and environment where the particular exercise is being performed (2).

Maximal oxygen consumption (VO_2 max) is primarily influenced by the determinants of cardiac output. Abnormality in VO_2 max may reflect either inability to increase heart rate or failure to augment stroke volume during exercise. During exercise, stroke volume increases up to approximately 50% to 60% of an individual's maximal exercise capacity (up to 100-200 ml/beat in well-trained subjects), after which, increases in cardiac output are caused by further increases in heart rate (3). However, in untrained subjects, cardiac output is increased almost entirely by an increase in heart rate. Physical training will improve augmentation of stroke volume, which results in better cardiovascular endurance during exercise. Cardiopulmonary assessment has therefore been utilized as a functional assessment tool that forms the basis for exercise prescription, to enhance athlete's performance or for cardiac rehabilitation.

The most common respiratory parameters assessed during exercise are changes in total minute ventilation (V_E), tidal volume (V_T) and respiratory rate (RR). In order to have effective consumption of oxygen during exercise, augmentation of ventilation is required to complement the increase in cardiac output. Increases in minute ventilation during exercise are initially achieved by increasing both the tidal volume and respiratory rate. Ventilatory limitation to exercise can be established by evaluating the individual's ventilatory reserve, defined as the difference between maximum voluntary ventilation (MVV) and maximum spontaneous ventilation (VE max) that is, VR=MVV-VE max. This parameter reflects the ability of ventilation to approach maximum volume that can be respired per minute (MVV), and is often reduced in patients with pulmonary diseases. Other ventilatory parameters which are often obtained during cardiopulmonary exercise testing and are indicative of gas exchange efficiency include ventilatory equivalents for O_2 (V_E/V_{O2}) and CO_2 (V_E/V_{CO2}), as well as the ratio of dead space volume to tidal volume (V_D/V_T). In addition, the measurement of differences in oxygen partial pressure between alveoli and pulmonary capillaries ($P(A\text{-}a)O_2$) is also helpful in ascertaining the cause of hypoxaemia during exercise.

The metabolic events during cardiopulmonary exercise can be evaluated by measuring respiratory exchange ratio (RER) and anaerobic threshold (AT). The ratio of oxygen consumption and carbon dioxide

output (VO_2/VCO_2) is called the respiratory exchange ratio (RER), which can be used as a rough index of metabolic activity. Anaerobic threshold (AT) is considered an estimator of the onset of metabolic acidosis, caused predominantly by increased rate of rise in arterial lactate during exercise. It is referred to the value of VO_2 at the onset of anaerobic metabolism, and is commonly expressed as a percentage from the VO_2max predicted value for each individual. In normal sedentary individuals, the AT occurs at about 40%-60% of predicted VO_2 max (4), with higher value in endurance-trained individuals. Values below 40% of predicted VO_2 max may indicate cardiac, pulmonary or other limitations in oxygen supply to the tissues, or other underlying cellular mitochondrial activity (for example, mitochondrial myopathies).

Cardiopulmonary exercise mode and protocol selection

Dynamic exercise involving large muscle groups is preferred for clinical exercise testing, since it initiates a more appropriate increase in cardiac output and oxygen exchange. Bicycle ergometer and the motorized treadmill are now the most commonly utilized dynamic exercise devices. Bicycle ergometer has the advantage of being relatively cheap and takes up less space compared to the treadmill. However, it requires the subject's cooperation to maintain the pedaling speed at the desired level, usually about 60 rpm, to ensure achievement of the desired workload. In addition, some subjects are not familiar with bicycling, as compared to walking exercise. Cycle ergometry has also been shown to result in 10% to 20% lower value of maximal oxygen consumption as compared to treadmill exercise (5). Thus, the treadmill is a generally more common dynamic testing modality, except in situations where the subject suffers from gait instability, or when simultaneous cardiac imaging is planned. Arm ergometry is an alternative method of exercise testing for patients with vascular, neurologic or orthopaedic conditions, who cannot perform leg exercises. However, at maximal effort, the extent of physiological responses in arm exercise is generally less than leg exercise due to recruitment of smaller muscle bulk.

The selection of appropriate workload protocol during cardiopulmonary test is of critical importance, as it has a considerable influence on the interpretation of physiologic parameters obtained during the exercise test. With each protocol, the measurement of workload or performance is expressed in basal metabolic equivalents (METs). One METs corresponds to the resting oxygen consumption rate of 3.5 mL O_2/kg/min^2. Before selecting the exercise protocol, the investigator must first decide whether to conduct the exercise test at a maximal or submaximal level. Patient's true maximal effort and functional capacity can be better evaluated from a maximal treadmill walking test. The protocol for maximal dynamic exercise testing can be classified according to the manner in which the workload is applied (that is, incremental or constant exercise workload). The traditional Bruce treadmill protocol is the most commonly used exercise protocol used in routine clinical setting (6). However, it involves vigorous exercise, commencing at five METs of energy, and increases both speed and gradient with each 3-minute stage. Because of its large unequal workload increment between stages and rapid exertion level, the protocol has been associated with overestimation of the subject's exercise capacity (VO_2max), particularly for patients with cardiac disease (7). Moderate increment in treadmill elevation at a constant speed, are preferable protocols to accurately estimate the subjects maximal oxygen consumption (2). Recently, the 'Ramp' protocol which involves small increments in work rate at 30 to 60-second interval, has been shown to accurately determine patients' functional capacity during exercise (8). Table 1 summarises the physiological profiles obtained and Table 2 illustrates some of the exercise protocols which can be applied during cardiopulmonary exercise test. Regardless of the specific protocol selected, it should be optimized to reach the individual's symptom-limited maximal effort, with exercise duration between 10 to 12 minutes. Shorter exercise duration may disrupt the linear relationship between VO_2max and work rate, whereas longer duration of more than 12 minutes may cause the subjects to terminate the exercise because of muscle fatigue, before reaching their true maximal effort.

Although maximal testing provides a more accurate determination of aerobic capacity, submaximal exercise testing may be desirable in certain situations which preclude strenuous physical activity. This includes predischarge cardiac evaluation after myocardial infarction, patients with dangerous dysrhythmias, assessment of frail elderly subjects who are unaccustomed with vigorous exercise, and field testing of a large number of subjects, particularly in the absence of clinical supervision. In the recent years, the six or 12-minute walk have been widely utilized to determine patient's submaximal functional capacity (9). Such test modality is found to be simpler, safe, very inexpensive and applicable to simulate performance of daily activities. The distance covered during 6-minute walk test was found to be a good prognostic indicator of patients with heart failure (9). It has also been employed as an assessment tool to evaluate therapeutic intervention, particularly pacemaker therapy, in heart failure patients (10,11).

Table 1. Summary of the physiological profiles obtained from cardiopulmonary exercise test

Physiological Variables	System Assessed
• VO_2max • O_2 pulse • Heart rate • Blood pressure • ECG	Assessment of cardiovascular response during exercise
• V_E • V_T • RR • VR • MVV	Assessment of respiratory mechanics during exercise
• V_E/VO_2 • V_E/VCO_2 • V_D/V_T	Assessment of gas exchange process during exercise
• RQ • AT	Assessment of metabolic activity during exercise

VO_2max = maximal oxygen consumption; O_2 = oxygen; ECG = electrocardiography; VE = total minute ventilation; VT= tidal volume; RR = respiratory rate; VR = ventilatory reserve; MVV = maximum voluntary ventilation; VO_2 = oxygen consumption; VCO_2 = carbon dioxide production; VD = volume of physiological dead space; RQ = respiratory quotient; AT = anaerobic threshold.

Table 2. Summary of various exercise protocols during cardiopulmonary exercise testing

Treadmill exercise protocols	
Bruce Protocol	Initial speed 1.7 mph and 10% slope; increments of 0.8 mph and 2% slope every 3 minutes
Balke Protocol	Constant speed and increase of slope by 1% per minute
Naughton Protocol	Initial speed 3.2 km/h with 3.5% slope every 3 minutes
Bicycle ergometer protocols	
Incremental exercise test	60 rpm; increase 5-25 watt/min; planned test duration 6-12 minutes
Ramp Protocol	Continuously increasing exercise; increase at a one-second interval

Research application of cardiopulmonary exercise test

Cardiopulmonary exercise test is regarded as an important research tool, which can be utilized as a mean of objective assessment of functional capacity and fitness level, in virtually any field of research, involving healthy and medically unfit individuals. In the area of clinical research, cardiopulmonary exercise test has been predominantly utilized to define the mechanism of exercise intolerance in various clinical disorders, as well as to objectively evaluate the efficacy of therapeutic interventions. Comprehensive cardiopulmonary data obtained from the test, provides an excellent research ground in the area of cardiovascular and respiratory medicine. The kinetics of changes in physiological responses during incremental exercise have previously been studied in many cardiorespiratory conditions such as asthma, obstructive and restrictive lung disorders, hypertension, peripheral vascular disease and cardiac dysfunction (12). One of the areas of research which extensively utilizes cardiopulmonary exercise testing as an assessment tool is heart failure. The cardiopulmonary exercise test facilitates the understanding of exercise pathophysiology in heart failure, in order to construct

appropriate treatment regime and rehabilitation program for the patients.

It has been documented that patients with congestive heart failure have a peak oxygen consumption that is generally half (range of eight to 21 mL/kg/min) of that observed in age-matched healthy subjects (13). Although it has been a common believe that physical activity is predominantly limited by the reduction in cardiac output, peripheral factors (impaired vasodilatation and muscle deconditioning) are now recognized as major concomitant contributors to exercise intolerance in heart failure patients. It has been shown that patients with congestive heart failure have generalized skeletal muscle atrophy, most notably in type II ('fast-switch') fibres, which contribute to diminution of exercise capacity (14). In a recent study which examined the relationship between myocardial dysfunction and peripheral haemodynamic factors of exercise intolerance in heart failure, it was found that in patients with mild-to-moderate heart failure, peak VO_2 significantly correlated with central haemodynamic factor (cardiac index and right atrial pressure), whereas in severe heart failure, peripheral factors (forearm blood flow, vascular resistance and venous tone) assumed greater importance in determining exercise capacity (15). The shift from central to peripheral haemodynamic factors limiting physical exertion in heart failure was suggestive of the increasing importance of peripheral component as exercise-limiting factor, in parallel to the progression of the disease.

Neurohormonal activation has been associated with limitation in exercise capacity in heart failure patients. Brain Naturetic Peptide (BNP) has recently been found to have a role in identifying chronic heart failure patients with moderate to severe impairment in exercise capacity. A recent study revealed significant correlation between BNP levels with oxygen uptake. A BNP above 316 pg/ml was associated with a risk ratio of 6.8 for a reduced exercise capacity with a peak VO_2 of below 14 ml/min/kg (16).

Cardiopulmonary exercise test is also a valuable research tool for assessing therapeutic interventions in heart failure. Treatment with Alacepril (long-acting sulphydryl-containing angiotensin-converting enzyme inhibitor) has been shown to improve functional status and exercise capacity in patients with mild-to-moderate chronic heart failure (17). In another recent study on pharmacological treatment for heart failure, 106 ambulatory heart failure patients were randomized to either spironolactone therapy (12.5 to 50 mg/day) or control group (18). Peak oxygen consumption was found to be significantly increased in patients treated with the highest administrated dose (50 mg) of spironolactone (17.7 ± 5.2 vs. 18.5 ± 5.9, $p = 0.01$) and decreased in control group (19.1 ± 5.6 vs. 17.9 ± 5.3) after twelve months of treatment. The data obtained from cardiopulmonary exercise test supported the use of spironolactone adjunctive to other novel pharmacological therapy, to optimize the clinical condition and prognosis of patients with chronic heart failure.

Anemia is common in elderly patients with chronic heart failure. An increase in haemoglobin level could enhance exercise performance by increasing oxygen delivery. In a recent randomized single blind prospective study (19), treatment with erythropoietin (EPO) for three months was shown to result in significant improvement of peak VO_2 (11.0 ± 1.8 to 12.7 ± 2.8 ml/kg/min, $p < 0.05$) and exercise duration (590 ± 107 to 657 ± 119 sec, $p < 0.004$) in patients with moderate to severe heart failure.

The research utility of cardiopulmonary exercise testing continues to expand in this recent era of evidence-based medicine. Cardiopulmonary exercise test is now utilized in virtually any domain of research that requires objective assessment of the subject's fitness level, particularly, the cardiovascular and pulmonary functional capacity, discrimination of the etiologic factors of exercise intolerance, evaluation of therapy, as well as for prognostic indication. The large body of data obtained from research utility of cardiopulmonary exercise test forms the basis of its application in the clinical practice.

Utility of cardiopulmonary exercise testing in clinical practice

Because of the important nature of the physiological profiles obtained during the cardiopulmonary exercise test, it has now been widely applied in a wide spectrum of clinical setting, including Respiratory Medicine, Cardiology, Sports Medicine, Occupational and Rehabilitative Medicine. It has a value in facilitating the clinicians in many different levels of clinical decision-making, including diagnosis, assessment of severity and progression of disease, prognosis and response to treatment. However, the interpretation of test results should be on an individual basis, after consideration of the patient's full clinical history, physical examination and other diagnostic modalities.

Clinical application of cardiopulmonary exercise test in respiratory medicine

Cardiopulmonary exercise test is clinically useful to objectively determine exercise capacity and establish exercise limitations in patients with lung disease. It helps to characterize limitations of breathing mechanics, peripheral deconditioning and gas exchange disorders, in the presence of restrictive and obstructive pulmonary diseases. Many patients with pulmonary disorders

also have concomitant disease of other organ systems that may affect exercise performance. Cardiopulmonary exercise test also helps to distinguish and identify other contributing factors of exercise intolerance in these patients.

Patients with chronic obstructive pulmonary disease may complain of gradual increase in exertional dyspnoea over time, which may be multi-factorial (ventilatory inefficiency, cardiovascular limitation, muscle deconditioning and psychological problem). The study of ventilatory reserve and breathing pattern during cardiopulmonary exercise test helps to objectively define the dominant cause of unexplained dyspnoea, especially when exertional symptoms are disproportionate to resting pulmonary function test (20). Patients with ventilatory-related exertional dyspnoea fail to reach anaerobic threshold or achieve VO_2max. They use more than 70% of their maximum voluntary ventilation at peak exercise and develop arterial desaturation with exercise. In contrast, cardiac patients with dyspnoea on exertion are able to attain VO_2max and anaerobic threshold, use less than 50% of their maximum breathing effort and do not develop desaturation during physical exertion (1).

In interstitial lung disease and pulmonary vascular disease, cardiopulmonary exercise test aid in early detection of subtle pulmonary gas exchange abnormalities, not revealed by routine testing. It also permits physiologic monitoring of severity of the illness and therapeutic intervention. Cardiopulmonary test also helps to quantify and qualify the response to oxygen therapy and pulmonary rehabilitation, as well as facilitate in the monitoring of disease progression in patients with chronic pulmonary disorders.

Determination of preoperative pulmonary function is crucial in avoiding complications from pulmonary resection surgery. Risk for perioperative complications can generally be stratified by the level of peak oxygen consumption (VO_2max) obtained from cardiopulmonary exercise test (21). Generally, patients with preoperative VO_2max more than 20 mL/kg/min are not at increased risk of complications or death. VO_2max less than 15 mL/kg/min indicates an increase risk of perioperative complications, whereas patients with VO_2max less than 10 mL/kg/min have a high risk for post-operative complications. Desaturation during exercise test has also been associated with an increased perioperative complication.

Clinical application of cardiopulmonary exercise testing in cardiovascular diseases

Cardiopulmonary exercise has been clinically utilized in the evaluation of patients with various forms of cardiovascular diseases, to objectively determine functional capacity and prognostic outcome, as well as to assess response to therapeutic interventions. Submaximal exercise testing is routinely performed in patients after an acute coronary event before hospital discharge to evaluate their functional capacity and predict future adverse cardiac events. In a recent study (22) involving 740 men with unstable angina or non-Q wave myocardial infarction, who underwent predischarge cycle ergometer exercise testing, the major predictors of one year infarction-free survival, were found to be the total number of leads with ischaemic ST-segment depression and peak workload attained during the cardiopulmonary exercise testing.

Cardiopulmonary exercise testing also offers an objective evaluation of functional capacity in patients with heart failure. Peak VO_2 provides important prognostic information in patients with chronic heart failure. Previous study has demonstrated a 77% one-year mortality rate for patients with peak VO_2 less than 10 mL/kg/min and a 21% mortality rate for those with VO_2 between 10 to 18 ml/kg/min (23). The value of peak exercise oxygen consumption in determining the optimal timing of cardiac transplantation has been established by a later study by others who performed cardiopulmonary stress test on 116 ambulatory heart failure patients referred for cardiac transplantation (24). The patients were divided into three groups based on peak oxygen consumption (VO_2max) cut-off point of 14 mL/kg/min. Group 1 consisted of 35 accepted candidates for transplant, who achieved VO_2max of less than 14 mL/kg/min. Group 2 included 52 patients with VO_2max more than 14 mL/kg/min, who had transplant deferred. Group 3 involved 27 heart failure patients with VO_2max less than 14 mL/kg/min but had a significant co-morbidity that precluded the decision for transplantation. The study revealed a good prognosis (one-year survival rate of 94%) in Group 1 patients, who obtained VO_2max more than 14 mL/kg/min. On the other hand, accepted transplant candidates with VO_2max less than 14 mL/kg/min had a one-year survival rate of 70%, whereas patients in Group 3 with low VO_2max and significant co-morbidity had a 47% one year survival rate. A more recent prognostic study (25) involving 154 heart failure transplant candidates with peak VO_2 less or equal to 14 mL/kg/min revealed a three-year survival rate of 55% in patients (n=77) who were unable to reach peak exercise systolic blood pressure of 120 mmHg, compared to 83% three-year survival rate in patients (n=74) who accomplished this peak exercise systolic blood pressure cut-off point. Multivariate analysis revealed that peak exercise systolic blood pressure (p = 0.0005) and per cent predicted VO_2 less or equal to 50% (p = 0.04) were the two most important variables for estimating prognostic risk. The data from these studies formed the basis of

the clinical application of cardiopulmonary stress testing for prognostic stratification and selection of potential candidates for heart transplant, as well as identifying nominated candidates whose transplant could be safely deferred in the event of limited resources.

Cardiopulmonary exercise test can be used to objectively monitor progression of disease and evaluate the effect of treatment on cardiac patient's functional capacity. Serial measurements of peak VO_2 have been used to determine the effect of electrical cardioversion on functional capacity of patients with chronic atrial fibrillation. A previous study concluded that the restoration of sinus rhythm was associated with a delayed improvement in exercise capacity (28 days post-cardioversion) (26), which may in part be due to a slow improvement in atrial contractility and peak cardiac output after electrical cardioversion. Maintenance of sinus rhythm following electrical cardioversion resulted in sustained improvement of functional capacity, which is reflected by the value of peak VO_2 (27).

Recently, the cardiopulmonary exercise test has also been utilized to evaluate the effect of both medical and non-pharmacological approach to management of patients with heart failure. A recent small randomized control trial evaluating the effect with beta-adrenergic blocking agent (Carvedilol) in patients with idiopathic dilated cardiomyopathy revealed improvement of submaximal exercise tolerance and cardiac haemodynamic indices following short (12 hours) and long-term (four months) administration of the drug (starting dose of 6.25 mg a day with weekly increments up to maximum of 25 mg twice a day), as compared to placebo (28). Recently, pacing therapy in heart failure has been widely accepted as part of the integrated management of advanced heart failure patients who are resistant to medical treatment. Cardiopulmonary exercise test has been routinely performed to evaluate the effect of pacing treatment in heart failure. The recent studies (11,29,30) have consistently shown that cardiac resynchronization therapy (biventricular pacing) improved exercise capacity, cardiac function and quality of life in symptomatic patients with severe chronic heart failure and ventricular conduction disturbances, who are non-responsive to pharmacologic therapy.

Application of cardiopulmonary exercise testing in sports medicine

As cardiopulmonary exercise testing measures an individual's physiological responses to exercise, it is often utilized to provide an objective evaluation of exercise performance in both the healthy and symptomatic subjects, in the field of sports medicine. The results obtained from the test are essential for constructing the appropriate training regimes for athletes and rehabilitative patients. Cardiopulmonary exercise test has been previously used to assist in confirming and elucidating different etiological factors of exercise limitations in debilitating conditions such as chronic fatigue syndrome (31) and in HIV+ individuals (32), for recommendation and optimization of their exercise training program. In the athlete population, cardiopulmonary exercise can distinguish between physiologic from pathologic hypertrophy of the left ventricle (33). Serial measurements of physiologic parameters obtained from the test can also objectively evaluate fitness progress and maximize athlete's performance, particularly in endurance sports such as marathon running, swimming, cycling and rowing.

Applications of cardiopulmonary exercise test in occupational and rehabilitative medicine

Cardiopulmonary exercise test is of great importance in the evaluation of disability and impairment. It provides an objective evaluation of exertion ability, beyond the assessment of patient's clinical history and examination findings. Apart from objective assessment of exercise capacity, cardiopulmonary exercise test also identifies exercise-induced arrhythmias, arterial desaturation and the timing of metabolic acidosis, all of which may contribute to exercise intolerance in patients with cardiopulmonary diseases. It provides objective and accurate evidence for occupational-related disability in patients who file workers' compensation claim.

Exercise prescription during cardiac rehabilitation is usually based on the documentation of patient's functional capacity, cardiac and haemodynamic responses, as well as signs and symptoms associated with exertion, obtained from the cardiopulmonary stress test (34). Serial measurements of peak VO_2 and ventilatory parameters are also useful to evaluate and optimize the safety and intensity of training, as well as to assess the therapeutic response to physical training in patients with cardiopulmonary diseases. Previous randomized controlled trial assessing the benefit of exercise training in patients with heart failure revealed varying degree of improvement of peak VO_2 from 16% (35) to 31% (36) after six months of moderate physical training. Pulmonary rehabilitation has been proven to improve quality of life and exercise capacity in clinically stable patients with chronic obstructive pulmonary disease (37). Patients with severe chronic obstructive pulmonary disease required rehabilitation program of at least six month duration to show significant benefit over the control group. Improvement of exercise tolerance following pulmonary rehabilitation in these patients is believed to be attributed to the improvement in neuromuscular coordination and desensitization in the perception of dyspnoea.

Role of cardiopulmonary exercise testing for pre-operative evaluation of the elderly

Major surgery is associated with high post-operative oxygen consumption and cardiac output requirement. Elderly patients may not have the ability to respond to the increased needs of surgery and trauma, due to the natural tendency for cardiac function to deteriorate with age. These patients may die from cardiac failure post-operatively, when oxygen delivery is insufficient to meet the oxygen requirement of the organs in the body. Cardiopulmonary exercise test is thus a reliable technique for pre-operative evaluation of the ability of the cardio-respiratory system to respond to the stress of surgical trauma. In a previous prognostic study (38), post-operative cardiovascular mortality was associated with oxygen uptake at anaerobic threshold (VO_2-AT) of less than 11 mL/kg/min. The investigator also found that an VO_2-AT of less than 11 mL/kg/min associated with angina or ECG evidence of ischaemia during exercise, resulted in approximately 40% mortality following major surgery in patients over 60 years of age. Elderly patients who exhibited neither cardiac failure nor ischaemia based on the exercise criteria had a mortality of less than one per cent.

Conclusion

Evaluation of exercise capacity involves assessment of the interaction and adaptation of various human physiological systems to physical activity. This can be achieved by a non-invasive exercise test with integrated gas exchange analysis. The cardiopulmonary exercise test provides comprehensive assessment of functional capacity, particularly, the cardio-respiratory fitness. It can be utilized in virtually any field of research that requires objective evaluation of the subject's cardiopulmonary as well metabolic function during exercise. The research data on utility of cardiopulmonary exercise test in various clinical conditions forms the basis of its application in the clinical field. Clinicians from various specialties can now utilize the cardiopulmonary exercise test as an integral part of a patient's overall clinical evaluation. Cardiologist and respiratory physician may use the test to further understand the factors which limit exercise capacity in patients with cardiopulmonary disorders, as well as to facilitate in distinguishing between cardiac or pulmonary cause of exertional dyspnoea. Cardiopulmonary exercise test also has a clinical role in determining the optimal time for heart or lung transplant, predicting prognosis and objectively monitor disease progression and response to therapeutic interventions. In sports medicine, it is often use as an assessment tool to monitor progress of exercise training program for further optimization of exercise performance in both the athlete population as well as chronically ill patients. In the field of occupational medicine, cardiopulmonary exercise test has a great importance in objectively determining disability and impairment for work-related compensation claims. Cardiopulmonary exercise test is now increasingly used in preoperative evaluation of patients undergoing major surgery due to its reliability in predicting peri-operative risk of morbidity and mortality. Regardless of the conditions in which the cardiopulmonary exercise test is applied to, the value of information obtained from it will only be evident when interpreted on an individual basis, after the consideration of patient's full clinical profile.

References

1. Myers JN. The physiology behind exercise testing. Prim Care 2001; 28(1):5-27.
2. Myers F. Special methods: Ventilatory Gas Exchange. In: Exercise and the Heart; Saunders 4th edition 2000; 39-58.
3. American Thoracic Society/American College of Chest Physician. ATS/ACCP Statement on Cardiopulmonary Exercise Testing. Am J Respir Crit Care Med 2003; 167:211-277.
4. Mitlehner W. Cardiopulmonary Exercise Testing: Practical guideline. VIASYS info Special Edition CPET 2002; 12-18.
5. Miyamura M, Honda Y. Oxygen intake and cardiac output during treadmill & bicycle exercise. J Appl Physiol 1972; 32:185-188.
6. Bruce RA. Exercise testing of patient with coronary heart disease. Ann Clin Res 1971; 3:323-330.
7. Myers J, Buchanan N, Walsh D *et al*. Comparison of the ramp vs. standard exercise protocols. J Am Coll Cardiol 1991; 17:1334-42.
8. Myers J, Bellin D. Ramp exercise protocols for clinical and cardiopulmonary exercise testing. Sports Med 2000; 30(1):23-29.
9. Cahalin LP, Semigran MJ, Dec GW. Assessment of oxygen uptake during the 6-minute walk test. Chest 1997; 111:1465-6.
10. Auricchio A, Stellbrink C, Sack S *et al*. The pacing therapies for congestive heart failure (PATH-CHF) study (abstract) Am J Cardiol 1999; 83:130D-135D.
11. Cazeau S, Laclereq C, Lavergne T, *et al* for Multisite Stimulation on Cardiomyopathies (MUSTIC) Study Investigators. Effect of multisite biventricular pacing in patients with heart failure and interventricular conduction disturbances. N Engl J Med 2001; 344: 873-880.
12. Vibhuti N, Singh. The role of gas analysis with exercise testing. Prim Care 2001; 28(1):159-178.

13. Brubaker, PH. Exercise intolerance in congestive heart failure: A lesson in exercise physiology. J Cardiopulm Rehabil 1997; 17(4):217-221.

14. Wilson JR, Mancini DM. Factors contributing to exercise limitation in heart failure. J Am Coll Cardiol 1993; 22:93A- 98A.

15. Florea VG, Mareyer VY, Archilov AA, *et al*. Central and peripheral components of chronic heart failure: Determinants of exercise intolerance. Int J Cardiol 1999; 70(1):51-6.

16. Myers S, Graft J, Kunz D, *et al*. Brain naturetic peptide levels predict functional capacity in patients with chronic heart failure. J Am Coll Cardiol 2002; 40(4):718-22.

17. Kinugawa T, Osaki S, Kato M, *et al*. Effect of angiotensin-converting enzyme inhibitor alacepril on exercise capacity and neurohormonal factors in patients with mild to moderate heart failure. Clin Exp Pharmacol Physiol 2002; 12:1060-1065.

18. Cicoira M, Zanolla L, Rossi A, *et al*. Long-term, dose-dependent effects of spironolactone on left ventricular function and exercise tolerance in patients with chronic heart failure. J Am Coll Cardiol 2002; 40(2):304-10.

19. Mancini DM, Katz SD, Lang CC, *et al*. The effect of erythropoietin on exercise capacity in patients with moderate to severe chronic heart failure. Circulation 2003; 107(2):294-9.

20. Steven K, Mohnssen, Idelle MW, *et al*. Heart or Lung Disease: Determining the primary cause for dyspnoea on exertion. Chest 1998; 113:1705-10.

21. Beckles MA, Spiro SG, Colice GL, *et al*. American College of Chest Physician. The physiologic evaluation of patients with lung cancer being considered for resectional surgery. Chest (Suppl 1) 2003; 123:105S-114S.

22. Nyman I, Larsson H, Areskog M, *et al*. The predictive value of silent ischaemia on an exercise test before discharge after an episode of unstable coronary artery disease: RISC study group. Am Heart J 1992; 123:324-331.

23. Szlahcic J, Massio B, Kramer B, *et al*. Correlations and prognostic implication of exercise capacity in chronic heart failure. Am J Cardiol 1985; 55:1037-1042.

24. Mancini DM, Eisen H, Kussumaul W, *et al*. Value of peak exercise oxygen consumption for optimal timing of cardiac transplant in ambulatory patients with heart failure. Circulation 1991; 83:778-786.

25. Osada N, Chaitman BR, Miller LW, *et al*. Cardiopulmonary exercise testing identifies low risk patients with heart failure and severely impaired exercise capacity considered for heart transplant. J Am Coll Cardiol 1998; 31(3):577-82.

26. Lipkin DP, Frenneaux M, Stewart R, *et al*. Delayed improvement in exercise capacity after cardioversion of atrial fibrillation to sinus rhythm. Br Heart J 1988; 59:572-7.

27. Gosselink ATM, Bulsma EBM, Landsman LJ, *et al*. Long-term effect of cardioversion on peak oxygen consumption in chronic atrial fibrillation: a two year follow-up. Eur Heart J 1994; 15: 1368-1372.

28. Metra M, Nardi M, Giubbini R, *et al*. Effect of short and long-term carvedilol administration on rest and exercise haemodynamic variables, exercise capacity and clinical conditions in patients with idiopathic dilated cardiomyopathy. J Am Coll Cardiol 1994; 24(7):1678-87.

29. Grass D, Cazeau S, Ritter P, *et al*. Long-term results of cardiac resynchronization for heart failure patients: The Insync Clinical Trial. Circulation (Suppl) 1999; 100:510-515.

30. Abraham WT, Fisher MG, Smith AL, *et al* for Multicenter Insync Randomized Clinical Evaluation (MIRACLE) Investigators and Coordinators. Double blind controlled trial of cardiac resynchronization in chronic heart failure. N Engl J Med 2002; 346:1845-1853.

31. Inbar O, Dlin R, Rotstein A, *et al*. Physiological responses to incremental exercise in patients with chronic fatigue syndrome. Med Sci Sports Exerc 2001; 33(9):1463-1470.

32. Stringer W. Mechanism of exercise limitation in HIV+ individuals (review). Med Sci Sports Exerc (Suppl) 2000; 32(7):S412-421.

33. Sharma S, Elliot PM, Whyte G, *et al*. Utility of metabolic exercise testing in distinguishing hypertrophic cardiomyopathy from physiologic left ventricular hypertrophy in athletes. J Am Coll Cardiol 2000; 34(3):864-70.

34. William MA. Exercise testing in cardiac rehabilitation: Exercise prescription and beyond. Cardiol Clin 2001; 19(3):415-31.

35. Keteyian SJ, Levine AB, Brawner, *et al*. Exercise training in patients with heart failure: A randomized controlled trial. Ann Int Med 1996; 124(12):1051-1057.

36. Hambrecht R, Niebauer J, Fiehn E, *et al*. Physical training in patients with stable chronic heart failure: effects in cardiorespiratory fitness and ultrastructural abnormalities of leg muscles. J Am Coll Cardiol 1996; 25:1239-49.

37. Salman GF, Mosier MC, Beasley BW, *et al*. Rehabilitation for patients with chronic obstructive pulmonary disease: Meta-analysis of randomized controlled trials. J Gen Int Med 2003;18(3):213-221.

38. Wasserman K. Preoperative evaluation of cardiovascular reserve in the elderly. Chest. 1993 Sep; 104(3): 663-4.

PERIPARTUM CARDIOMYOPATHY: AN OVERVIEW

Wan Azman WA and Haizal HK
The Division of Cardiology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur

ABSTRACT: Peripartum cardiomyopathy (PPCM) is a life-threatening cardiomyopathy of an unknown cause that occurs in the peripartum period in previously healthy women and this article discusses the challenges that lie in diagnosing and managing this rare yet lethal disease. ***(JUMMEC 2003-2005; 8: 18-22)***

KEYWORDS: Peripartum, cardiomyopathy, pregnancy, cardiac failure

Definition

Peripartum cardiomyopathy (PPCM) is defined on the basis of four criteria, adapted from the work by Demakis, *et al* (1) which are (a) the development of cardiac failure during pregnancy or within five months of delivery, (b) the absence of a determinable cause for cardiac failure, (c) the possibility of occurrence in patients with coincidental heart disease, and (d) the demonstration of impairment of left ventricular systolic function. The peripartum period is as defined to exclude preexisting causes of cardiomyopathy that may be exacerbated by pregnancy rather than arising as a result of pregnancy.

Incidence

The actual incidence of PPCM is not known because population-based estimates are not available and there may be a lot of undiagnosed cases. The reported incidence ranges from one per 1,300 to one per 15,000 with a higher incidence in Africa (2). However, the currently accepted incidence is approximately one per 3,000 to one per 4,000 live births (3).

Predisposing Factors

Classical risk factors for PPCM include multiparity, advanced maternal age, multifoetal pregnancy, pre-eclampsia and gestational hypertension, and African-American race (1).

Aetiology

The reported incidence of PPCM is higher than the incidence of idiopathic cardiomyopathy. As such, it is thought to be a distinct entity, rather than a clinically silent underlying cardiomyopathy unmasked by the haemodynamic stresses of pregnancy (4).

A number of possible causes have been proposed for PPCM, including myocarditis, abnormal immune response to pregnancy, maladaptive response to the haemodynamic stresses of pregnancy, stress-activated cytokines, and prolonged tocolysis. In addition, there have been a few reports of familial PPCM (5-7), raising the possibility that some cases of PPCM are actually familial dilated cardiomyopathy unmasked by pregnancy. Some of the key hypotheses are discussed below.

Myocarditis

Myocarditis has been shown by endomyocardial biopsy in PPCM (8) and its incidence can be as high as 76% of cases (9). The absent or muted immune response during pregnancy may allow for unchecked viral replication and thus a greater likelihood of myocarditis in the setting of a viral infection. Studies in pregnant mice demonstrated enhanced susceptibility to viral myocarditis due to coxsackie viruses and echoviruses (10). The hypothesis is that if viral genetic products are evident, the postviral immune response of the patient may have been inappropriately targeted against otherwise cryptic cardiac tissue proteins, leading to ventricular dysfunction.

Correspondence:
Dr Haizal Haron Kamar
Faculty of Medicine,
University of Malaya,
50603 Kuala Lumpur.
Tel: 603-7950 2429
Email: haizal@um.edu.my

Abnormal immune response to pregnancy

The occurrence of chimerism of the haematopoietic lineage cells from the foetus to the mother during pregnancy have been reported (11-12). If these cells, which are weakly immunogenic, escape into the mother's circulation and reside in cardiac tissue during the immunosuppressed pregnant state, then following postpartum recovery of immune competence, they are recognized as nonself by the maternal immune system and a pathologic autoimmune response may be triggered leading to myocarditis.

Response to haemodynamic stresses of pregnancy

During pregnancy, blood volume (preload) and cardiac output increase and afterload decreases. In addition, the left ventricle remodels in response to the haemodynamics of pregnancy, resulting in transient hypertrophy. The research (13) and other studies (14) have shown a reversible decrease in left ventricular systolic function in the second and third trimesters that persisted into the early postpartum period, but returned to baseline shortly thereafter. It is possible that PPCM may be due, in part, to an exaggeration of this decrease in systolic function.

Other aetiologic factors

There are other causes for PPCM that merit further study such as: (a) prolonged tocolysis (15), (b) stress-activated proinflammatory cytokines such as tumor necrosis factor-alpha or interleukin-6 that have been implicated in the pathophysiology of idiopathic dilated cardiomyopathy (16), and (c) abnormalities of relaxin, primarily an ovarian hormone produced during pregnancy, recently found in cardiac atria, shown to have positive inotropic and chronotropic properties (17) and potentially involved in excessive relaxation of the cardiac skeleton.

Clinical Presentation

PPCM can present in a number of different ways. Some of the known clinical presentations are arrhythmias (18), thromboembolic events (1,19) and cardiac arrest during anaesthesia (20). However, by far the commonest symptoms and signs are those of congestive cardiac failure, such as dyspnoea, orthopnoea, and paroxysmal nocturnal dyspnoea (21-22).

This presents a challenge because many women in the last month of a normal pregnancy experience dyspnoea, fatigue, and pedal oedema, symptoms identical to early congestive heart failure. PPCM may, therefore, go unrecognized, leading to underestimation of incidence. There are no specific criteria for differentiating subtle symptoms of heart failure from normal late pregnancy, so it is important that a high index of suspicion be maintained to identify the rare case of PPCM.

Management

A few issues need to be considered when managing PPCM cases. Firstly, is the stage of PPCM, that is, prepartum versus postpartum period. Secondly, in the prepartum period, management also takes into account the welfare of the foetus. Thirdly, is the mode of cardiac failure presentation, which is either acute (unstable) or chronic (stable).

In the prepartum period, the principle issue is the timing of delivery. Many factors must be taken into consideration including the success of medical therapy, perception of cardiac stress and anaesthesia risk. In selective cases, conservative management with medical therapy may be appropriate. If pulmonary maturity on amniocentesis can be demonstrated, prompt delivery of the patient would appear to be the best mode of therapy. In patients with unstable maternal haemodynamics, the maternal and secondary foetal risks demand prompt delivery as part of the patient's treatment protocol.

The postpartum management is similar to that of other non-ischaemic dilated cardiomyopathies, which is preload and afterload reduction, and increase inotropy.

Management of stable PPCM patient

(a) Non-pharmaceutical therapy

These include low sodium diet (less than 4 gm a day), fluid intake restriction and modest daily exercise (e.g. walking).

(b) Pharmaceutical therapy

The cornerstone of optimal outpatient oral pharmacologic therapy for cardiomyopathy begins with afterload reduction with the use of angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARB) (23-25). Unfortunately, pregnancy is a contraindication to the use of ACEI and ARB. In this instance, the use of hydralazine and nitroglycerine can be safely used in pregnancy to provide the much needed afterload reduction (26).

Preload reduction can be achieved with diuretic and low dose oral nitrates. In pregnancy, diuretics must be used with caution to avoid dehydration.

Oral inotropic therapy can be provided by digoxin (27). The deleterious effect of excessive sympathetic nervous system may be blocked and reversed with b-blockers (28-30).

Calcium channel blockers have negative inotropic properties that may make them unacceptable for use in this situation but amlodipine, a dihydropyridine calcium channel blocker, has been shown to improve survival in non-ischaemic cardiomyopathy patients (31) and may have a role in management of PPCM.

A suggested treatment regimen for stable PPCM is outlined in Table 1.

Management of unstable PPCM patient

In acutely ill or highly symptomatic patients, intravenous preload- and afterload-reducing agents (e.g. nitroglycerin) and/or inotropic agents (e.g. dopamine and dobutamine) should be considered. These agents can be used in pregnancy if medically indicated.

Table 1. Suggested treatment plan in stable peripartum cardiomyopathy

1. Start diuretic therapy (e.g. frusemide 40 mg od) to control symptoms due to volume excess. Use with caution in prepartum patients.
2. In postpartum patients, institute ACEI and titrate up to the maximum tolerated dose. In prepartum patients, use hydralazine and isosorbide dinitrate combination therapy to lower the systolic blood pressure to no less than 100 mmHg.
3. Start digoxin, especially if atrial fibrillation is present.
4. Start β-blockers, such as carvedilol, metoprolol or bisoprolol. Begin with small doses and titrate up to the maximum tolerated dose. Use with caution in prepartum patients.
5. Consider the use of small dose spironolactone (e.g. 12.5 mg od).
6. Consider the use of amlodipine.
7. Dietary consultation for fluid-restricted, low-salt diet.
8. Detailed patient education and counseling.
9. Referral to an exercise rehabilitation programme, if appropriate.
10. Vigilant and frequent follow-up, especially during the prepartum period.

Invasive haemodynamic monitoring is used if available to guide the acute phase of illness and therapy. The haemodynamic goals would be to achieve and maintain a mean arterial pressure of approximately 75 mmHg, and heart rate between 60 to 80 beats per minute, systemic vascular resistance between 800 and 1,200 dynes/sec/cm, pulmonary capillary wedge pressure between 16 to 20 mmHg, and cardiac index of more than 2.5 L/min/m^2.

Other forms of treatment to be considered

Anticoagulation

From natural history studies, there is a high incidence of thromboembolism in this population. Thrombi are the result of hypercoagulable state of pregnancy and of stasis and turbulent flow in dilated heart. Mortality due to embolic phenomena has been reported to be as high as 30%. Therefore, anticoagulation with heparin (either unfractionated or low molecular weight heparin) or warfarin is advised.

Immunosuppressive therapy

Midei *et al* (9) studied 14 patients with PPCM who had biopsy-proven myocarditis. Nine out of 10 patients who received immunosuppressive therapy (prednisolone and azathioprine) had symptomatic improvement, but so too were the other four patients who were not given immunosuppression (32). One retrospective study suggested that women with PPCM treated with intravenous immune globulin had a greater improvement in ejection fraction during early follow-up than patients treated conventionally (33). More recently, it was shown that the addition of pentoxifylline, a drug known to inhibit the production of TNF-alpha, to conventional treatment, improves outcome in patients with PPCM (34).

Cardiac transplantation

Women who fail maximal medical management may be candidates for cardiac transplantation. One study of 10 PPCM patients who underwent cardiac transplantation reported survival comparable to age-matched women undergoing heart transplantation for other indications, but noted a marginally higher rate of biopsy-proven early rejection, necessitating increased cytolytic therapy (35).

Prognosis

Reported mortality of PPCM ranges from 25 to 50%. Approximately 50% of patients show full recovery by six months after delivery. 10 to 20% will deteriorate despite treatment and die. Another 30 to 40% of patients will have partial or no recovery.

The prognosis for women with PPCM appears to depend on the normalisation of left ventricular size and function within six months after delivery. In one study, approximately half of the 27 women studied had persistent left ventricular dysfunction. In this group, the cardiac mortality rate was 85% over five years, compared with the group in whom cardiac size returned to normal, who experienced no reported cardiac mortality in the same time interval (1). A more recent study corroborates these results: 50% (7/14) of patients had dramatic improvement soon after delivery, but six of the seven remaining patients died (36). Survivors were found to have a higher mean ejection fraction (23% vs. 11%) and smaller mean left ventricular cavity size (5.8 cm vs. 6.9 cm) at diagnosis. Other good prognostic indicators are normal pulmonary artery pressure, younger age, delay in diagnosis and low parity (37). The presence or absence of myocarditis is thought not to influence prognosis (38).

The effect on the foetus of PPCM patients has been reported in a study where there was an increase incidence of premature and low birth weight infants. There was, however, no foetal death (15).

Future Obstetric Recommendations

Currently, there is no consensus regarding recommendations for future pregnancy after PPCM. Patients whose left ventricular size or function does not return to normal should be counseled strongly against subsequent pregnancy (1) and treated accordingly, including adopting a heart-healthy diet and lifestyle.

Patients whose cardiomyopathy apparently resolves completely are a more difficult group to counsel. In the long-term follow-up study, eight out of 14 patients whose heart size returned to normal after the first episode of PPCM had subsequent pregnancies. Of the eight patients, two developed PPCM with subsequent pregnancies (1). Others (39) reported normal subsequent pregnancies and normal left ventricular function (by echocardiography) in four women whose heart size returned to normal after PPCM in a prior pregnancy. As PPCM has been associated with multiparity in some studies, the risk of irreversible cardiac damage may increase with each subsequent pregnancy. In addition, even though the left ventricular size and function return to normal, there is evidence that contractile reserve is impaired (40) and recurrence of PPCM despite rapid return of heart size and function to normal in the prior affected pregnancy has been reported (41). Therefore, subsequent pregnancies, if they cannot be avoided, should be managed in collaboration with a high-risk perinatal centre.

References

1. Demakis JG, Rahimtoola SLI, Sutton, GC *et al*. Natural course of peripartum cardiomyopathy. Circulation 1971; 44:1058-61.
2. Seftel H, Susser M. Maternity and myocardial failure in African women. Br Heart J 1961; 28:157-67.
3. Manolio TA, Baughman KL, Rodeheffer R, *et al*. Prevalence and etiology of idiopathic cardiomyopathy (summary of a National Heart, Lung, and Blood Institute Workshop). Am J Cardiol. 1992; 69:1458-1466.
4. Ventura SJ, Peters KD, Martin JA, *et al*. Births and deaths: United States, 1996. Mon Vital Stat Rep. 1997; 46(1 suppl 2):1-40.
5. Familial occurrence of postpartal heart failure. Arch Intern Med. 1962; 111:163-166.
6. Massad LS, Reiss CK, Mutch DG, *et al*. Family peripartum cardiomyopathy after molar pregnancy. Obstet Gynecol. 1993; 81:886-888.
7. Pearl W. Familial occurrence of peripartum cardiomyopathy. Am Heart J. 1995; 129:421-422.
8. Melvin KR, Richardson PJ, Olsen EG, *et al*. Peripartum cardiomyopathy due to myocarditis. N Engl J Med. 1982; 307:731-734.
9. Midei MG, DeMent SH, Feldman AM, *et al*. Peripartum myocarditis and cardiomyopathy. Circulation. 1990; 81: 922-928.
10. Farber PA, Glasgow LA. Viral myocarditis during pregnancy: encephalomyocarditis virus infection in mice. Am Heart J. 1970; 80:96-102.
11. Artlett CM, Jimenez SA, Smith JB. Identification of fetal DNA and cells in skin lesions from women with systemic sclerosis. N Engl J Med. 1998; 338:1186-1191.
12. Nelson JL, Bianchi DW, Ober C, *et al*. Microchimerism and HLA compatible relationships of pregnancy in scleroderma. Lancet. 1998; 351:559-562.
13. Geva T, Mauer MB, Striker L, *et al*. Effects of physiologic load of pregnancy on left ventricular contractility and remodeling. Am Heart J. 1997; 133:53-59.
14. Mone SM, Sanders SP, Colan SD. Control mechanisms for physiological hypertrophy of pregnancy. Circulation. 1996; 94:667-672.
15. Witlin AG, Mable WC, Sibai BM. Peripartum cardiomyopathy: An ominous diagnosis. Am J Obstet Gynecol. 1997; 176:182-188.
16. Sliwa K, Skudicky D, Bergemann A, *et al*. Peripartum cardiomyopathy: analysis of clinical outcome, left ventricular function, plasma levels of cytokines and Fas/APO-1. J Am Coll Cardiol. 2000; 35(3):701-705.
17. Coulson CC, Thorp JM Jr, Mayer DC, *et al*. Central haemodynamic effects of recombinant human relaxin in the isolated, perfused rat heart model. Obstet Gynecol. 1996; 87:610-612.

18. Brito O, de Lacerda AP, Freitas P, *et al.* Incessant atrial tachycardia and peripartum cardiomyopathy – a therapeutic challenge. Rev Port Cardiol. 1997; 16(2):157-163.

19. Janssens U, Klues HG, Hanrath P. Successful thrombolysis of right atrial and ventricle thrombi in a patient with peripartum cardiomyopathy and extensive thromboembolism. Heart. 1997; 78(5):515-516.

20. Melndoe AK, Hammond EJ, Babington PC. Peripartum cardiomyopathy presenting as a cardiac arrest at induction of anaesthesia for emergency Caesarian section. Br J Anaesth. 1995; 75(1):97-101.

21. O'Connel JB, Costanzo-Nordin MR, Subramaniam R, *et al.* Peripartum cardiomyopathy: Clinical, haemodynamic, histologic and prognostic characteristics. J Am Coll Cardiol. 1986; 8:52-56.

22. Van Haevan KH, Kitsis RN, Katz SD. Peripartum versus idiopathic dilated cardiomyopathy in young women – a comparison of clinical, pathological and prognostic features. Int J Cardiol. 1993; 40:57.

23. CONSENSUS Trial Study Group. Effects of Enalapril on mortality in severe congestive cardiac failure. N Engl J Med. 1987; 316:1429-1435.

24. Pitt B, Poole-Wilson PA, Segal R, *et al.* Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: Randomized trial – the losartan heart failure survival study (ELITE II). Lancet. 2000; 355(9215):1582-1587.

25. Cohn JN, Tognoni G, Valsartan Heart Failure Trial (Val-HeFT) Investigators. A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure. N Engl J Med. 2001; 345(23):1667-1675.

26. Cohn JN, Johnson G, Ziesche S, *et al.* A comparison of enalapril with hydraline and isosorbide dinitrate in the treatment of chronic congestive heart failure. N Engl J Med. 1991; 325:303-310.

27. Packer M, Gheorghia de M, Young JB, *et al.* Withdrawal of digoxin from patients with chronic heart failure treated with angiotensin-converting enzyme inhibitors. N Engl J Med. 1993; 329:1-7.

28. CIBIS Investigators and Committees. A randomized trial of beta-blockade in heart failure: The Cardiac Insufficiency Bisoprolol Study (CIBIS). Circulation. 1994; 90: 1765-1773.

29. MERIT-HF Study Group. Effect of Metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF). Lancet. 1999; 353:2001-2007.

30. Packer M, Coats AJ, Fowler MB, COPERNICUS Study Group. Effect of carvedilol on survival in severe chronic heart failure. N Engl J Med. 2001; 344(22): 1651-1658.

31. Packer M, O'Connor CM, Ghali JK, *et al* for the PRAISE Study Group. Effect of amlodipine on morbidity and mortality in severe chronic heart failure. N Engl J Med. 1996; 335:1107-1114.

32. Midei MG, Dement SH, Feldmon AM, *et al.* Peripartum myocarditis and cardiomyopathy. Circulation. 1990; 81:922-928.

33. Bozkurt B, Villaneuva FS, Holubkov R, *et al.* Intravenous immune globulin in the therapy of peripartum cardiomyopathy. J Am Coll Cardiol. 1999; 34:177-180.

34. Sliwa K, Skudicky D, Candy G, *et al.* The addition of pentoxifylline to conventional therapy improves outcome in patients with peripartum cardiomyopathy. Eur J Heart Fail. 2002; 4(3):305-309.

35. Keogh A, Macdonald P, Spratt P, *et al.* Outcome in peripartum cardiomyopathy after heart transplantation. J Heart Lung Transplant. 1994; 13:202-207.

36. Sutton MS, Cole P, Plappert M, *et al.* Effects of subsequent pregnancy on left ventricular function in peripartum cardiomyopathy. Am Heart J. 1991; 121:1776-1778.

37. Carvalho A, Brandao A, Martinez EE, *et al.* Prognosis is peripartum cardiomyopathy. Am J Cardiol. 1989; 64: 540-542.

38. Felker GM, Jaeger CJ, Klodas E, *et al.* Myocarditis and long-term survival in peripartum cardiomyopathy. Am Heart J. 2000 Nov; 140(5):785-91.

39. Sutton MS, Cole P, Plappert M, *et al.* Effects of subsequent pregnancy on left ventricular function in peripartum cardiomyopathy. Am Heart J. 1991; 121: 1776-1778.

40. Lampert M, Weinert L, Hibbard J, *et al.* Contractile reserve in patients with peripartum cardiomyopathy and recovered left ventricular function. Am J Obstet Gynecol. 1997; 176(1 pt 1):189-195.

41. Ceci O, Berardesca C, Caradonna F, *et al.* Recurrent peripartum cardiomyopathy. Eur J Obstet Gynecol Reprod Biol. 1998; 76:29-30.

ISOLATION OF *LEGIONELLA* FROM COOLING TOWERS AND POTABLE WATER SYSTEMS IN HOSPITAL AND NON-MEDICAL BUILDINGS IN A UNIVERSITY CAMPUS

Chin KS[1], Rosli AA[1], Wee CSL[2] and Ngeow YF[2]
[1] *MBBS Phase 2, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur*
[2] *Department of Medical Microbiology, Faculty of Medicine. University of Malaya, 50603 Kuala Lumpur*

ABSTRACT: Six cooling towers and eleven sources of potable water in a university campus in Kuala Lumpur were surveyed for the presence of *legionellae*. One non-medical building cooling tower and three hot water systems from one ward of the hospital tested positive for *Legionella*, two of which contained *Legionella pneumophila* serogroup 1. The identification of *Legionella* was based on isolation, immunofluorescence and polymerase chain reaction (PCR). *(JUMMEC 2003-2005; 8: 23-27)*

KEYWORDS: *Legionella* isolation, hot water system, cooling towers

Introduction

Legionella spp. are Gram-negative bacteria that occur ubiquitously in soil and aquatic environments (1). The most well-known of these is *Legionella pneumophila*, which is the causative agent of Legionnaires' Disease, an atypical form of pneumonia characterized by a non-productive cough coupled with pneumonia symptoms. Ever since its discovery in an air-conditioning system in 1976, this organism, along with other members of its genus, has been found with increasing frequency in both natural and man-made environments, especially in air-conditioning cooling towers and potable water systems (1-3). These organisms are dispersed in the form of aerosolized water droplets which, if inhaled by the susceptible, may be brought into the lungs where they cause disease.

Because of the *Legionella* organism's association with outbreaks of community and nosocomial pneumonia as well as a milder, self-limiting form of infection called Pontiac Fever, there has been an increasing need to monitor water systems for their presence, especially in hospital environments, where equipment relying on potable water sources, for example, humidifiers and nebulizers, which provide vehicles of transmission for these organisms, are used on a regular basis.

Until recently, there have been very few reports of Legionnaires' Disease in South-East Asia; however, several cases have been reported of late in Singapore (4) and China (5), in conjunction with the development of this region. In Malaysia, however, the last reported survey of the prevalence of *Legionellae* was carried out in 1990 (6). This paper describes a study carried out in 2002 as a follow-up of the study in a university campus in Kuala Lumpur.

Methods

Media

A commercial Buffered Charcoal Yeast Extract Agar with α-ketoglutarate (Oxoid) supplemented with cysteine and ferric ions (Oxoid) and added with the selective agents glycine, vancomycin, polymyxin and cycloheximide (Oxoid) was used for the isolation of *Legionella* spp.

Samples

Water samples were collected from air-conditioning cooling towers and potable water systems from different sites in the university campus, including the university hospital according to the standard procedures of the American Public Health Association (APHA 1998). One litre of water was collected from

Correspondence:
CSL Wee
Department of Medical Microbiology
Faculty of Medicine
University of Malaya
50603 Kuala Lumpur
Tel: 603-7950 2205

each cooling tower as well as hot water from taps and showers, using sterile bottles. These water samples were kept at 4°C and processed within 24 hours. Temperature and pH readings for the water samples were also determined by using a handheld temperature probe and pH indicator paper, respectively.

Water processing

The water samples were filtered by negative pressure through 47 mm polycarbonate membrane filters of 0.22 µm pore size. The filter membranes were subsequently washed in 10 ml sterile distilled water to dislodge any trapped organisms. The suspension was then centrifuged at 4,000 rpm for 10 minutes. The supernatant was poured out, and the sediment was re-suspended in 1 ml of the original water sample.

Acid buffer treatment

The water samples were subjected to acid buffer treatment as described by Bopp *et al* (7). The HCl-KCl buffer was prepared by mixing 3.9 ml of 0.2 M HCl with 25 ml of 0.2 M KCl, producing a solution of approximately pH 2.2. The 1 ml suspensions were diluted 1:10 with the acid buffer and incubated at room temperature for 15 minutes. 0.1 ml of each treated water sample was then removed from the acid suspension and inoculated onto BCYE-α agar by the spread plate method. The plates were incubated in a moist chamber at 37°C for up to 14 days.

Screening suspect Legionella *isolates*

Colonies which appeared after three to five days of incubation, and were greyish-white in colour with round edges and shiny appearance were presumed to be *Legionella*. These suspect isolates were plated onto Horse Blood Agar (HBA) as well as BCYE-α agar and incubated at 37°C. *Legionella*-like organisms were identified by positive growth on BCYE-α agar but absence of growth on HBA. Verification of *Legionella* was carried out by a direct immunofluorescence assay (*Legionella* Direct Fluorescent Test System, Scimdex Corp., USA) and DNA amplification.

DNA extraction and amplification

A loopful of each suspected *Legionella* isolate was suspended in 200 µl of TBE buffer (5 mM Tris, 5 mM boric acid, 0.1 mM EDTA), pH 8.0. The suspensions were centrifuged at 10,000 g for 30 minutes to pellet the bacterial cells. The cells were then lysed with lysis buffer containing 0.5% (v/v) Nonidet P-40, 0.5% Tween 20 (v/v) and 0.1 mg/mL Proteinase K at 60°C for one hour. The enzymes were subsequently deactivated by boiling the mixture at 100°C for 10 minutes. The extracts were then stored at -20°C until use.

Amplification of the DNA was carried out using primers that amplified a 386-bp region of the *Legionella* 16S rRNA, as described by Jonas *et al (8)*. The two 20-base oligonucleotides (5'-AGGGTTGATAGGTTAAGAGC-3' (JFP) and 5'-CCAACAGCTAGTTGACATCG-3' (JRP)) were complementary to positions 451 to 470, and 836 to 817 respectively.

Polymerase chain reaction (PCR) was performed in a 40 µl reaction mixture containing 1X PCR buffer (20 mM Tris-HCl (pH 8.4), 50 mM KCl), 3.0 mM $MgCl_2$, 200 µM of dNTP (dATP, dCTP, dGTP, dTTP), 1 µM of each primer, 2 U of Platinum Taq DNA polymerase (Invitrogen, USA) and 4 µl of each extracted template DNA. Thermal cycling was performed on a PTC-100™ progammable thermal controller (MJ Research, Inc. USA). The cycling conditions began with a 5-minute hot start at 95°C to activate the DNA polymerase and was followed by 35 cycles consisting of 95°C for 45 s, 57°C for 45 s, and 72°C for 60 s, ending with a final extension at 72°C for 10 minutes. The mixture was held at room temperature until analysis by gel electrophoresis.

Ten µl of each amplified product was mixed with 5 µl of loading buffer and electrophoresed on 1.5% agarose gel containing ethidium bromide, in TBE buffer at 90V for 45 minutes. The gel was viewed on a UV transilluminator. The migration distance of the amplified fragment was compared to that of the Gene Ruler 100-bp marker to determine its approximate size.

Results

Out of the 17 water samples collected, four yielded *Legionella*-like organisms. All four isolates grew on BCYE-α after three to eight days of incubation, forming shiny grayish-white colonies with round edges. These were presumed to be *Legionella* by their inability to grow on HBA, which did not contain cysteine. DNA amplification yielded bands of 386-bp size (Figure 1), confirming their identity as *Legionella* spp., and direct fluorescence assay using monoclonal antibodies determined that two of the four isolates were *L. pneumophila* serogroup 1. The remaining two were non-reactive with the *L. pneumophila* serogroup 1 antiserum but were identified as *Legionella* by PCR.

Table 1 shows the breakdown of isolation based on sampling site. Out of a total of 17 sites around the university campus, six were from non-hospital ground-based cooling towers from various faculties that could be accessed without written permission. The remaining 11 were from different sites in the university hospital where potable water was available, namely the taps and showers in ward bathrooms. One of the six

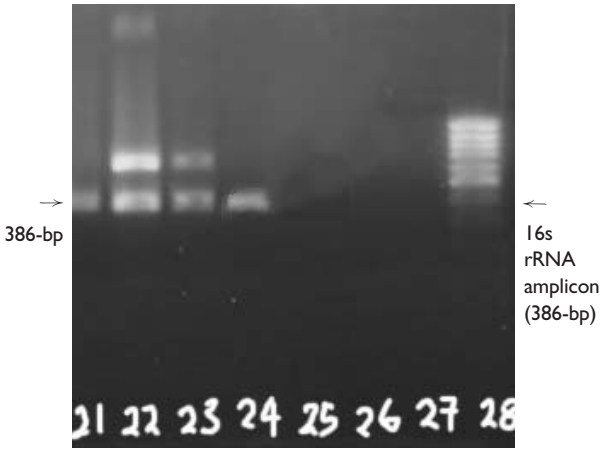

Figure 1. Gel electrophoresis picture of 16s rRNA gene PCR for *Legionella* spp. Lanes 21-24: water samples positive for *Legionellae*; lanes 25-27: negative controls; lane 28: 100-bp marker. The specific 16s rRNA amplicon appears as a 386-bp band. The second (649-bp) band in lanes 22 and 23 is the product of amplification of a virulence gene in *Legionella pneumophila* (not described in this study).

cooling towers tested positive for *Legionella*. The other three samples that yielded *Legionellae* were two hot water taps and a shower head from a paediatrics ward of the hospital. This gives an overall isolation rate of 23.5% (16.7% from the water cooling towers and 27.3% from hospital warm water supplies).

The mean pH and temperature of the water samples obtained from the cooling towers and wards are as shown in Table 1. Hot water systems in the hospital were targeted for sampling because, as previously reported, (a) *Legionellae* can multiply in waters of temperatures that are not favourable to many other pathogens, and (b) these organisms are found more frequently and in larger numbers in hot water systems than cold water systems.

Discussion

The isolation of *Legionella* from natural waters without association with disease (3) was the first indication that this organism was not merely an accidental contaminant in the air-conditioning cooling tower involved

Table 1. Breakdown of isolation based on sampling site

Sample Type	Cooling Towers	Ward Hot Water Supply
Sampling location	• Pathology department • Business faculty 1 • Business faculty 2 • Symphonic Band headquarters • Hospital 1 • Hospital 2	Adult Oncology Unit • Bone marrow transplant bathroom shower head • Water tap 1 • Water tap 2 Milk kitchen • Preparation area tap • Wash area 1 • Wash area 2 Paediatrics 4 ward • Shower head • Water tap (dirty utility room) • Water tap (clean utility room) Intensive Care Unit (ICU) • Water tap 1 • Water tap 2
Total no. sampled	6	11
No. positive for *Legionella*	3	3
Mean pH of water	4.7	4.6
Mean temperature (°C)	31.2	46.6

in the 1976 Philadelphia outbreak, but actually dwelled in aquatic habitats. Since then, there have been reports of *Legionella* being found in potable water systems such as plumbing systems (3,9), and luxury items such as fountains, spas (10) and misting devices (11).

In our study, we have pinpointed certain areas in a university hospital as harbouring *Legionella*. Two of the four sites were found to be contaminated with *L. pneumophila* serogroup 1, which is responsible for 50-70% of Legionnaires' Disease cases (8), and the two other sites by non-serogroup 1 *Legionella*. The detection rate of 23.5% is somewhat lower than the 40% previously reported from this country and its neighbour (6); however, the lower detection rate may be accounted for by the filtration isolation technique, which has a reported success rate of 53%, and the acid buffer treatment which, while necessary to eliminate other microorganisms in the water, has been reported to reduce the recovery rate by 30% (12). With the development of molecular biology, it may be more prudent to couple these tools with traditional culture methods to increase detection accuracy and sensitivity in future studies.

It has long since been established that *Legionella* infests waters as intracellular parasites of amoebae and protozoa. This carries serious implications since it has recently been shown that not only does this provide *Legionella* with sanctuary from harsh environmental conditions (13) – and thus increases its resistance against elimination by chemical methods – it also enhances its infectivity (14). In the hospital environment especially, its proliferation in plumbing systems is encouraged by the relatively high temperature of the water which, while hot enough to eliminate most other pathogens, is usually not high enough to kill *Legionella* spp. as they thrive in temperatures of about 32-42°C (1,3), although they cannot survive temperatures of over 60°C. This study found that the *Legionellae* were able to survive in hospital hot water systems with an average water temperature of 46°C.

Many previous studies have reported heavy contamination of *Legionella* in the plumbing systems of hospitals and other health care facilities (3,15), and these organisms have been associated with nosocomial outbreaks (5,7,12,14). The presence of *Legionella* in the hot water supply to the paediatrics ward poses a potential infection hazard as immunocompromised patients in the ward would be at risk for Legionnaires' Disease; furthermore, *Legionella pneumophila* has been associated with bacteremic coinfection (16).

Until recently there has been very little concern about this disease in this region, and there is no data regarding the extent of endemic *Legionella* infections in Malaysia (6); however, the case reports from Singapore (4) and China (5) serve as warning of the health issues Malaysia may face in the future, especially since there is a fast-growing trend towards the use of misting devices in both places of residence and public locations. If legionellosis is to be avoided, especially in health care establishments, then monitoring of water supplies and chemical disinfection with oxidizing agents or thermal disinfection (17), coupled with regular scouring of the cooling towers to remove the slime and sediments that would harbour *Legionellae* should be carried out as a preventive measure, and not as corrective action after disease occurs.

References

1. Yee RY, Wadowsky RM. Multiplication of *Legionella pneumophila* in unsterilized tap water. Appl Environ Microbiol 1982; 43:1330-34.
2. Hsu SC, Martin R, Wentworth BB. Isolation of *Legionella* species from drinking water. Appl Environ Microbiol 1984; 48:830-32.
3. Wadowsky RM, Yee RB, Mezmar L, *et al*. Hot water systems as sources of *Legionella pneumophila* in hospital and non-hospital plumbing fixtures. Appl Environ Microbiol 1982; 43:1104-110.
4. Goh KT, Ed. Surveillance of Legionellosis and *Legionella* bacteria in Singapore, 1999. Epidemiol Bull 2000; 26:39-44.
5. Chen YS, Lin WR, Liu YC, *et al*. Residential water supply as a likely cause of community-acquired Legionnaires' Disease in an immunocompromised host. Eur J Clin Microbiol Infect Dis 2002; 21:706-09.
6. Ngeow YF, Tan CH, Lim SY. *Legionella* species isolated from cooling towers in Kuala Lumpur. Med J Malaysia 1992; 47:15-19.
7. Bopp CA, Sumner JW, Morris GK, *et al*. Isolation of *Legionella* spp. from environmental water samples by low-pH treatment and use of a selective medium. J Clin Microbiol 1981; 13:714-19.
8. Jonas D, Rosenbaum A, Weyrich S, *et al*. Enzyme-linked immunoassay for detection of PCR-amplified DNA of *Legionellae* in bronchoalveolar fluid. J Clin Microbiol 1995; 33:1247-52.
9. Tobin JO'H, Beare J, Dunnill MS. Legionnaires' Disease in a transplant unit: isolation of the causative agent from shower baths. Lancet 1980; 2:118-121.

10. Hershey J, Burrus B, Marcussen V, *et al*. Legionnaires' Disease Associated with a Whirlpool Spa Display – Virginia, September-October, 1996. MMWR 1997; 46: 83-6.

11. LaMaire W, Jackson H, McFarland L. Epidemiologic Notes and Reports: Legionnaires' Disease Outbreak Associated with a Grocery Store Mist Machine – Louisiana, 1989. MMWR 1990; 39:108-110.

12. Boulanger CA, Edelstein PH. Precision and accuracy of recovery of *Legionella pneumophila* from seeded tap water by filtration and centrifugation. Appl Environ Microbiol 1995; 61:1805-09.

13. Gao LY, Harb OS, Kwaik YS. Utilization of similar mechanisms by *Legionella pneumophila* to parasitize two evolutionarily distant host cells, mammalian macrophages and protozoa. Infect Immun 1997; 65:4738-46.

14. Cirillo JD, Falkow S, Tompkins LS. Growth of *Legionella pneumophila* in Acanthamoeba castellanii enhances invasion. Infect Immun 1994; 62:3254-61.

15. Sabria M, Yu VL. Hospital-acquired *Legionellosis*: solutions for a preventable infection. Lancet Infect Dis 2002; 2:368-73.

16. Tan MJ, Tan JS, File TM Jr. Legionnaires' Disease with bacteremic coinfection. Clin Infect Dis 2002; 35:533-9.

17. Kim BR, Anderson JE, Mueller SA, *et al*. Literature review – efficacy of various disinfectants against *Legionella* in water systems. Water Res 2002; 36:4433-44.

THE ANTIULCER AND CYTOPROTECTIVE EFFECT OF *AGERATUM CONYZOIDES*–HONEY COMBINATION IN RATS

Fathihah B, Mahmood AA, Sidik K and Salmah I
Department of Molecular Medicine, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur

ABSTRACT: Six groups of adult male *Sprague Dawley* rats, each consisting of six animals were used throughout the experiment. The gastroprotective effects of aqueous plant extract alone, honey alone or honey in combination with ethanolic or aqueous extracts of *A. conyzoides* and cimetidine were investigated in rats against ethanol-HCl-induced gastric ulcer. Efficacy was assessed by determination of ulcer index and inhibition percentage. Oral administration of ethanol-HCl (5 ml kg^{-1} body weight) to fasted rats produced extensive lesions of gastric mucosa (Group 1). Pre-treatment with honey (2.5 g kg^{-1} body weight) alone (Group 2), aqueous plant extract alone (10% w/v 5 ml kg^{-1}) (Group 3), or honey in combination with each of alcoholic extract (10% w/w 5 ml kg^{-1}) (Group 4), aqueous extract (10% w/w 5 ml kg^{-1}) (Group 5) or cimetidine (10 mg/ml honey 5 ml kg^{-1}) (Group 6) orally 30 minutes before administration of absolute ethanol-HCl significantly ($p < 0.05$) protected gastric lesions by 46.74%, 61.50%, 76.68%, 78.39% and 56.55% respectively. Although the mechanism of gastric protection is unknown, honey in combination with each plant extract appears to increase the resistance of gastric mucosal cells to the necrotizing effect of strong irritants in the absolute ethanol-HCl mixture. The results suggest that honey in combination with each plant extract might be beneficial in the treatment of a variety of diseases in which gastric mucosal injury is present. *(JUMMEC 2003-2005; 8: 28-32)*

KEYWORDS: Honey, *A. conyzoides*, cimetidine, rats, ulcer

Introduction

Ageratum conyzoides is a plant that is used for traditional herbal medicine in many countries especially in the tropical and subtropical region. *A. conyzoides* is very common in West Africa and some parts of Asia and South America. The plant is native to tropical America and has been introduced and naturalized in India (1). The phytochemicals in *A. conyzoides* include alkaloids, cumarins, essential oils, flavonoids and tannins. It also consists of conyzorigum, chromene and flavones (2). Borthakor and Baruah found procene I and procene II in 1987 in a plant collected in India (3).

The formation of peptic ulcers depends on the presence of acid and peptic activity in gastric juice plus a breakdown in mucosal defences. There are two major factors that can disrupt the mucosal resistance to injury: non-steroidal anti-inflammatory drugs (NSAIDs) e.g. aspirin and *Helicobacter pylori* infection (4). As a matter of fact, many drugs were used to treat this disease but many of them cause adverse effects and recurrent infections frequently occur within a few weeks because of difficulty in eradication of *H. pylori* (5).

Honey is a remarkable liquid, prepared by honeybees from the natural solutions called nectar obtained from various flowers (6). Honey consists of 70-80% of carbohydrates, which is the major constituent and various substances found in low amounts in honey are organic acid, proteins, amino acids, vitamins, enzymes, minerals and different other molecules such as pigments, flavonoids and antibacterial factors (7).

The curative properties of honey have been known since ancient times. The ancient Greeks, Romans, Chinese and Egyptians used honey to cure gut disease (8). The curing properties of honey for mankind were also clearly described in the Holy Quran (7). There is also a report that honey was able to induce adaptive cytoprotection against ethanol-induced gastric lesion in rats because of its high carbohydrate concentrations (7).

Therefore, the present study was performed to evaluate the efficacy of cytoprotective properties of honey alone or in combination with each of alcoholic and aqueous plant extract of *A. conyzoides* and its antiulcer effect against experimental gastric ulcer in rats.

Methods

Plant material

A. conyzoides was collected at Faculty of Medicine, University of Malaya, Kuala Lumpur in the months of March to April 2004. The plant were identified and deposited at the Department of Pharmacy, Faculty of Medicine, University Malaya (Voucher No. 30).

Preparation of aqueous and alcoholic extracts

A. conyzoides fresh leaves were cut into small pieces, labeled, washed with distilled water and dried in an oven at 50°C for five to seven days until fully dried. The leaves were ground to a fine texture form using a grinder. The leaf powder was used for aqueous extraction and 95% ethanol extraction.

Forty grams of leaf powder was mixed with 800 ml of sterile distilled water in a conical flask using a ratio of 1:20. The mixture was then heated and stirred on a hotplate for three hours. After being left to cool, the residue was removed by filtration using a mesh and filter funnel. A rotary evaporator was used to extract the filtered material.

Forty grams of *A. conyzoides* powder was mixed with 800 ml of 95% ethanol in a conical flask using a ratio of 1:20. The flask was then covered with aluminium foil and left at room temperature (25°C) for seven days. The residue was removed by filtration using a filter funnel, and the solvents were distilled under reduced pressure in an EYELA rotary vacuum evaporator until excess solvent evaporated.

Both extracts were then lyophilized in a freeze-dryer, to produce powdered forms of the extracts. Lyophilization removes the solvents from the solutes and stabilizes the formulation so that it can retain satisfactory pharmacological activity during long-term storage. The freeze-dried products were mixed with honey in a concentration of 100 mg extract/gram of honey (w/w).

Honey

Pure, unprocessed, unboiled commercial honey obtained from Faculty of Agriculture, University Putra Malaysia, Serdang, Selangor was used for the present study.

The oral pre-treatment applicant of honey alone or in combination with the plant extract was prepared. For the pre-treatment of honey alone (5 ml/kg body weight), the honey was filtered before use and kept in room temperature to become homogenous. Pre-treatment of aqueous extract alone 10% (w/v) (5 ml kg^{-1}) was prepared. Meanwhile, for pre-treatment with honey in combination with aqueous extract of *A. conyzoides*, (10% w/w) (5 ml kg^{-1}) was prepared. As for the preparation of working solution for pre-treatment with honey in combination with ethanol extract of *A. conyzoides*, (10% w/w) (5 ml kg^{-1}) was prepared. For the preparation of dose of drug used in pre-treatment with honey in combination with cimetidine, 10 mg/1 ml honey (5 ml kg^{-1}) was used.

Cimetidine

This drug was obtained from the University of Malaya Medical Centre (UMMC), Kuala Lumpur. The drug's gastroprotective effect in combination with honey was to be determined.

Experimental animals

Experimental animals consisted of 36 healthy female *Sprague Dawley* rats. The rats were obtained from the animal house, Faculty of Medicine, University of Malaya. *Sprague Dawley* rats weighing between 200-225 grams were deprived of food for 48 hours, but they were allowed free access tap water until 17 hours before the experiment. They were housed in standard environmental conditions (24°C, 60-70% humidity) under natural lighting. During the fasting period, the animals were placed individually in cages with wide-mesh wire bottoms to prevent coprophagy. On the day of the experiment, the rats were divided into five groups and were assigned to different control and treatment groups. 1.0 ml of distilled water was given orally to each rat in Group 1 (ulcer control). Meanwhile, for Group 2 (honey alone), 1.0 ml of honey was given to each rat. Each treated rat in Group 3, received 1.0 ml of honey in combination with aqueous extract of *A. conyzoides* whereas 1.0 ml of honey in combination with ethanol extract of *A. conyzoides* was administered orally to each treated rat in Group 4. For the animals in Group 5, each of them received 1.0 ml of honey in combination with cimetidine.

Thirty minutes after their pre-treatment, the rats were administered with 1.0 ml of absolute ethanol-HCl (5 ml/kg body weight) to induced ulceration except for the rats in Group 1, where they received the same amount of distilled water by the same route.

They were killed 30 minutes later under anaesthesia, using diethyl ether. Their stomachs were rapidly

removed after ligating both the oesophageal and pyloric ends. The stomach of each rat was excised and opened along the greater curvature.

Gross lesion evaluation

The stomachs were inflated with 10 ml of 1% buffered formalin to fix the outer layer of the stomachs. After rinsing with normal saline, the mucosa of the stomach was examined under a dissecting microscope with a square-grid eyepiece to assess the formation of ulcers (haemorrhagic lesions). The sum for the number of gastric lesions for each stomach was used as ulcer index (UI) and the inhibition percentage was calculated by the following formula:

$$\text{Inhibition \%} = [(\text{UI control} - \text{UI treated}) / \text{UI control}] \times 100$$

Statistical analysis of data

Results are expressed as means ± S.E.M. The statistical difference between the mean ulcer index of the positive control and negative control, and the mean ulcer index of the treated group and positive control, both were calculated by using Student's t-test, SPSS for Windows Student Version 11.0.

Histopathology

The stomachs were fixed in freshly made 10% buffered formalin for four to six hours. Next, they were processed in an automated machine (TISSUE PROCESSOR LEICA TP 1020). Then, the biopsies were embedded in paraffin and sectioned (3-5 µm), and were stained with haematoxylin and eosin. Then the sections were analyzed using a light microscope.

Results

The results of the present study are summarized in Table 1. The findings of this study showed that rat mucosa gastric injury induced by absolute ethanol-HCl was significantly reduced by ethanol extract of *A. conyzoides* in combination with honey as well as its aqueous extract.

Administration of absolute ethanol-HCl resulted in severe gastric damage. Thick reddish-black lines visible from outside indicate the formation of severe haemorrhagic lesions. After opening the stomach, lesions were found in the mucosa. They were located mostly in the corpus (the portion of the stomach secreting acid and pepsin). No haemorrhagic lesions developed in the forestomach (the non-secretory part of the stomach) due to the presence of squamous epithelium that coated the forestomach. The stomach rugae were almost flattened.

The result was substantiated by histopathological findings. Histology analysis of all rats treated with absolute ethanol-HCl revealed the tremendous infiltration of polymorphonuclear leucocytes in the mucosa up to submucosa region. There was a complete destruction of mucosa, which indicated severe haemorrhagic lesions formation. The depth of the ulcer extended up to the muscularis mucosae. The submucosa was markedly thickened by oedema.

Pre-treatment with ethanol and aqueous extract of *A. conyzoides* in combination with honey, very mild gross lesions were visible. The gross section of stomach of rats treated with ethanol extract of *A. conyzoides* showed only mild congestion compared to the stomachs of rats treated with aqueous extract of the plant, otherwise the stomach appearance was normal. In histopathologically findings, they were found to inhibit the absolute ethanol-HCl induced necrosis, congestion, haemorrhage and oedema in gastric mucosa.

Grossly, the stomach of the cimetidine in combination with honey (10 mg/rat/1 ml honey) resulted in less formation of gastric lesions compared to ulcer control. Histologically, it showed superficial erosion in the mucosa and a moderate degree of oedematous submucosa with less neutrophilic infiltration in the submucosa.

Pre-treatment with honey alone resulted in grossly moderate presence of haemorrhagic lesions. In histopathological finding, there was moderate erosion of gastric mucosa with necrotic patches and moderate gastric oedema with infiltration of neutrophils in the submucosa. Pre-treatment with aqueous plant extract also reduced the haemorrhagic lesions of mucosa grossly and histologically compared to ulcer control.

Discussion

The ethanol and aqueous extract of *A. conyzoides* in combination with honey exhibited marked cytoprotection in absolute ethanol-HCl induced rats by increasing gastric mucosal content through its phytochemical constituent, flavonoids which possess antioxidant activity. Ethanol has been shown to produce free radicals and induce peptic ulcers (4).

Earlier studies verified that antioxidants play a major task in protection of cellular damage by scavenging free radicals. The flavonoids kaempferol and quercetin are the constituents in *A. conyzoides* that are known to possess antioxidant activity (9). They act by increasing the gastric mucosal content, which is accompanied by

Table 1. Effect of *A. conyzoides* on induction of gross lesions in the absolute ethanol-HCl induced gastric ulcer model

Group	Treatment	No. of Rats	Dose Orally	Ulcer Index (Mean ± S.E.M)	Inhibition (%)
1	Absolute ethanol-HCL (ulcer control)	6	5 ml kg^{-1}	1194.83 ± 78.352	0
2	Honey alone	6	5 ml kg^{-1}	636.33 ± 29.71*	46.74
3	Aqueous extract *A. conyzoides* only	6	5 ml kg^{-1}	460 ± 18.62*	61.50
4	Aqueous extract *A. conyzoides* + Honey	6	5 ml kg^{-1}	278 ± 13.02**	76.68
5	EtOH extract *A. conyzoides* + Honey	6	5 ml kg^{-1}	258 ± 16.67**	78.40
6	Cimetidine + Honey	6	5 ml kg^{-1}	519.17 ± 15.60**	56.55

* $p < 0.05$ significant from (Absolute ethanol-HCl) ulcer control
** $p < 0.05$ significant from honey alone and aqueous *A. conyzoides*

a proportionate increase in protein and hexosamine. Hence, they inhibit gastric damage (10) and (11). A recent review bears out those flavonoids are good anti-inflammatory agent and are furthermore able to shield gastric mucosa against a variety of ulcerogenic agents via several mechanisms predominantly free-radical scavenging and antioxidant properties, enhance mucus production, anti-secretory action and inhibition of the *H. pylori* progression (1).

Regulation of gastric acid secretion involves Ca^{2+} ion. Ca^{2+} ions also mediate free radical generation in peptic ulcers. As a consequence Ca^{2+} channel blockers like nifedepine and verapamil are needed to restrain the Ca^{2+} ion activity (12). There has been a report that crude extract of *A. conyzoides* can possess Ca^{2+} channel blocking activity comparable to verapamil (13). Therefore, it can be hypothesized that the Ca^{2+} channel blocking activity of *A. conyzoides* may contribute towards its cytoprotective effect.

A. conyzoides belongs to the Asteraceae family. Polysaccharides are a main constituent of the Asteraceae family, which holds many therapeutic properties of the plants under this family. Alginic acid, which is categorized as heterogeneous polysaccharide are believed to be effective in treating gastric ulcer. Alginic acid was suggested to form gel layer and acts as barrier against excessive pH and thus protects gastric mucosa (14). It is speculated that the polysaccharide constituent contributes to the production of cytoprotective effect in *A. conyzoides*.

As for honey, it seems to share with sucralfate a common mechanism of action, indicating the presence of 'sucralfate-like' substances in honey, which afford the protection to gastric mucosa. Moreover, presence of catalase that possesses the antioxidant properties prevents formation of gastric ulcer (15). High concentration of carbohydrates honey behave as mild irritants that can induce adaptive cytoprotection (7). Meanwhile, cimetidine is an acid suppressant, which functions to inhibit the secretion of gastric acid and thus lead to diminishing ethanol-induced gastric damage.

Conclusion

This study demonstrated that honey and *A. conyzoides* attenuates gastric lesion and mucosal injury induced by absolute ethanol-HCl by increasing gastric mucosal content. Further work is necessary to isolate active principles and clarify the actual mechanism concerned in the anti-ulcer activity of this plant and to explore the active ingredients that are responsible for the protective effects of honey.

References

1. Shirwaikar A, Bhilegaonkar PM, Malini S, *et al.* The gastroprotective activity of the ethanol extract of *Ageratum conyzoides*. Journal of Ethnopharmacol 2003; 86(1): 117-121.

2. Vyas AS, Mulchandani NB. Polyoxygenated flavones from Ageratum conyzoides. (abstract). Phytochemistry 1986; 25(11):2625.

3. Borthakor N, Baruah AKS. Search for precocenes in *Ageratum conyzoides* Linn. Of North-East India. J Indian Chem Soc 1987; (64):580-581.

4. Soll AH. Pathogenesis of Peptic Ulcer and Implications from Therapy. N Engl J Med 1990; (322):909-916.

5. Chan FKL, Leung WK. Peptic Ulcer Disease. Lancet North Am Ed 2002; (360):933-941.

6. Subrahmanyam M. Topical application of honey in the treatment of burns. Br J Surg 1991; 78:497-8.

7. Gharzouli K, Gharzouli A, Amira S, *et al*. Prevention of ethanol-induced gastric lesions in rats by natural honey and glucose-fructose-sucrose-maltose mixture. Pharmacol Res 1999; 2(39):151-56.

8. Zumla A, Lulat A. Honey: a remedy rediscovered (Editorial). J R Soc Med 1989; 82:384-385.

9. Halliwell B. Free radical, antioxidant and human disease: curiosity, cause or constipation? (abstract). Lancet 1994; 334:721.

10. Alarcon DLLC, Martin MJ, Lacasa C, *et al*. Antiulcerogenic activity of flavonoids and gastric protection. J Ethnopharmacol 1994; (42):161-70.

11. Parmar NS, Parmar S. The antiulcer potential of flavonoids (abstract). Indian J Physiol and Pharmacol 1998; 343-51.

12. Mandal S, Roy RK, Das HN, *et al*. Potentiation of gastric antiulcer effect of famotidine by calcium channel blockers in rats (abstract). Indian J of Physiol Pharmacol 1998; 30:390.

13. Achola KJ, Munenge RW. Activity of *Ageratum conyzoides* on isolated rat phrenic nerve diaphragm and blood pressure on anaesthetized rats (abstract). Int J Pharm 1997; 35:31.

14. Wiart C. Medicinal Plants of Southeast Asia. Kuala Lumpur: Pelanduk Publications; 2000.

15. Ali ATMM, Al-Swayeh OA. Natural honey prevents ethanol-induced increased vascular permeability changes in the rat stomach. J Ethnopharmacol 1997; (55):231-238.

LIFESTYLE PRACTICES AND PREVALENCE OF OBESITY IN A COMMUNITY WITHIN A UNIVERSITY CAMPUS

Moy FM and Atiya AS
Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur

ABSTRACT: Malaysia has undergone rapid pace of industrialization and urbanization in recent decades and this has brought about imminent changes in the lifestyle of Malaysians. This is a cross-sectional study which attempts to examine the lifestyle practices and the prevalence of obesity of a group of security guards and their spouses of the University of Malaya, Kuala Lumpur. Data collection was conducted by both the methods of face-to-face interview and self-administered questionnaire. The respondents were surveyed on lifestyle practices such as smoking habits, exercise and eating pattern. Anthropometric measurement such as weight and height were also taken to establish the extend of obesity by using Body Mass Index (BMI). This study reveals that the community did have some unhealthy lifestyle practices such as smoking (27.7%; 95%CI 20.2%, 36.2%), low prevalence of adequate exercise (13.8%; 95%CI 8.4%, 21.0%); high prevalence of overweight and obesity (64%; 95%CI 55.1%, 72.3%); and high prevalence of co-morbidities such as diabetes mellitus and cardiovascular diseases. In conclusion, the community is considered to be a vulnerable and high-risk group for morbidity and mortality with the above predisposed risk factors. *(JUMMEC 2003-2005; 8: 33-38)*

KEYWORDS: Lifestyle practices, overweight and obesity

Introduction

Malaysia has undergone a rapid pace of industrialization and urbanization in recent decades and this has brought in changes in the lifestyles of Malaysians. These changes include reduction of physical activities, changes in dietary habits and food preferences which are more prone to high fat and high calorie diet (1). This has resulted in changes of nutritional status among the people in both the urban and rural dwellings where there is an increase of prevalence of overweight and obesity.

The Second National Health and Morbidity Survey (NHMS-II) in 1996 demonstrated an overall national prevalence (among population > 18 years of age) of overweight (BMI > 25 kg/m^2) of 16.6% and obesity (BMI > 30 kg/m^2) 4.4% (2). In urban areas, it was revealed that 29% males were overweight and 5% obese while 26% of females were overweight and 8% obese (3). As compared to another study conducted on urban executives in 1988, the prevalence of overweight and obesity was 28.7% and 2.7% respectively (4).

Overweight and obesity has resulted in the increase risks of premature death as well as increase morbidities such as diabetes mellitus, hypertension, hyperlipidaemia, atherosclerosis, coronary heart disease, gout, gall bladder disease, respiratory diseases, arthritis and certain types of cancer (5-6). The objectives of this survey were to study the lifestyle practices and the prevalence of overweight/obesity of the community. This paper reports the findings of the community of Kampung Awal, which is located in the University of Malaya campus.

Methods

Description of study area and study population

Kampung Awal is a residential area built by the management of the University of Malaya for the security staff in the 70s. It is located in the main campus of the University of Malaya, close to the Faculty of Medicine. The purpose of having them staying in was for the security of the campus as well as convenience for the guards who have to work round the clock (shift work). There are 100 units of houses in this residential area with 102 staff and 96 spouses

Correspondence:
Moy Foong Ming
Department of Social and Preventive Medicine
Faculty of Medicine, University of Malaya
50603 Kuala Lumpur

staying in. The study population included was mainly the heads of households and their spouses who were aged 18 to 58 years old. House to house visits were conducted and only those who were available during the home visits at the above mentioned period were surveyed. The total study population who responded was 136 respondents with 84 males and 52 females which made up a response rate of 68.7%. The majority of males who did not respond were security guards with secondary education, while the female non-respondents were mainly working away from their houses and therefore unavailable during our home visits.

Questionnaire

Socio-demographic data, medical history and some lifestyle practices (including the habits of exercise, smoking, pattern of eating out, etc.) of the respondents were collected through a set of questionnaire which was pre-tested and modified before the study was implemented. Approval was obtained from the relevant authorities and informed consent was obtained from the respondents. All information was collected either by face-to-face interviews (58.8%) or self-administered (41.2%) questionnaire. The filled questionnaires were checked with the respondents to clarify the unfilled questions or confused answers.

Anthropometric measurement

Anthropometric measurements including measurement of body weight and height of the respondents were taken. Respondents' weight was taken with bathroom weighing scale (spring balance scale). The weighing scale was calibrated regularly to ensure accuracy. Measurement was taken to the nearest 0.1 kg. Two readings were taken for each respondent and the average weight was recorded.

Height of the respondent was taken by using a modified tape measure, Microtoise, which measured up to two metres. A direct reading of height to the nearest millimeter was obtained. Two readings were taken for each respondent and the average height was recorded.

Body Mass Index (BMI)

Body Mass Index (BMI) which is a weight (kg) to height^2 (m^2) ratio was derived. Classification of BMI following the WHO (7) criteria is used.

Data analysis

All the variables listed in the questionnaire form was coded and entered into SPSS for Windows version 9.0. Appropriate statistical analyses were performed on the testable hypotheses using the same software. Students' t-test was conducted on continuous data while χ^2 test was conducted on categorical data. Significant level was preset at p = 0.05. Confidence interval at 95% was also included wherever appropriate.

Results

Demography data

Out of the 136 respondents, 95.5% (n=130) were Malays and the remainder Indians. All respondents were included in the description of socio-demography data but for the analysis of lifestyle practices and anthropometric measurement, the Indians were excluded due to their small number. Another two female respondents who were pregnant were excluded too. Therefore, the total number of respondents analysed for anthropometric measurement was 128.

Table 1 shows some of the socio-demographic data of the study population. There were 60.3% of males and 39.7% females. The mean age of the population was 43.4 (sd = 7.5 years). Majority of them were married, working as security guards and had secondary education.

Family history and prevalence of chronic diseases

Twenty-three per cent (n=32) of the study population had family history for diabetes mellitus and 47.1% (n=64) for cardiovascular diseases which 36.0% (n=49) for hypertension and 11.0% (n=15) for heart disease (Figure 1). Family members who had the above diseases could be their parents or siblings.

Table 1. Socio-demographic data of the study population

Characteristics		*n* (%)
Gender	Male	82 (60.3)
	Female	54 (39.7)
Marital status	Married	133 (97.8)
	Single	3 (2.2)
Occupation	Security guard	84 (61.8)
	Housewife	41 (30.1)
	Unskilled worker	11 (8.1)
Education	No education	2 (1.5)
	Primary	39 (28.6)
	Secondary	93 (68.4)
	Unknown	2 (1.5)
Age (mean ± sd)	43.4 ± 7.5 (years)	

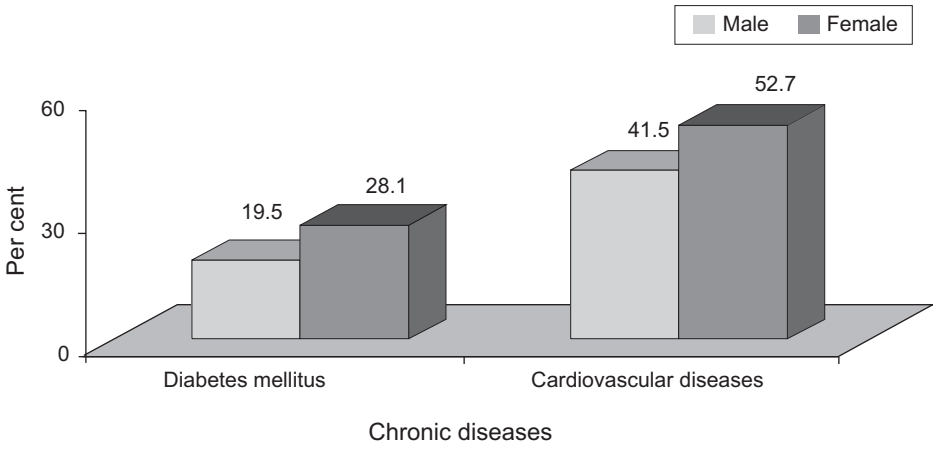

Figure 1. Family history of chronic diseases of the study population by gender

Prevalence rate of such diseases was also obtained from the study by means of self-reporting by the respondents. The prevalence rate of known diabetes among the study population was 13.2% (95%CI 7.8%, 20.1%), whereas for cardiovascular diseases was 29.5% (95%CI 21.6%, 37.8%) including hypertension and heart disease which were 22.1% (95%CI 15.5%, 30.4%) and 7.4% (95%CI 3.7%, 13.7%) respectively, and gout with a prevalence rate of 4.3% (95%CI 1.9%, 9.4%).

Figure 2 shows more information on the prevalence rate by gender. It could be observed that gout predominantly attacked the males in this study population. There was no statistical significant difference in the prevalence rates of diabetes mellitus (p = 0.845), hypertension (p = 0.585) and heart disease (p = 0.548) between the males and females.

Physical exercise

A person is considered to have ever exercise if he/she answered 'Yes' to the question whether he/she has ever carried out any type of exercise in the last two weeks. Exercise was considered to be adequate if he/she has performed one of the following 10 types of exercise: jogging, brisk walking, cycling, rope skipping, rowing, swimming, aerobics, team sports, racket sports and callisthenics sports (such as *Taichi*, *Silat*) for at least three times a week with each duration lasted 20 minutes or more (2).

Out of the total population (n=130), only 51 respondents (39.2%, 95%CI 30.8%, 48.2%) ever exercised. There are significantly more males (49.4%) taking part in exercise compared to females (24.5%) (p = 0.004).

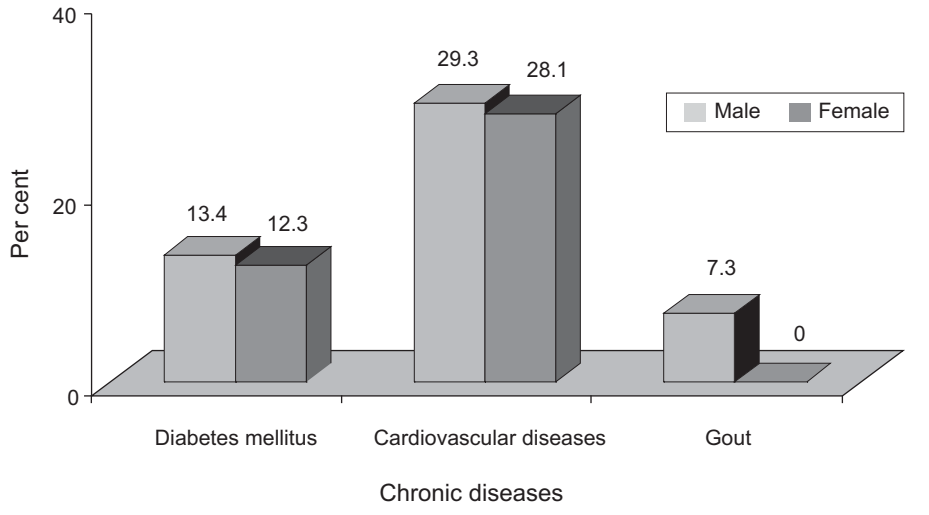

Figure 2. Prevalence rates of chronic diseases among the study population by gender

When the respondents were asked why they did not exercise, the most frequently cited reasons were busy (84.8%), not feeling well (7.6%) and others (dislike, unnecessary, etc.).

The three most common types of exercise carried out by the respondents (*n*=51) were jogging (34.6%), walking (19.2%), team sports (13.5%) and others (30.7%), which included racket games, weight lifting, cycling, exercise on machines, body movement and rope skipping. Team sports such as hockey, football were mainly participated by males. The frequencies of exercise among those who ever exercised were daily (17.3%), three times a week (34.6%), once a week (26.9%) and less than once a week (17.3%). The duration of each session was less than 20 minutes (29.4%, *n*=15), 20 to 60 minutes (47.1%, *n*=24) and more than an hour (19.6%, *n*=10) with 3.9% (*n*=2) unknown.

When the prevalence rate of adequate exercise was calculated, it was found that only 13.8% (*n*=18) (95%CI 8.4%, 21.0%) of the respondents exercised adequately. This gives a percentage of only 35.3% of those who ever exercised did it adequately.

Smoking habits among the study population

The prevalence rate of smoking among the study population was 27.7% (*n*=36) (95%CI 20.2%, 36.2%) with all smokers being males. The prevalence rate of smoking among the males (*n*=77) was 46.8%. The mean year of smoking was 18.4 (sd = 6.0 years). Most of the smokers (86.1%) had smoked from 10 to 29 years.

All of the smokers were smoking cigarettes. The mean number of cigarettes smoked a day was 15.3 (sd = 8.6). Among those who did not smoke currently (*n*=94), 13 (13.8%) of them had smoked before and all of them were males. The mean duration of smoking before cessation for these ex-smokers was 11.9 (sd = 9.1 years).

Eating pattern

Eating pattern of the study population was surveyed. The respondents were asked if they have the habits of eating out. It was found that 59 respondents (45.4%, 95%CI 36.6%, 54.3%) did have the habits of eating out with 47 males (61.0%) compared to 12 females (22.6%). The most frequently visited eating places were hawker stalls (44.3%) and cafeteria/canteen (39.3%) while fast food restaurants (9.8%) such as KFC, McDonalds were the favourite among the younger couples with younger children. Other places of eating out were restaurants (3.3%) and the remainder unknown.

Consumption of vegetables and fruits

This study shows that 118 of the respondents (90.8%, 95%CI 84.4%, 95.1%) took vegetables daily. Those who did not consume vegetables regularly gave reasons such as dislike, unnecessary, etc.

The consumption of fruits among the study population was lower where only 96 of the respondents (73.8%, 95%CI 65.4%, 81.2%) consumed fruits daily. There were significantly more males (84.4%) who consumed fruits daily compared to females (58.5%) ($p < 0.01$). Types of fruits consumed were mainly local fruits (37.1%) or imported fruits (9.3%) or both (53.6%). Reasons for not consuming fruits daily were mainly unavailability (61.1%), dislike (16.7%), expensive (5.5%) and others unknown. More female respondents cited the reason of unavailability compared to males.

Anthropometric measurement

The mean weight and height of the respondents (*n*=128) were 68.9 (sd = 11.9 kg) and 161.1 (sd = 8.5 cm) respectively. For the mean weight and height of the males and females, the results were as shown in Table 2. The males were statistical significantly heavier and taller than the females ($p < 0.01$).

Table 2. Anthropometric indicators of the study population by gender

Anthropometric Indicators	Total Population (*n*=128) $\bar{x}$ ± sd	Males (*n*=77) $\bar{x}$ ± sd	Females (*n*=51) $\bar{x}$ ± sd
Weight (kg)	68.9 ± 11.9	72.6 ± 10.5	63.2 ± 11.8
Height (kg)	161.1 ± 8.5	166.5 ± 5.2*	152.9 ± 5.4
BMI (kg/m^2)	26.5 ± 4.0	26.2 ± 3.4*	27.0 ± 4.8

** $p < 0.05$ within gender*

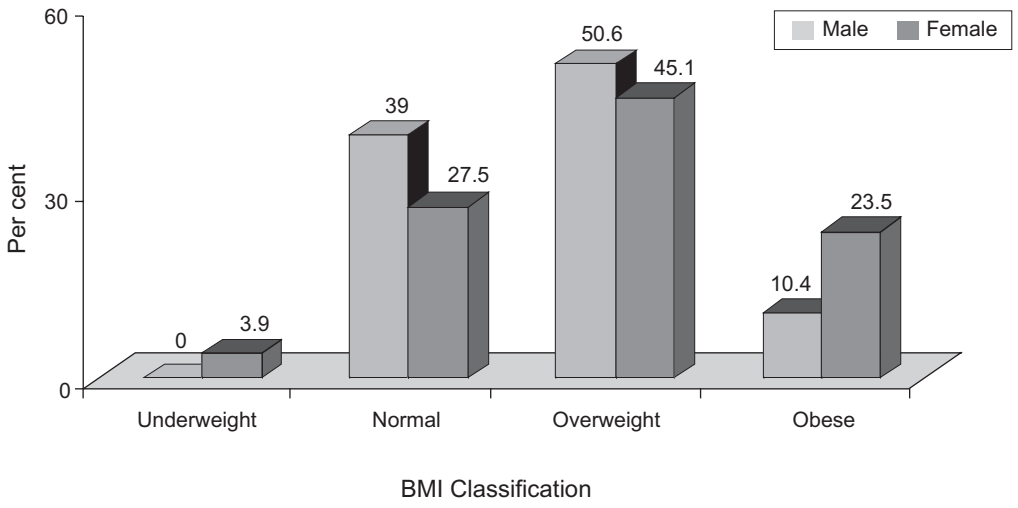

Figure 3. Classification of subjects into BMI categories by gender

The mean BMI of the population was 26.5 (sd = 4.0 kg/m^2) with males' and females' BMI being 26.2 (sd = 3.4 kg/m^2) and 27.0 (sd = 4.8 kg/m^2) respectively (Table 2). The difference of BMI among gender was not statistically significant (p = 0.246). Figure 3 shows the BMI of the respondents in categories of underweight, normal, overweight and obese following WHO *(7)* criteria by gender.

From Figure 3, it could be observed that only 34.4% of the study population was of normal weight with more males (39.0%) than females (27.5%). While 64% (95%CI 55.1%, 72.3%) of the study population were overweight (BMI > 25.0 kg/m^2). However, there were 15.6 per cent (95%CI 9.8%, 23.1%) of the population in the obese category (BMI > 30 kg/m^2). For the overweight group, the proportion of males and females were about the same (50.6% and 45.1% respectively). But for the obese group, there were 10.4% males compared to 23.5% females. There was only 1.6% of the study population underweight who were primarily females.

Discussion and Conclusions

The results show that majority of this study population is overweight with increased risk of co-morbidity and having higher prevalence of chronic diseases such as diabetes mellitus and cardiovascular diseases as compared to the national figures (2).

When the respondents were classified into categories of underweight, normal, overweight and obese following the WHO criteria (7), it was found that over 60% of the respondents were either overweight or obese. Compared to the NHMS-II (2) data for both the prevalence of overweight/obesity for all races or only Malay population only, the prevalence of this study population is very much higher. This could be attributed to their older age compared to the NHMS-II since it is noted that overweight and obesity tend to increase with age (8-9).

Although the difference of BMI among gender was not statistically significant, but the proportion of overweight males (50.6%) were higher compared to females (45.1%) while the proportion of obese females (23.5%) were higher than males (10.4%). These findings are comparable to the study of (3) in urban areas and the Singapore National Health Survey (9) conducted in 1998 where both studies had more overweight males and more obese females. Obesity in females was found to be rising after marriage and with parity (8).

Although the prevalence rates of ever exercise and adequate exercise of this study population were higher than the national figures (2), but it still is considered low since there are about 60% of the respondents who did not exercise at all. This sedentary lifestyle will lead to increase in body weight as well as higher risk of chronic non-communicable diseases. Therefore, it is important to motivate the respondents to adopt healthy lifestyle in particularly in exercise.

Among the ethnic groups in the NHMS-II (2), Malays had higher prevalence of smoking (27.9%) compared to Chinese (19.2%) and Indians (16.2%). This study population which predominantly was from the Malay ethnicity had a current smoking prevalence (27.7%) which is close to the national figure (2).

Cigarette smoking is a major risk factor for hypertension, heart disease, stroke, cancer and chronic obstructive lung disease (10) and has been identified as the single most avoidable cause of death in countries such as United Kingdom (11) and the United States (10). The WHO estimates that annual tobacco attributable death will reach 8.4 million in 2020 and 10 million in 2030 (10). In view of the adverse consequences of cigarette smoking, health intervention needs to be initiated for this community to quit smoking.

Dietary habits such as consumption of fibre (contributed by vegetables and fruits) as well as pattern of eating out are also surveyed in this community. It could be observed that the habit of consuming vegetables regularly was being practiced by most of the respondents. However, the adequacy of fibre intake in this community is not available due to the inaccessibility of quantitative data. Respondents who used to eat out need to be advised on healthier food choices which are lower in calorie, fat, sugar and salt. Those who frequented the fast food outlets also need to be advised to reduce or stop this eating habit since fast food has high calorie, high fat and high sodium contents.

No significant association was found among the status of obesity (BMI) with the above mentioned variables such as gender, education, exercise, medical history such as diabetes mellitus and heart diseases, cigarette smoking, pattern of eating out, consumption pattern of vegetable and fruits. This could be due to the small sample size of the study population. More thorough investigation needs to be carried out to verify these findings.

The non-respondents who might be the less healthy and less motivated to practise healthy lifestyle could also serve as a confounding factor in the analysis.

In conclusion, this study finds that the community of Kampung Awal practises unhealthy lifestyle such as smoking, low prevalence of exercise; had high prevalence of diabetes mellitus and cardiovascular diseases and high prevalence of overweight/obesity. On the other hand, the habits of consuming vegetables and fruits are still being practised. Nevertheless, the unhealthy lifestyle practices and the obesity status are indicative of their vulnerability for chronic diseases such as diabetes mellitus, hypertension and cardiovascular diseases. Health promotion and health education targeted to increase awareness on healthy lifestyles should be specially planned for them.

Acknowledgements

The authors express their most sincere gratitude to the Department of Social and Preventive of Medicine, the Registrar of the Human Resource and the Director of the Security Office of University of Malaya; the Penghulu and all the residents of Kampung Awal in giving their support in the conduct of the survey. Our gratitude also goes to Encik Mohd Shukri for his assistance in the field and all those who helped in the survey.

References

1. Tee ES. Obesity in Asia: prevalence and issues in assessment methodologies. Asia Pac J Clin Nutr 2002; 11(3):S694-S701.
2. Report of the Second National Health and Morbidity Survey (NHMS-II). Ministry of Health Kuala Lumpur, 1997.
3. Ismail MN, Zawiah H, Chee SS, *et al*. Prevalence and obesity and chronic energy deficiency (CED) in adult Malaysians. Malays J Nutr 1995; 1:1-9.
4. Teo PH, Chong YH, Zaini AR. Coronary risk factors among Malaysian male executives in two urban areas. Med J Malaysia 1988; 43:125-133.
5. Pi-Sunyer FX. Medical hazards of obesity. Ann Intern Med 1993; 119:655-660.
6. American Obesity Association. 2000. Justification for obesity as a leading health indicator. Internet communication at http://www.obesity.org/AOA_HP2010.html (accessed on 10.6.00).
7. WHO. *Obesity: preventing and managing the global epidemic*. Report of a WHO consultation on Obesity. Geneva: World Health Organisation. 1997.
8. McNulty SJ, Williams G. Obesity: an overview. 2000. Internet communication at http://www.rcpe.ac.uk/public/volume29_3a.html (accessed on 15.12.00).
9. Singapore National Health Survey. 1998. Internet communication at http://www.gov.sg/moh/health_survey/NHSODF.htm (accessed on 14th June 2000).
10. WHO 2001. Tobacco Free Initiative. Health Impact. Internet communication at http://tobacco.who.int/en/health/index.html (accessed on the 22.2.01).
11. Erens B, Primatesta P. (eds) Risk factors for cardiac diseases: cigarette smoking. In: *Health Survey for England: Cardiovascular Disease 98, Volume 2*. 1999; London: The Stationary Office.

TERM BREECH TRIAL AND ITS CONSEQUENCES ON PRACTICE: A RETROSPECTIVE STUDY OF THE UNIVERSITY OF MALAYA MEDICAL CENTRE'S EXPERIENCE

Noor Azmi MA and Aniza A
Department of Obstetrics & Gynaecology, University of Malaya Medical Centre, 50603 Kuala Lumpur

ABSTRACT: To see the trend in managing singleton breech pregnancy after the term breech trial. Secondly to compare the safety of different modes of delivery for term, singleton breeches by looking at the immediate neonatal outcome, based on our own experience. Breech infants were identified by examining computer-stored maternal discharge records of hospitalization for the years 1990 and 2000 respectively. Parameters studied included planned mode of delivery, actual mode of delivery, parity, previous vaginal delivery, Apgar score at five minute, birth weight, referral to special care nursery and neonatal morbidity. Of 6,496 deliveries in 1990 and 5,081 in 2000, there were 220 (3.4%) and 148 (2.9%) term breech infants respectively, of which 115 (for 1990) and 102 (for 2000) case records were available. In 1990, 62.6% of the women had trial of vaginal breech delivery but only 24.5% of the women in 2000 were allowed to do so ($p < 0.05$). Caesarean section rate for singleton breeches increased from 51.3% in 1990 to 84.3% in 2000 ($p < 0.05$). Mean Apgar score at five minutes was significantly lower after vaginal breech delivery (9.40 ± 1.36) compared to after Caesarean section (9.72 ± 0.712) but there was no clinical significance. There was a noticeable trend towards Caesarean section and less trial of vaginal delivery. Neonatal outcomes of babies born abdominally were statistically better than those born vaginally but there was little clinical impact. Perhaps in properly selected cases, a planned vaginal breech delivery still has a role to play. *(JUMMEC 2003-2005; 8: 39-44)*

KEYWORDS: Breech deliveries, Caesarean section, Apgar score

Introduction

Incidence of breech presentation is inversely related to the gestational age (that is, the relative of liquor volume to fetal size) at birth (1), where it occurs in 40% of babies at 26 weeks gestation, in 20% at 30 weeks and 3% to 4% at term.

The mode of the delivery in term singleton breeches has always been a controversial issue in the obstetric literature (2-4). Assisted vaginal delivery continues to be one of the challenging problems in obstetrics because of its association with high perinatal mortality and morbidity after excluding congenital malformation. In the past, if there were no contraindications, most women with breech presentation were allowed to undergo labour and deliver vaginally (5). This allows the doctor to perfect their techniques and enhance confidence. Caesarean section was reserved only for the primigravida or the multiparous patients with footling breech or evidence of poor progress or fetal distress. Nowadays, after the published randomized trial in the Lancet (6), Caesarean section has become the delivery route of choice for most women with a breech presentation, regardless of parity and estimated fetal size. This will definitely increase the Caesarean section rate and cost to the already tight health budget of any government.

Although the results of the trial and a few others (7-8) were supportive of elective Caesarean delivery, experience tells us that in properly selected cases and in experienced hands, assisted breech deliveries are

Correspondence:
Dr Noor Azmi Mat Adenan
Lecturer
Department of Obstetrics and Gynaecology
University of Malaya
50603 Kuala Lumpur
Email: azmiadenan@yahoo.co.uk

reasonably safe (9-11). If all cases are delivered abdominally, soon the skills of vaginal delivery will be lost and will join the fate of the rotational forceps. This may lead to disaster when the doctor is called for an inevitable assisted breech delivery or a delay in delivery of a breech second twin (12).

This study was conducted to demonstrate the safety or hazards of assisted breech delivery by looking at the differences in the immediate neonatal outcomes such as 5-minute Apgar scores and referral to special care nursery (SCN).

Methods

This was a retrospective cohort study. The cases were identified by searching through the computer-stored maternal discharge records of hospitalisation in the Department of Obstetrics and Gynaecology, University of Malaya Medical Centre (UMMC), using search terms such as assisted breech delivery, vaginal breech delivery and Caesarean section for breech. The search was confined from the 1st January to 31st December 1990 and 1st January to 31st December 2000. Preterm deliveries (< 37 completed weeks), infants with congenital anomalies, intrauterine fetal death and those of multiple pregnancies were excluded.

Of 6,496 deliveries in 1990 and 5,081 in 2000, there were 220 (3.4%) and 148 (2.9%) presented by the breech respectively. After excluding twins, infants with congenital anomalies, intrauterine fetal death and undetected case records, a total of 217 original case records (115 for year 1990 and 102 for year 2000) were available for analysis. The parameters included were the demographic data of the mothers, the intended mode of delivery, the actual mode of delivery (assisted vaginal delivery, elective Caesarean section and emergency Caesarean section), Apgar scores at one and five minutes, parity, previous vaginal delivery, birth weight, referral to SCN and neonatal morbidity.

Intended and actual modes of delivery were compared according to year of admission (1990 and 2000). Primary outcome measures were Apgar scores less than seven at five minutes, referral to SCN, and any neonatal morbidity. The analysis of outcome was done according to actual mode of delivery.

Data entry and analysis were done using SPSS version 8.0. For statistical analysis, the chi square test was used for binominal variables if all expected numbers exceed five, and Fisher's exact test if any expected number was five or less. For continuous variables, student t-test was used if the variables were normally distributed variables.

Results

The study group comprised 217 women who delivered singleton term breech infants. There were 115 respondents in 1990 and 102 in 2000. More than half (129, 59.4%) of the subjects were Malays, followed by Chinese, Indian and others (Figure 1). This racial distribution is proportional to the group of population that this centre is serving. Most of the subjects were in the age group of 26 to 30. The mean (± sd) age was 28.77 ± 4.98 years.

Table 1. Intended (planned) mode of delivery in study population for 1990 and 2000

Year of Admission	Trial of Vaginal Delivery	Caesarean Section (CS)	Total
1990	72 (62.6%)	43 (37.4%)	115
2000	25 (24.5%)	77 (75.5%)	102
Total	97 (44.7%)	120 (55.3%)	217

In the year 1990, 62.6% women underwent a trial of vaginal breech delivery compared to only 24.5% in the year 2000. The difference was statistically significant with the p value < 0.05 (p = 0.0001). As expected, the Caesarean sections (CS) were more frequently performed among the study population in the year 2000.

Of the total 97 women who underwent trial of vaginal delivery, 25 (25.8%) ended up having emergency Caesarean section. The success rate of vaginal breech delivery for 1990 and 2000 were 77.8% and 64.0% respectively. However, the difference was not statistically significant. The result is presented in Table 2.

Table 2. Success rate of vaginal breech delivery for 1990 and 2000

Year	Trial of Vaginal Delivery	Successful (%)	Unsuccessful (Emergency CS)
1990	72	56 (77.8%)	16
2000	25	16 (64.0%)	9
Total	97	72 (74.2%)	25

Table 3. Actual mode of delivery in study population for 1990 and 2000

Year of Admission	Vaginal Delivery	Elective CS	Emergency CS	Total
1990	56 (48.7%)	43 (37.4%)	16 (13.9%)	115
2000	16 (15.7%)	77 (75.5.%)	9 (8.8%)	102
Total	72 (33.2%)	120 (40.6%)	25 (11.5%)	217

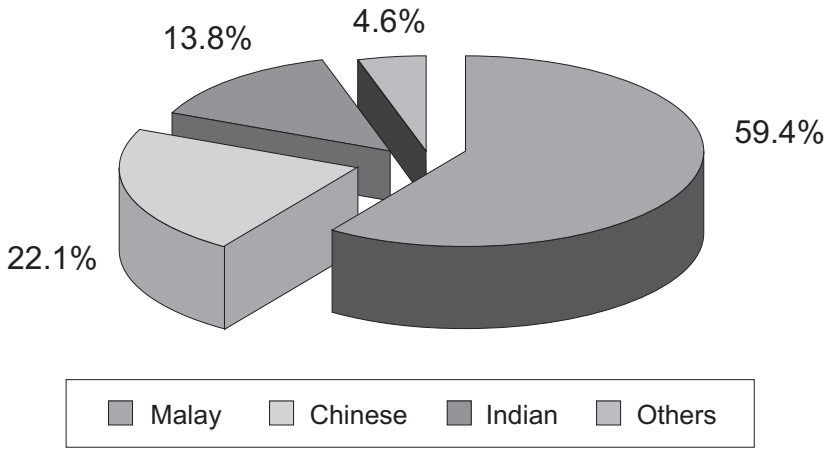

Figure 1. Racial distribution of the study population

A cross tabulation between the actual mode of delivery and those women who had previous vaginal delivery to see whether there is any relationship in these two variables (Table 4).

Table 4. Association between mode of delivery and previous vaginal delivery in the study population

	Mode of Delivery			
Previous Vaginal Delivery	Vaginal Breech	Elective CS	Emergency CS	Total
Yes	44 (61.1%)	47 (39.2%)	6 (24.0%)	97 (44.7%)
No	28 (38.9%)	73 (60.8%)	19 (76.0%)	120 (55.3%)
Total	72 (100%)	120 (100%)	25 (100%)	217 (100%)

A higher percentage of women (61.1%) was noted in vaginal delivery group who had previous vaginal delivery compared to only 39% and 24% in elective and emergency Caesarean section groups respectively. The difference was statistically significant at *p* value of 0.001). This means that there was an association between previous vaginal delivery and mode of delivery.

Regarding the birth weight of the infants in this study, most of them weighed between 2.6 kg and 3.5 kg. The mean (± sd) birth weight in 1990 was 3.017 kg ± 0.477, while in 2000, the mean was 2.975 kg ± 0.384.

Birth weight by mode of delivery is shown in Figure 2. Most of the infants who weighed between 2.6-3.5 kg were delivered abdominally. In the less than 2.5 kg, more babies were born vaginally. There were only two infants whose birth weight was more than four kg and both were delivered by emergency Caesarean section due to spontaneous rupture of membrane in one case and the other one was due to meconium stained liquor. Infants delivered by Caesarean section (elective and emergency) were slightly heavier than those in vaginal group. The mean (± sd) birth weight for Caesarean group was 3.054 kg ± 0.395 and for vaginal breech group was 2.927 kg ± 0.47. However, the difference between these two groups was not statistically significant (p = 0.178).

Table 5 shows the immediate neonatal outcomes, which were Apgar scores at five minutes and referral to special care nursery (SCN) according to mode of delivery.

For both outcomes, vaginal delivery had higher rates of adverse outcomes in comparison with Caesarean group.

Out of 217 respondents, only six (2.8%) infants got Apgar scores of less than seven at five minutes. All of them were born in 1990 with four infants delivered by assisted vaginal breech delivery. The vaginal breech group (n=72) had a lower mean Apgar scores at five minutes with 9.40 ± 1.36 compared to those in the Caesarean group (9.72 ± 0.712). Although the difference was significant statistically (p = 0.0001), but in clinical practice the scores were quite similar. Another interesting observation was the fact that of the 25 babies intended for vaginal delivery but failed and delivered abdominally, none recorded Apgar score less than seven at five minutes or admission to the SCN.

For both years, a total of 14 infants were referred to SCN for further evaluation and close monitoring.

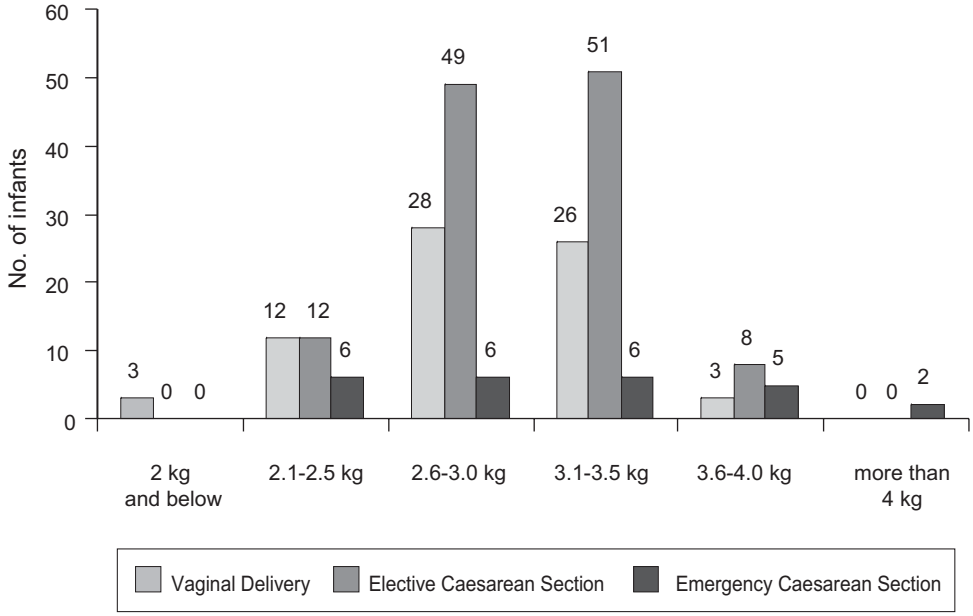

Figure 2. Birth weight by mode of delivery

Table 5. Immediate neonatal outcome according to mode of delivery

Immediate Neonatal Outcome	1990 Vaginal Delivery (%)	1990 Elective Caesarean Section (%)	1990 Emergency Caesarean Section (%)	2000 Vaginal Delivery (%)	2000 Elective Caesarean Section (%)	2000 Emergency Caesarean Section (%)
Apgar score (5 min)						
< 7	4 (7.1)	2 (4.7)	–	–	–	–
≥ 7	52 (92.9)	41 (95.3)	16 (100)	16 (000)	77 (100)	9 (100)
Referral to SCN						
Yes	7 (12.5)	5 (11.6)	–	–	2 (2.6)	–
No	49 (87.5)	38 (88.4)	16 (100)	16 (100)	759 (7.4)	9 (100)

Seven of them were delivered vaginally and another seven by Caesarean section (Table 5). Two infants were transferred due to low birth weight, two because of chorioamniotis in mothers and one due to suspected herpes zoster infection contracted from the mother. Another 11 infants did not have obvious reasons for referral stated in their mothers' case notes. However, there was no death of any of the infants.

Discussion

A change with a tendency towards Caesarean section in the delivery for term breech presentation between years 1990 and 2000 was noted. This finding was consistent with a study conducted by staff of National Hospital, University of Oslo (13) where the Caesarean section rate increased from 8.1% in 1972-75 periods to 32.6% in 1976-79. The same tendency has been observed in many countries, often with an even higher Caesarean section rate.

Caesarean section is not free of its share of morbidity and mortality (14-15). The risks are more in the developing countries and even higher in any remote hospital. We all know that in these settings, juniors and overworked staff usually perform the operative procedure. Of course, Caesarean section is indicated if labour is protracted, breech baby is high, there is poor cervical dilatation or when there is insufficient descent of the breech in spite of adequate uterine contractions and cervical dilatation. Of course, in the

presence of additional risk factors such as diabetes mellitus, intrauterine growth retardation and pathological CTG, an elective Caesarean section should be appropriately considered as a safer option (15-17).

Many obstetricians consider previous vaginal parity as an important factor for selection of parturient to deliver vaginally (4-5). In a large retrospective study of more than 10,000 singleton breech deliveries of normal infants in 86 hospitals, the benefit of Caesarean section was significantly greater for primiparae than multiparae (18). Nevertheless, two studies of 159 and 580 singleton breech deliveries did not find any significant difference in neonatal mortality (13), or pH in the umbilical cord vein between primiparae and multiparae (19).

The selection of parturients for vaginal breech delivery or Caesarean section is also governed by the estimated fetal birth weight. This was evident as more infants with the birth weight of 2.5 kg or less were delivered by assisted breech delivery. Nevertheless, estimation of birth weight by clinical palpation of the gravid uterus or by ultrasound had been shown to be inaccurate (20). Therefore, correct assessment on the progress of labour and timely intervention in deciding on continuation or stopping any trial of vaginal breech delivery cannot be overlooked (16).

In this study and in some others (9-11), the immediate neonatal outcomes (Apgar score) between those infants delivered by vaginal breech delivery and by Caesarean section were statistically significant but with little impact clinically. Only a small number of breeches recorded low Apgar score at five minutes and four out of six were delivered vaginally. This was not the finding of others that found otherwise (8,13). However, it has been shown that in properly selected cases, slightly more than 70% of cases can be delivered vaginally with very little morbidity (21).

Interestingly, those cases that went into labour spontaneously but failed in their trial of vaginal delivery and had Caesarean section, all recorded good Apgar score. If induction and augmentation of breech is not a practice and early recourse to Caesarean if progress is poor, a fail trial is still safe for the baby.

Whether external cephalic version was offered to each of these parturient was not the main objective of this study. Ideally, external cephalic version should be offered or attempted in selected cases as this was shown to reduce the non cephalic presentation at term (22). In the era of increasing litigation, proper and comprehensive counselling is a must and the wishes of the mothers must be respected. The attending doctor or midwife must be well versed in breech delivery and this ability can then be applied to delivery of the breech second twin without having to resort to unnecessary Caesarean section which usually will delay delivery (23), and be potentially harmful to the baby (12) and the mother. Avoiding unnecessary Caesarean delivery also helps to reduce the potential iatrogenic induced cases of respiratory morbidity in newborns of elective Caesarean cases, which would normally be planned at 38 weeks gestation (24-25).

Sometimes we are so much into patients' rights and allow them to make the decision after a thorough counselling. There is also a move nowadays towards an elective Caesarean for a normally presented fetus at term for those who are too posh to push and some obstetricians are condoning this (26). Many a time, we have discussed cases of delayed Caesarean for poor progress with non-assuring CTG running into hours, all for the sake of reducing the Caesarean rates, with bad outcome on the fetuses. Why don't we give those who had vaginal delivery before with an appropriate fetal size and wish to deliver their child vaginally, their rights to choose? Anyway, we still monitor closely all delivering mothers and make appropriate intervention if necessary. Only then can we talk about how to reduce our relatively high Caesarean rate.

There were some limitations in this study and they were as follows:

1. small sample size (*n*=217),
2. this study was meant to analyze all the cases of breech in 1990 and 2000. However, due to missing records the results do not totally represent the whole number of breech deliveries in these years, and
3. since this was a retrospective study, some information like external version offering were not clearly stated or some were not completed.

Conclusion

In conclusion, there was a trend towards Caesarean section in delivering singleton term breech with fewer women allowed to undergo trial of labour in 2000 compared to those in 1990. A low five minute Apgar score occurred at a slightly higher rate after vaginal breech delivery than after Caesarean section but without much clinical implication. External cephalic version should be offered to all suitable cases. Individualization of cases should be the appropriate approach and those with previous vaginal parity with no obvious contraindication, should be given the options to deliver vaginally if they wish. Further study to examine the latest trend in the past three or four years will show the true impact of The Term Breech Trial in our practice.

Acknowledgement

I wish to express my thanks to my student for extracting and compiling the data. My gratitude also to the staff of the Department of Obstetrics and Gynaecology and Medical Record Unit, the University of Malaya Medical Centre, Kuala Lumpur for their kind co-operation during this study.

References

1. Weisman AI. An antepartum study of fetal polarity and rotation. Am J Obstet Gynecol 1944; 448:550-52.
2. Thorpe Beeston JG, Banfield PJ, Saunders NJ. Outcome of breech delivery at term. Br Med J 1992; 305:746-47.
3. Arulkumaran. Acta Obstet Gynecol Scand Suppl, 76 Supplement No. 167, August 1997:5. Ovid Abstract.
4. Roumen FJ, Luyben AG. Safety of term vaginal breech delivery. Eur J Obstet Gynecol Reprod Biol. 1991 Jul 25; 40(3):171-7.
5. Ghosh MK. Breech presentation: evolution of management. J Reprod Med. 2005 Feb; 50(2):108-16. (abstract).
6. Hannah ME, Hannah WJ, Hewson SA, *et al*. Planned Caesarean section versus planned vaginal birth for breech presentation at term: A randomized multicentre trial. Lancet 2000; 356:1375-83.
7. Pradhan P, Mohajer M, Deshpande S. Outcome of term breech births: 10-year experience at a district general hospital. Br J Obstet Gynecol. 2005 Feb; 112(2):281-22.
8. Rietberg CC, Elferink-Stinkens PM, Brand R, Van Loon AJ, Van Hemel OJ, Visser GH. Term breech presentation in the Netherlands from 1995 to 1999: mortality and morbidity in relation to mode of delivery of 33,824 infants. Br J Obstet Gynecol. 2003 Jun; 110(6):604-9.
9. Doyle NM, Riggs JW, Ramin SM, Sosa MA, Gilstrap LC. Outcome of term vaginal breech delivery. Am J Perimatol. 2005 Aug; 22(6):325-8.
10. Orji EO, Ajenifuja KO. Planned vaginal delivery versus Caesarean section for breech presentation in Ile-Ife, Nigeria. East Afr Med J 2003 Nov; 80(11):89-91. Abstract.
11. Uotila J, Tuimala R, Kirkinen P. Good perinatal outcome in selective vaginal breech delivery at term. Acta Obstet Gynecol Scand. 2005 Jun; 84(6):578-83.
12. Roopnarinesingh AJ. Abdominal delivery of the second twin. J Obstet Gynecol. 2002 Jul; 22(4):379-80.
13. Pal O, Inge S, Einar H, Knut B. Breech delivery: An obstetrical analysis. Acta Obstet Gynecol Scand 1988; 67:75-79.
14. Henci Goer. The case against elective Caesarean section. J Perinat Neonatal Nurs. Gaithersburg: Dec 2001; 15(3):23-38.
15. Annapoorna V, Arulkumaran S. Controversies in the management of breech presentation. Singapore J Obstet Gynecol 1998; 29(1):5-9.
16. Songane FT, Himansugekhar M, Bingham P, *et al*. Balancing the risks of planned Caesarean section and trial of vaginal delivery for the mature, selected, singleton breech presentation. J Perinat Med 1987; 15:531-43.
17. Caesarean childbirth: Summary of a National Institute of Health consensus statement. Br Med J 1981; 282:1600-4.
18. Fortney JA, Higgins JE, Kennedy KI, *et al*. Delivery type and neonatal mortality among 10,749 breeches. Am J Public Health 1986; 76(8):980-85.
19. Luterkort M, Marsal K. Umbilical cord acid-base state and Apgar score in term breech neonates. Acta Obstet Gynecol Scand 1987; 66:57-60.
20. Nahum, Gerard G., Stanislaw, *et al*. Ultrasonic prediction of term birth weight: How accurate is it? Am J Obstet Gynecol. Feb 2003; 188(2):566-574.
21. Mohammed NB, Noor Ali R, Anandakumar C, *et al*. Management trend and safety of vaginal delivery for term breech fetuses in a tertiary care hospital of Karachi, Pakistan. J Perinat Med 2001; 29(3):250-9.
22. Hofmeyr GJ, Kulier R. External cephalic version for breech presentation at term. Cochrane Database Syst Rev 3, 2003.
23. Helmy WH, Jolaoso AS, Ifaturoti OO, *et al*. The decision-to-delivery interval for emergency Caesarean section, is 30 minutes a realistic target? Br J Obstet Gynecol 2002 May; 109(5):505-8.
24. Anomone DB, Ruurd M, Hernan P, *et al*. Neonatal respiratory morbidity following elective Caesarean section in term infants. A 5-year retrospective study and a review of the literature. Eur J Obstet Gynecol Reprod Biol. Sept 2001; 98(1):9-13.
25. Wax JR, Herson V, Carignan E, *et al*. Contribution of elective delivery to severe respiratory distress at term. Am J Perimatol 2002 Feb; 19(2): 81-6.
26. Cozias CS, Paterson-Brown S, Fisk NM. Obstetricians say yes to maternal request for elective Caesarean section: a survey of current opinion. Eur J Obstet Gynecol Reprod Biol. 2001 Jul; 97(1):15-6.

A PROSPECTIVE AUDIT OF DESFLURANE ANAESTHESIA IN THE UNIVERSITY OF MALAYA MEDICAL CENTRE DAY SURGERY UNIT

Chiu CL, Mansor M and Wang CY
Department of Anaesthesia, University of Malaya Medical Centre, 50603 Kuala Lumpur, Malaysia

ABSTRACT: We evaluated the use of Desflurane anaesthesia in this prospective observational audit in the University of Malaya Medical Centre Day Surgery Unit. Fifty ASA I-II unpremedicated day surgery patients received fentanyl and propofol induction after preoxygenation. Desflurane was introduced initially at 2% and the concentration was increased gradually to 4%, then 6%, 8% and 10% in nitrous oxide and oxygen. Patients breathed spontaneously throughout the surgery. Desflurane was switched off at the end of surgery and patients breathed 100% oxygen. The haemodynamic effect, perioperative complications and recovery profiles were recorded. Systolic arterial pressure and heart rate decreased after induction of anaesthesia but returned to baseline value at discharge. Adverse airway event such as coughing and postoperative nausea and vomiting are two unwanted complications. *(JUMMEC 2003-2005; 8: 45-49)*

KEYWORDS: Desflurane, day surgery, propofol induction

Introduction

The desire to contain the costs of anaesthesia and surgery, as well as the changes in surgical practice such as the adoption of minimally invasive technologies, have seen an evolution of anaesthetic practice in the past two decades. One result has been an increase in the numbers of outpatient surgical procedures. In support of this trend we have seen the development of drugs which permit greater, more precise control over the course of anaesthesia and more rapid recovery. For inhaled anaesthetics, Desflurane was developed as a result and has now become widely used in the developed country.

Day Surgery Unit in the University of Malaya Medical Centre was officially opened in June 2002. Desflurane was introduced to the unit a few months later. The aim of this communication is to report the haemodynamic effect, recovery profiles and perioperative complications of Desflurane anaesthesia in daycare patients in the University of Malaya in a prospective observational audit of 50 patients.

Methods

We audited prospectively 50 consecutive ASA physical status I-II patients who fulfilled our hospital's criteria for ambulatory surgery and who breathed spontaneously under Desflurane anaesthesia. Celebrax 200 mg or Vioxx 25 mg were given as premedication immediately after patients were seen by the anaesthetists. After cannulation of an appropriate vein, patients were preoxygenated for three minutes before induction of anaesthesia. Circle breathing system was used. Anaesthesia was induced with 1 mcg.kg^{-1} of fentanyl and 2-4 mg.kg^{-1} of propofol until loss of eyelash reflex. An oral airway or laryngeal mask airway or airway management device was inserted thereafter. Desflurane was introduced at 2% concentration together with 66% of nitrous oxide in oxygen and the total flow rate was 9 L.min^{-1}. The concentration was increased gradually to 4%, 6%, 8% and 10% every two breaths. Patients breathed spontaneously throughout the operation with 66% nitrous oxide and 6-10% of Desflurane in oxygen depending on the depth of the anaesthesia as evidence from clinical signs. The total flow rate was decreased to 1.5 L.min^{-1} after surgery started. Small boluses of fentanyl or propofol was

Correspondence:
Dr CL Chiu
Department of Anaesthesia
University of Malaya Medical Centre
50603 Kuala Lumpur
Malaysia.
Tel: 603-7950 2052
Fax: 603-7725 8439
Email: chiucl@um.edu.my

given to deepen the anaesthesia if necessary, during the operation, at the discretion of the anaesthetists. At the end of the surgery, Desflurane and nitrous oxide were both switched off at the same time. Patients breathed 10 L.min^{-1} of 100% oxygen. Airway devices were removed with the patient fully awake and obeying commands.

A specially designed audit form was used to collect relevant data. Age, sex, weight, ASA physical status, cardiorespiratory data, total fentanyl dosage, total propofol dosage and duration of Desflurane anaesthesia (from switching on the Desflurane vaporizer to turning it off at the end of surgery) were recorded. Baseline systolic arterial pressure (SAP) and baseline heart rate (HR) was recorded before the induction and at 1 min, 2 min, 5 min, 10 min and 15 min after induction, as well as at disharge to PACU II and at discharge home. The time of eye opening (from turning off the Desflurane to eye opening) and the time of obeying command (from turning off the Desflurane to obeying simple command such as sticking the tongue out), together with the time when patients were discharged to PACU II (*Appendix 1*: Criteria for discharge to PACU II) and discharged home (*Appendix 2*: Criteria for discharge home) were documented. Note was made of any problems that occurred before induction, at induction, during the maintenance period, on awakening, and in the recovery period postoperatively. Arterial desaturation and bradycardia requiring intervention were defined as a pulse oximetry saturation < 95% and heart rate of < 40 bpm, respectively.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) version 10.0 for Windows was used for statistical analysis. Paired Student t-test was used to analyze systolic arterial pressure and heart rate.

Results

Patient characteristics and recovery profiles were presented in Table 1. Haemodynamic data were presented in Figure 1. Systolic arterial pressure and heart rate at 1 min, 2 min, 5 min, 10 min and 15 min after induction of anaesthesia was significantly lower when compared to baseline value. However, at discharge, SAP returned to baseline value. Eight patients coughed shortly after the introduction of Desflurane at the beginning of an operation. A small bolus of propofol was given to rectify the problem and there was brief desaturation in one of these eight patients. One patient developed hypotension of about 30% when Desflurane was at 10% concentration but responded to intravenous crystalloid fluid therapy. At emergence a total of nine patients coughed, five of them were smokers and the other four were non-smokers. Six patients, one male and five females complained of postoperative nausea, which responded to metoclopramide 10 mg. Two patients required admission as an inpatient for surgical reason. There were no other complications documented.

Discussion

From this small audit we observed that Desflurane provides controllable anaesthesia, and it is haemodynamically similar to other commonly used inhalational anaesthetics.

The systolic arterial blood pressure decreased after the induction of anaesthesia and continued to be lower than the baseline value. This reduction in arterial blood pressure is in agreement with other studies and is similar to other commonly used inhaled anaesthetics (1-2).

Previous studies showed that heart rate is unchanged at lower steady state concentrations, but increases with higher concentrations (1-2). Studies also showed that when end tidal concentration is increased very rapidly to more than 1 MAC, in the absence of premedication, Desflurane increases heart rate (3-4). In our audit heart rate decreased after induction of anaesthesia and continued to be lower than baseline value by 15 mins. This is probably due to the prior administration of fentanyl (5-6).

Desflurane has two unwanted complications, postoperative nausea and vomiting and adverse airway events. Our incidence of nausea and vomiting in the

Table 1. Demographic data, duration of anaesthesia, fentanyl and propofol dosage

Parameters	$\bar{x}$ ± sd
Age; years	32 ± 12
Weight; kg	56 ± 12
Sex; M:F	9:41
ASA; I:II	48:2
Fentanyl; mcg	65 ± 17
Fentanyl per weight; mcg.kg^{-1}	1.2 ± 0.3
Propofol; mg	151 ± 40
Propofol per weight; mg.kg^{-1}	2.7 ± 0.6
Duration of Desflurane anaesthesia; min	20 ± 17

Table 2. Recovery profiles

Parameters	$\bar{x}$ ± sd
Eye opening; min	4.8 ± 2.3
Following command; min	5.6 ± 2.8
Discharge to PACU II; min	40 ± 17
Discharge home; min	109 ± 45

recovery room was 12%, which is lower than the 35% rate quoted by Ghouri *et al* (7). This may be because we used fentanyl-propofol as the induction agent whilst Ghouri used fentanyl-thiopentone as the induction agent. It has been shown that the incidence of vomiting is lower with propofol when compared to thiopentone. Twenty-four hours postoperative nausea and vomiting rate has been reported to be as high as 67% (8) and 52% (9). In this audit our patients were not followed up beyond discharge, this may also explain our relatively low incidence of postoperative nausea and vomiting.

Desflurane is an irritant agent and when it is used at high concentration during induction, adverse airway events can occur (9-12). Some studies have shown that even in early maintenance of anaesthesia, following intravenous induction, irritation of the upper airway is still a problem (13). Our audit agreed with this finding. 16% of the patients coughed shortly after introduction of Desflurane, following fentanyl and propofol induction. This incidence is slightly lower than reported by Wilkes *et al* (13). This may be because we did not increase the concentration beyond 10% whilst Wilkes *et al* used up to 12% of Desflurane in early maintenance phase. We were surprised to find that coughing occurred quite frequently at emergence although there was no incidence of laryngospasm and desaturation. Whether the incidence of coughing at emergence was higher with Desflurane anaesthesia compared with other inhaled anaesthetics is not known.

In conclusion, we showed that Desflurane may be a suitable agent for daycare anaesthesia in our population. However, more randomised controlled trial would be needed to evaluate its complications such as upper airway irritation and postoperative nausea and vomiting.

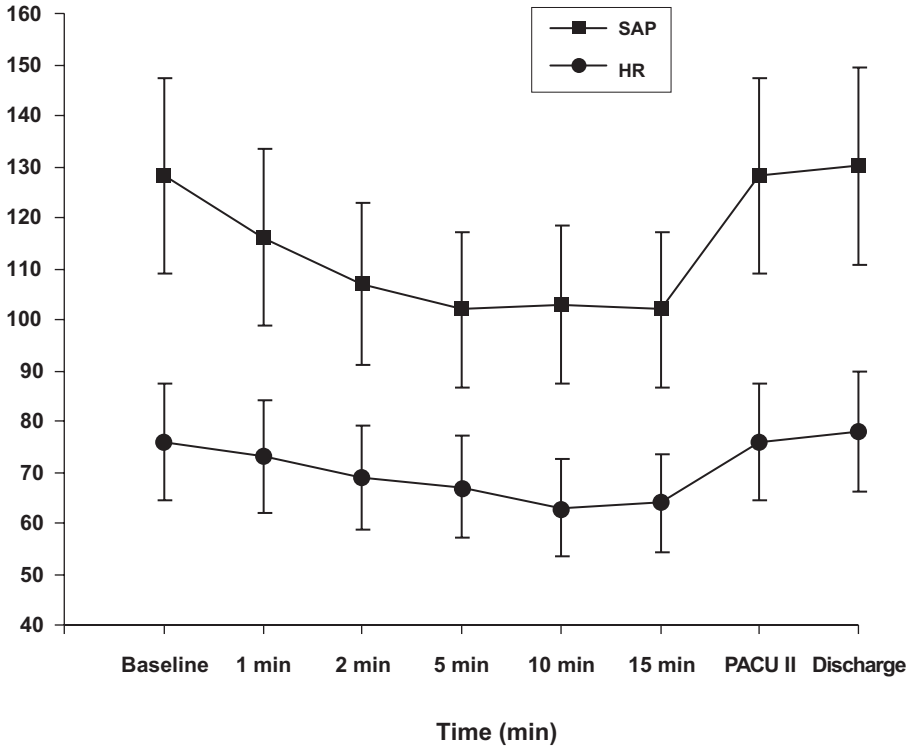

Figure 1. Systolic arterial pressure (SAP) and heart rate (HR) at different time intervals. Systemic arterial pressure is in mmHg and heart rate is in beats/minute.

Data presented are mean (sd). SAP at 1 min, 2 min, 5 min, 10 min and 15 min after induction were all significantly lower than baseline SAP (P < 0.001, by paired student t-test). Heart rate at 1 min, 2 min, 5 min, 10 min and 15 min after induction were all significantly lower than baseline heart rate (p < 0.005, by paired student t-test).

References

1. Weiskopf RB, Cahalan MK, Eger EI II, *et al*. Cardiovascular actions of Desflurane in normocarbic volunteers. Anesth Analg 1991; 73:143-156.
2. Cahalan MK, Weiskopf RB, Eger EI II, Yasuda N. Haemodynamic effects of Desflurane in normocarbic volunteers. Anesth Analg 1991; 73:157-164.
3. Moore MA, Weiskopf RB, Eger EI II, Noorani M *et al*. Rapid 1% increases of end tidal Desflurane concentrations above 5% transiently increase heart rate and blood pressure in humans. Anesthesiology 1994; 81: 94-98.
4. Ebert TJ, Muzi M. Sympathetic hyperactivity during Desflurane anaesthesia in healthy volunteers. A comparison with isoflurane. Anesthesiology 1993; 79: 444-53.
5. Weiskopf RB, Eger EI II, Noorani M, *et al*. Fentanyl, esmolol, and clonidine blunt the transient cardiovascular stimulation induced by Desflurane in humans. Anesthesiology 1994; 81:1350-1355.
6. Joshi GP, Warner DS, Twersky RS, *et al*. A comparison of the remifentanil and fentanyl adverse effect profile in a multicentre phase IV study. J Clin Anesth 2002; 14:494-499.
7. Ghouri AF, Bodner M, White PF. Recovery profile after desflurane-nitrous oxide versus isoflurane-nitrous oxide in outpatients. Anesthesiology 1991; 74:419-424.
8. Karlsen KL, Persson E, Wennberg E, *et al*. Anaesthesia, recovery and postoperative nausea and vomiting after breast surgery. A comparison between Desflurane, sevoflurane and isoflurane anaesthesia. Acta Anaesthesiol Scand 2000; 44:489-493.
9. Van Hemelrijck J, Smith I, White PF. Use of Desflurane for outpatient anaesthesia. A comparison with propofol and nitrous oxide. Anesthesiology 1991; 75:197-203.
10. TerRiet MF, DeSouza GJ, Jacobs JS, *et al*. Which is most pungent: Isoflurane or Desflurane? Br J Anaesth 2000; 85:305-307.
11. Bunting HE, Kelly MC, Milligan KR. Effect of nebulized lignocaine on airway irritation and haemodynamic changes during induction of anaesthesia with Desflurane. Br J Anaesth 1995; 75:631-633.
12. Kong CF, Chew ST, Ip-Yam PC. Intravenous opiods reduce airway irritation during induction of anaesthesia with Desflurane in adults. Br J Anaesth 2000; 85:364-367.
13. Wilkes AR, Hall JE, Wright E, *et al*. The effect of humidification and smoking habit on the incidence of adverse airway events during deepening of anaesthesia with Desflurane. Anaesthesia 2000; 55:685-689.

Appendix 1

Criteria for Discharge to PACU II

Ventilation/Respiration	**Score**
Spontaneous ventilation needs no support, respiratory rate is at least 10	2
Spontaneous ventilation – requires artificial airway – respiratory rate abnormally high or low – shallow or limited respiratory effort	1
Apnea – requires ventilation	0
Circulation	
BP ± 20% of preanaesthetic level	2
BP ± 20-50% of preanaesthetic level	1
BP ± 50% of preanaesthetic level	0
Consciousness	
Responding to verbal stimuli – may or may not initiate conversation, but answers questions appropriately (verbally or by nodding head). Eye open spontaneously. Carries out commands	2
Responding to tactile stimuli – actively responds to physical stimulation (e.g. Position change, BP monitoring) by movement and/or vocalization	1
No response – unresponsive to verbal or non-painful stimuli	0
Muscle strength	
Moves four extremities spontaneously and keeps head up	2
Moves two extremities spontaneously	1
Does not move extremities when painful, non-verbal stimuli applied	0
Colour	
Pink skin colour and mucous membrane	2
Pale dusky blotchy discoloration: jaundice discoloration	1
Cyanotic	0
Total score should be 8-10 on discharge	

Appendix 2

Post Anaesthetic Discharge Scoring System

Vital signs
2 = within 20% of preoperative baseline
1 = 20-40% of preoperative baseline
0 = 40% of preoperative baseline

Activity level
2 = steady gait, no dizziness, consistence
1 = requires assistance
0 = unable to ambulate/assess

Nausea and vomiting
2 = minimal: successfully treated with no medication
1 = moderate: successfully treated with IM medication
0 = severe: continuous after repeated treatment with preoperative level

Pain relief acceptable to patient
2 = yes
1 = no

Surgical bleeding
2 = minimum: does not require dressing change
1 = moderate: required up to two dressing changes with no further bleeding
0 = severe: require three or more dressing changes and continuous bleeding

Patients that score 9 or > are considered for discharge

CARPAL TUNNEL SYNDROME: BETWEEN CONSERVATIVE TREATMENT AND THOSE TREATED SURGICALLY AFTER FAILED CONSERVATIVE TREATMENT

Omar BMI
Department of Orthopaedic Surgery, University of Malaya Medical Centre, 50603 Kuala Lumpur, Malaysia

ABSTRACT: A retrospective study of 102 hands with carpal tunnel syndrome which were treated conservatively initially. Patients who were successfully treated with this method were then compared with those who had failed with this method and had to be treated with surgical decompression. This study found that it took a mean period of about 5.1 months of conservative treatment before deciding on surgery. Generally, the study shows a predominant involvement of the right hand and the female sex as full-time homemakers. Those who finally needed surgery had a longer duration of symptoms prior to consultation. Surgery brought a faster relief from both pain and numbness. It is recommended that conservative treatment be abandoned after a trial period of at least three to five months in order to encourage a speedier recovery. *(JUMMEC 2003-2005; 8: 50-55)*

KEYWORDS: Carpal tunnel syndrome, phalen, pinel, median nerve motor latency, median nerve sensory latency

Introduction

The carpal tunnel is narrowest 2.0 to 2.5 cm distal to its proximal margin (mean of 20 cm), widening both proximally and distally (mean of 2.5 cm) (1-2), which corresponds to the recognized greatest morphologic changes in cases of carpal tunnel syndrome (CTS) (3).

The volume of the carpal tunnel is not static and significant changes occur with flexion and extension as shown by the MRI. Some studies have shown that patients afflicted with CTS have smaller carpal canals than the normal population. This suggests that certain individuals have a hereditary predisposition on the development of CTS on the basis of carpal size.

Acute CTS is a syndrome in which there is a rapid rise and sustained increase in interstitial pressure within the carpal tunnel. This may result from haemorrhage, injection injuries, burns and pyogenic infection. Others have suggested that the primary pathophysiologic mechanism underlying the nerve conduction block in acute CTS is related to acute intracompartmental and intraneural ischaemia (4-5).

External compression of the peripheral nerve by 20 to 30 mmHg results in a decreased epineural venous blood flow and at levels of 60 to 80 mmHg, there is an immediate complete cessation of intraneural blood flow (6).

Chronic CTS is a compressive neuropathy in which there is an insidious rise in the carpal tunnel interstitial pressure of moderate degree (7). It ranges from early stage where there is no gross morphologic changes in the median nerve to the intermediate stage of numbness and paraesthesia and median nerve demonstrates epineural and intrafascicular oedema and to the advanced stage of fibrillation potentials and with endoneural oedema, intraneural fibrosis, partial demyelination and axonal degeneration (6). The changes in the intermediate stage are reversible with decompression but in the advanced stage it is irreversible.

The increased pressure also has a direct mechanical effect on axonal transport. Experimental data suggests that persistent compression at 20 mmHg results in the reduction in orthograde fast axonal transport with progressive dysfunction almost complete with pressure above 200 mmHg (8).

Correspondence:
Dr Omar Md Isa
Department of Orthopaedic Surgery
University of Malaya Medical Centre
50603 Kuala Lumpur
Malaysia

The sequelae of local ischaemia is destruction and replacement of the epineurium and endoneurium with dense fibrous tissue. This causes distal nerve fibre degeneration resulting in abnormal impulse generation and transmission, conduction delay or complete nerve block. These manifest as pain, paraesthesia and numbness (9).

Methods

This is a retrospective study involving 120 patients with the diagnosis of CTS seen at the Hand and Microsurgery Unit, Kuala Lumpur General Hospital from January 1993 to December 1996 with a follow-up period was fifteen months. The source of information was the patients' medical records.

A criteria for the diagnosis of the CTS in the study was determined by the Unit such as:

1. symptoms of pain, tingling sensation or numbness either at night, during activities only or at all times, clumsiness of the hand and sensation of heaviness in the affected hand or hands, and
2. either positive Phalen's test or positive Tinel's sign.

From the number, 24 patients were excluded due to incomplete data and another 14 due to associated medical conditions like cervical spondylosis, chronic renal failure, diabetes, rheumatoid arthritis and history of wrist trauma. From the remaining 82 patients, there were 102 hands taken into study. Twenty patients had bilateral involvement but each hand was treated differently and thus regarded as a separate hand.

Demographic data

Data taken included age, occupation, dominant hand, the side of hand involved, duration of symptoms and the date of the first visit.

Those chosen were the ones whose symptoms as defined by the criteria above.

Clinical examination

The areas of altered sensation or paraesthesia were determined using a pinwheel. The wheel was passed in turn from the digits into the palm, moving from the area of absolute innervation by the median nerve into that supplied by the palmar cutaneous nerve. In CTS, a change will occur at some point between the two areas. Repeated comparison was made with the ulnar-innervated digits and with those on the other hand, and particular attention was paid to the palmar triangle whose sensation was derived from the palmar cutaneous nerve.

The strength of the abductor pollicis brevis muscle was graded according to the Medical Research Council (MRC) scale and any thenar muscle wasting noted. The Phalen's test was performed either actively by the patient or assisted and considered positive when the abnormal sensation was felt within 60 seconds. If this was negative, a reversed Phalen's test was performed.

Investigation

Nerve conduction studies of both the distal sensory and motor latencies of only the median nerve were taken into account. There were then categorized into no response, normal, mild, moderate and severe responses according to the criteria set by Choi and Ahn (10).

Treatment

All patients underwent conservative treatment with splintage, oral tablets of vitamin B6 with or without analgesics depending on the circumstances. Those who were successfully treated with this method were classified under group A. There were 51 hands in this group.

During the course of conservative treatment, about 24 patients were given steroid injection into the carpal tunnel, whereby seven of them finally ended with surgical treatment. However, their numbers were quite small to influence the study significantly.

The criteria for surgical treatment were:

- worsening of symptoms,
- poor compliance, and
- abductor pollicis brevis muscle power of grade three or less.

Seven patients gave persistent symptoms and two gave worsening of symptoms as reasons to discontinue conservative treatment.

Those patients who finally had to undergo surgery were categorized as Group B. There were 51 hands in this group, too.

Surgical decompression was performed either via endoscopic (four hands) or open surgical technique. Endoscopic surgeries were abandoned later due to a high complication rate.

Result of treatment

The two factors taken into account that indicated success of treatment were resolution from pain and numbness.

Results

Their mean age was from 43.5 years (range of 23-65 years). Out of 82 patients, 71 (82.6%) were females.

There were 76 (92.6%) right hand dominant patients. There were 66 (80.5%) right hands involved out of 102 hands. 20 (24.2%) patients had bilateral involvement.

There were 42 (51.2%) patients in the sedentary jobs who were mainly office workers. There were 30 (36.5%) patients who were considered as full-time homemakers and finally 10 (12.3%) patients who were labourers.

For the Group A patients (those who were successful with conservative treatment), the mean duration of symptoms prior to consultation was 16.1 months (range of 0.3-96 months). For the Group B patients (those who finally needed surgery) the mean duration of symptoms prior to consultation was 29.1 months (range of 0.3-120 months). Using a two independent t-test, there was a significance difference in the duration of symptoms prior to consultation between the two groups ($p < 0.001$).

The distribution of paraesthesia on various regions of the hand showed a preponderance towards the area of the radial three and a half digits.

There were three hands from each group that demonstrated involvement of more than one region (Table 1).

The result of the abductor pollicis brevis muscle power testing is shown in Table 2. It shows that the distribution is almost equal for both groups.

In Group B, there were seven hands with thenar muscle wasting compared to six hands in Group A.

The Phalen's test has a higher sensitivity compared to the Tinel's sign (Table 3).

Except for one, all patients with bilateral involvement reported that the duration of symptoms occurred simultaneously for both hands.

With the nerve conduction studies, Group A showed a slightly higher number of hands with severe grade with the median motor latency test but for the sensory latency test, the number of hands with no response and with severe grade were almost equal for both groups (Table 4).

Table 1. A table on the distribution of altered sensation in the hands according to three regions. The extra three hands in each group had paraesthesiae of more than one region.

	Group A *n*=51	Group B *n*=51
Paraesthesiae of whole palm	11	15
Paraesthesiae of the radial three and a half digits	34	30
Paraesthesiae of all the digits	9	9
Total number of hands	54	54

Table 2. A table of the abductor pollicis brevis motor power

	Group A *n*=51	Group B *n*=51
Grade 3	1	1
Grade 4	15	23
Grade 5	35	27

Table 3. A table on the results of the Phalen's test and Tinel's sign

		Group A *n*=51	Group B *n*=51
Phalen's test	*positive*	47	46
	negative	4	5
Tinel's sign	*positive*	26	26
	negative	25	25

The mean duration period of failed conservative treatment before proceeding to surgery in Group B was 5.1 months (range of 0.3-15 months).

Post treatment period of resolution from pain

For Group A patients, the mean duration time was 4.8 months (range of 0.3-13 months). For the Group B patients, the mean duration time was 1.8 months (range of 0.3-6.5 months) after surgery.

Post treatment period of resolution from numbness

For the Group A, the mean duration time was 4.8 months (range of 0.3-13 months) versus Group B patients, who took a mean period of 2.5 months (range of 0.2-6.5 months) after surgery.

Table 4. A table on the results of the median nerve latency test

		msec	Group A *n*=51	Group B *n*=51
Median motor nerve latency	*no response*	0	4	11
	normal	4.0 <	1	0
	mild	4.0 – 4.9	6	5
	moderate	5.0 – 7.0	8	6
	severe	> 7.0	32	29
Median sensory nerve latency	*no response*	0	15	22
	normal	3.0 <	3	2
	mild	3.0 – 3.9	10	5
	moderate	4.0 – 6.0	4	1
	severe	> 6.0	19	21

One hand from the Group B did not gain any relief from pain and numbness and was thus discounted.

Using the t-test, there was significant difference statistically in the period of resolution from both pain ($p < 0.001$) and numbness ($p < 0.001$) between the two groups.

Discussion

It is still controversial whether work-related hand or wrist overuse is a risk factor for developing carpal tunnel syndrome. Phalen and co-workers (11) maintained that it was not an occupational disease. They stated that, whereas hand overuse might provoke symptoms, it was unlikely that occupation alone could be considered a causative factor or the condition would be encountered more frequently.

It has been reported that there was no consistent association between the prevalence of carpal tunnel syndrome and the type and level of occupational hand activity, duration of employment or bilateral versus unilateral activity (12).

It has also been shown that the volume of the carpal tunnel is relatively smaller in women than in men and this difference may be a predisposing factor for the development of carpal tunnel syndrome and thus a higher prevalence amongst women (13).

Others have reported that the mean duration of symptoms was 24 months for both the left and right hands (14). This almost coincides with this study whereby the duration of symptoms was 16.1 months for those successful with conservative treatment and 29.1 months for those who finally needed surgery. There was so much nerve destruction in those hands that had to undergo operative treatment probably due to the delay in seeking treatment.

Both the Phalen's and the Tinel's tests are quite unreliable in diagnosing carpal tunnel syndrome. The sensitivity of Phalen's test is estimated to range from 10% to 88% and of Tinel's sign from 26% to 79%. The estimates of the specificity of Phalen's test ranges from 47% to 100% and of Tinel's sign from 45% to 100% (15).

In patients with prolonged distal motor and sensory latencies preoperatively, significant improvement in conduction times were seen after surgical decompression, correlating with relief of symptoms. It was suggested that the relief of symptoms after surgery is the result of a reduction in spontaneous activity generated by the compressed nerve fragment than from the recovery from conduction block (16). In severe cases, localized demyelination is the main cause of nerve conduction delay and in more severe cases there may also be loss of larger fibres. In order to reduce false negatives, the Choi and Ahn criteria were used rather than that of DeKrom *et al* (17) and Martinez (18) (who opined that motor latency of less than 4.0 msec and sensory latency of less than 3.7 msec be considered normal). The DeKrom and Martinez's have only a 40% to 50% diagnostic rate (17).

The nearly 10% incidence of false-negative electrodiagnostic tests result in most large studies of CTS, perhaps is the biggest pitfall. There are patients with obvious CTS but with normal test. If only a small number of medium or small-sized nerve fibres are blocked, there will be no measurable effect on the conduction speed or the size of action potential, but it is likely that such a situation could cause clinical symptoms. The paraesthesia in early and mild CTS are caused by ectopic excitation of impulses within the

nerve by ischaemia or mechanical irritation even before any conduction block has developed.

Others have recommended a waiting period of six months after the initial diagnosis before performing surgery (19). In this study, surgery was performed after a median period of 12 weeks after the initial diagnosis. Those undergone conservative treatment needed a period of median 13 weeks before embarking on surgery.

It was also found that the mean time for the resolution of symptoms was between six and nine months (20), while in this study, the mean time for resolution from both pain and numbness was 4.8 and 1.8 months respectively. While for those treated surgically, the mean time for resolution from pain and numbness was 4.8 and 2.5 months respectively.

Surgery itself is not without complications. The endoscopic surgery gives the most complication in terms of recurrence and pillar pain. Probably that is the reason for it's abandonment six months later. Open surgery too, has it's share of complications predominantly pillar pain and scar tenderness.

There are several limitations in this study. Apart from a small sample, there is a lack of a third observer to eliminate the bias occurring between the examiner and the patient during the conduct of the physical examination. There is poor documentation of the nerve conduction study records as the majority only showed latency velocities without the amplitude. Bias may also occur in the period of resolution of symptoms as those hands which have undergone surgery might have gained some benefit from the initial conservative treatment.

There was also more emphasis on conservative treatment in the later period of the study. Given adequate time the symptoms may resolve by themselves. Public awareness, too played a role as the patients either came on their own or were referred.

Conclusion

The hands which failed with conservative treatment and later have to undergo surgery have a longer duration of symptoms before seeking treatment. Surgery offered a faster relief from pain and numbness. It would be unreasonable to deny surgery after failed non-surgical treatment for a period of five to six months.

Acknowledgements

This paper is a summary of a thesis of the same name submitted for the Masters of Orthopaedic Surgery for the academic year of 1999. I thank Dr. K. Pathmanaban, the Head of Department of the Hand and Reconstructive Unit of the Hospital Besar, Kuala Lumpur. Although he was not directly involved in the production of the thesis, he was helpful in allowing me access to his patients' data.

I also thank Dr. Noran Naqiah Mohd Khairi from the Department of Social and Preventive Medicine for helping me with the statistics.

References

1. Cobb TK, Dalley BK, Posteraro RH, *et al*. Anatomy of flexor retinaculum. J Hand Surg 1986; 11A:512-514.
2. Robbins H. Anatomical study of the median nerve in the carpal tunnel and etiologies of the carpal tunnel syndrome. J Bone Joint Surg 1963; 45A:953-966.
3. Armstrong TJ, Castelli WA, Evans FG. Some histological changes in carpal tunnel contents and their biomechanical implications. J Occup Med 1984; 26:197-201.
4. Gelberman RH, Szabo RM, Williamson RV, *et al*. Tissue pressure threshold for peripheral nerve viability. Clin Orthop 1983; 178:285-293.
5. Szabo RM, Gelberman RH, Williamson RV, *et al*. Effects of increased pressure on the tissue fluid pressure threshold of peripheral nerve. J Orthop Res 1983; 1:172-179.
6. Rydevik B, Lunborg G, Bagge U, *et al*. Effects of graded compression on intraneural blood flow: An in vivo study on rabbit tibial nerve. J Hand Surg 1981; 6:3-11.
7. Gelberman RH, Rydevik BL, Pess GM, *et al*. Carpal tunnel syndrome: A scientific basis for clinical care. Clin Orthop 1988; 178:285-295.
8. Dahlin LB, McLean WG. Effects of graded experimental compression on slow and fast axonal transport in rabbit vagus nerve, J Neuro Sci 1986; 72:19-27.
9. Ditmars DM Jr. Patterns of carpal tunnel syndrome. Hand Clin 1993; 9:241-248.
10. Choi SJ, Ahn DS. Correlation of clinical history and electrodiagnostic abnormalities with outcome after surgery for carpal tunnel syndrome. Plast Reconstr Surg 1998: 102; 2374-2379.
11. Phalen GS. The carpal tunnel syndrome: clinical evaluation of 598 hands. Clin Orthop 1972: 83; 29-35.

12. Nathan PA, Meadows KD, Doyle LS. Occupation as a risk factor for impaired sensory conduction of the median nerve at the carpal tunnel. J Hand Surg 1988: 13B; 167-172.

13. Dekel S, Papaioannou T, Rushworth G, *et al*. Idiopathic carpal tunnel syndrome caused by carpal stenosis. Br Med J 1980: 280; 1297-1302.

14. Gunnarsson LG, Amilon A, Hellstrand P, *et al*. The diagnosis of carpal tunnel syndrome; sensitivity and specificity of some clinical and electrophysiological tests. J Hand Surg 1997: 22B:1; 34-37.

15. Gerr F, Letz R. The sensitivity and specificity of tests for carpal tunnel syndrome vary with the comparison subjects. J Hand Surg 1998: 23B; 151-155.

16. Yates SK, Hurst LN, Brown WF. Physiological observations in the median nerve during carpal tunnel surgery. Ann Neurol 1981: 10; 227-229.

17. DeKrom MCTFM, Khipschild PG, Kester ADM, *et al*. Efficacy of provocative tests for diagnosis of carpal tunnel syndrome. Lancet North Am Ed 1990: 335; 393-395.

18. Martinez AC. Diagnostic yield of different electrophysiological methods in carpal tunnel syndrome. Muscle Nerve 1991: 14; 183-189.

19. Muhlau G, Both R, Kunath H. Carpal tunnel syndrome. Course and prognosis. J Neurol 1984: 231; 83-86.

20. DeStefano F, Nordstrom DL, Vierkant RA. Long-term symptoms outcomes of carpal tunnel syndrome and its treatment. J Hand Surg 1997: 22A; 200-210.

SKIN CLOSURE USING SIMPLE INTERRUPTED AND CONTINUOUS SUBCUTICULAR NYLON SUTURES: A COMPARISON OF RESULTS

Loo JT and Md Razif MA
Department of Orthopaedic Surgery, University of Malaya Medical Centre, 50603 Kuala Lumpur

ABSTRACT: Skin closure using simple interrupted nylon sutures was compared with closure using subcuticular nylon sutures in 80 consecutive patients undergoing semi-emergency surgery, involving open reduction and internal fixation of either the forearm bones or femur. The simple interrupted technique was shown to be slower than the subcuticular technique with higher early postoperative wound complication rate. It may use an extra packet of sutures particularly if the average wound length is 19.8 cm. There is, however, no statistical difference demonstrated for the late scar complaints or subjective and objective scoring of cosmetic outcomes six months after the surgery. ***(JUMMEC 2003-2005; 8: 56-60)***

KEYWORDS: Simple interrupted, subcuticular, skin closure, nylon, cosmetic outcome

Introduction

The skin as a barrier between the internal structures and the external environment is exceptionally susceptible to injury, either through accidental injury or planned surgical incision. Today, as surgery increases in complexity, and the heightened public awareness of scar cosmesis and skin healing need to be optimized to ensure the overall success of the surgery. The technique of suturing which is a method of closing wounds is thousands of years old. Although suture materials and techniques have changed, the goals remain the same: closing dead space, supporting wounds until healing increases their tensile strength, approximating skin edges for an aesthetically pleasing and functional result, and minimizing the risks of bleeding and infection.

A number of studies published have discussed the various aspects of the wound closure (1-5). However, direct comparison between different suturing techniques is lacking. There is also no standardized protocol for the methods, lack of agreement in the outcome measurement and scoring system. In general, simple interrupted technique of wound closure is commonly performed, as it is easy to learn and master. However, it is thought to be time-consuming with high complication rate and inferior cosmetic result. On the other hand, subcuticular technique is considered an elegant but difficult suturing technique. Running subcuticular closure is also time-consuming and does not evert wound edges well. It may show superior cosmetic result in certain locations of the body. Many studies have been performed on general surgical procedures, a number of which were often low tissue trauma and short incisions (1-4,6,7). Orthopaedic trauma surgical procedures have the following features. Firstly, the surgery is complicated by pre-existing and extensive soft tissue injury. Secondly, the dissection needs to be deep and must reach the bone before any meaningful internal fixation could be done. There is relatively rough tissue handling and surgical trauma, particularly during the implants insertion. Thirdly, the presence of the implants increase the tissue tension and this is worse if the bulky plate is used on the thin patients. The skin is subjected to excessive distraction force. Last but not least, the surgery is usually time-consuming with lengthy wounds. Therefore, a randomized prospective study was carried out to examine the advantages and disadvantages of the two commonest suturing techniques, that is, simple interrupted and continuous subcuticular, in closing the wound in clean orthopaedic surgery. Attempt is made to compare the short-term outcome of the cosmetic result between the suturing techniques, which is seldom mentioned in most previous publications due to the very subjective nature of this parameter.

Methods

Eighty consecutive healthy patients with either closed fracture of radius-ulna or femur operated between September 2001 and March 2002 were included in this study. The patients were considered for the study if they were above 12 years old, sustained isolated closed fracture of radius-ulna or femur and treated by open reduction and internal fixation with metallic implants. The following patients would be excluded: those with open fracture, personal or family history of keloid or hypertrophic scar formation, presence of abrasion, previous surgery and preexisting skin disease at the operating site, medical conditions for example, steroid usage, diabetes mellitus, blood clotting disorder, peripheral vascular disease and haemoglobin level less than 100 g/l. The patients were randomized into two groups, simple interrupted and continuous subcuticular groups. To reduce the inter-surgeon variability during the surgery, only the medical officer in the Masters program third year and above, were performing the final wound closure. To further reduce the variation, a handout of protocol was distributed to each of the medical officers involved. At the operation theatre, the starting time of the surgery was recorded once the skin incision was made. The fracture site would be identified. The fracture was mobilized, reduced and stabilized. At the end of surgery, the wound was cleaned with copious amount of normal saline. For both groups, the deep fascia was closed continuously with polyglactin 910 size 1 or 0, and dermal layer was closed with polyglactin 910 size 2/0 or 3/0 with simple interrupted method. Depending on the randomization, the final skin closure would be either simple interrupted or continuous subcuticular techniques, using nylon 3/0 or 4/0, 3/8c, reverse cutting, (75 cm in length, Ethilon; ethicon).

The patients were followed up on day 14, 3rd month and 6th month postoperatively. Early wound complications and late scar complications were recorded. At the 6th month follow-up, the cosmetic outcome was assessed. These included subjective assessment by the patient and assessment by the author using modified clinical scar scoring (8). Digital photographs of each scar were also taken in the standardized fashion throughout the study period for later assessment by a panel of medical personnel who were blind to the study.

Results

Demographic data

A total of 80 patients were available. At subsequent visits, the number of patients declined gradually as some of them defaulted the follow-up. The surgery to close the wound was performed by different surgeons of varying skill levels. To eliminate the influence of operator variability, the number of simple interrupted data entries from a given surgeon must equal his subcuticular data entries. In cases in which the data did not meet this criterion, data from the larger group were selected in a random manner, so that both groups would have equal number of entries for that particular surgeon.

For this reason, only 76, 66 and 59 patients at day 14, 3rd month and 6th month respectively were available for analysis (Table 1).

In Table 2, both simple interrupted and continuous subcuticular groups were comparable with no significant difference at different time interval for the following parameters: number of patients, age, sex and racial distribution and smoking status. No significant difference was found between the groups in terms of mode of injury, number of day spent in the hospital before and after the surgery, duration of the surgery, the length of the wound at different time interval, sites of surgery and types of implants used.

Clinical outcomes

For comparison purposes, the time taken to close the wound was divided by the length of the wound. Subcuticular closure was accomplished at a significantly faster rate (mean 35.66 sec/cm) than simple interrupted closure (46.84 sec/cm) ($t = 3.56$, $p = 0.001$).

Most of the wounds required only one packet (75 cm/packet) of suture to close the wound. However, four out of 38 patients in the simple interrupted group needed extra packet of suture. All wounds in the subcuticular group were accomplished with single packet of suture. None of the patients in either group needed more than two packets of suture to close the wound. Further analysis showed that the simple interrupted group that needed one and two packets to close the wound, the average length of the wound was 10.7 and 19.8 cm respectively.

The wounds closed with subcuticular technique showed a significantly lower frequency of postoperative complication, for example, tissue reactivity, gapping infection etc., compared to the simple interrupted group ($p = 0.004$).

However, at the 3rd month and 6th month postoperatively both groups had almost equal number of patient who developed complications of the scar. There was no significant difference between the groups.

Table 1. Number of patients

	At Beginning	Day 14	3rd Month	6th Month
Defaulters	–	0	8	7
Patients available	80	80	72	65
*Actual number of patients used for analysis (after randomized selection)	76	76	66	59

**The patient was selected in a randomized manner so that the number of simple interrupted data entries from a given surgeon equaled his subcuticular data entries.*

Table 2. General characteristics of the patients at various time intervals

General characteristics of the patients according to the group at the beginning and day 14 of the study

	Simple Interrupted	Subcuticular	Statistic
Number of patients	38	38	
Age, (yrs ± sd)	42.26 ± 20.63	45.11 ± 23.34	No difference
Sex, Male:Female	26:12 (68.4%:31.6%)	25:13 (65.8%:34.2%)	No difference
Race, Malay:Chinese:Indian:Others	12:13:10:3	14:11:11:2	No difference
Smoker:Non-smoker	7:31	9:29	No difference

General characteristics of the patients according to the group at the 3rd month of the study

	Simple Interrupted	Subcuticular	Statistic
Number of patients	32	34	
Age, (yrs ± sd)	41.28 ± 19.64	42.74 ± 22.43	No difference
Sex, Male:Female	24:8 (75%:25%)	22:12 (64.7%:35.3%)	No difference
Race, Malay:Chinese:Indian:Others	10:10:10:2	13:9:10:2	No difference
Smoker:Non-smoker	6:26	9:25	No difference

General characteristics of the patients according to the group at the 6th month of the study

	Simple Interrupted	Subcuticular	Statistic
Number of patients	31	28	
Age, (yrs ± sd)	41.74 ± 19.79	43.86 ± 23.26	No difference
Sex, Male:Female	23:8 (74.2%:25.8%)	18:10 (64.3%:35.7%)	No difference
Race, Malay:Chinese:Indian:Others	9:10:10:2	10:7:9:2	No difference
Smoker:Non-smoker	6:25	7:21	No difference

Similarly, both groups showed no significant difference in the cosmetic outcomes whether this was assessed by the patients using grading system, visual analogue scale, rating by the author using modified clinical scar scoring or objective scoring by the panel of medical personnel using visual analogue scale.

Discussion and Conclusions

The study was designed as a randomized prospective study. Every effort was taken to ensure the similarity between the two groups. This was evident when both the simple interrupted and subcuticular groups showed the near equal if not perfect result in the demographic and clinical features.

For the first parameter, that is, speed of wound closure, after eliminating the influence of the length of wound on the closure time, the subcuticular closure was accomplished at a faster rate compared to the simple interrupted group. The reason this difference exists most likely due to the following factors:

- Time was spent while waiting for the assistant to cut the suture in the simple interrupted method. In the subcuticular method, the suture was only cut once, that is, at the end of skin closure.

- The needle was much nearer to the wound before the start of next stitch in the subcuticular group compared to the simple interrupted group.
- Extra time spent on tying the multiple knots in the simple interrupted closure, whereas there was no such requirement for the subcuticular method.

For the second outcome measured, almost all the wounds were closed with a single packet of suture. A few wounds in the simple interrupted group needed two packets of sutures to complete the closure. None in the subcuticular group needed two packets of suture. Analysis showed that the average length of wound for those who needed two packet of sutures was 19.8 cm, as compared to 10.7 cm for those whose wound closed with single packet of suture in the simple interrupted group. The tendency for the extra packet of suture in the simple interrupted group can be explained by the following facts:

- By the nature of the technique, some length of suture was left behind for the ease of removal. Typically about 1-2 cm of the suture was used for this purpose. The length would vary among the surgeons.
- Surgeons differ in their ability to secure a knot with a shorter length of suture. Some surgeons were much more comfortable to tie a knot with excessive length of suture. This would be a waste, as the excess suture would be removed after completion of the knot. No such waste would ever occur in the subcuticular closure, as no knot tying is necessary except at the end of the closure.
- At the very end of suture, it is very difficult to utilize fully the short remnant of the suture attached to the needle.

Subcuticular closure was not necessarily more economical. Frequently the subcuticular closure could not oppose the wound well, leaving a mildly gapped wound at multiple loci. This was commonly treated with secondary reinforcement methods, for example, steristrip. The overall economic cost resulting from the use of this additional reinforcement would have equaled the cost of the extra packet of suture.

The simple interrupted group showed higher incidence of early wound complication as compared to subcuticular group. Most of the complications were due to the development of tissue reactivity. The overall incidence of wound infection in this study was about 2.5%, which is comparable to the worldwide figure quoted for clean surgery (9, 1-2). All infected wounds were cleared successfully with daily dressing and five-day course of antibiotic. Most studies in English literature with similar designs showed no apparent difference in the postoperative wound complication regardless of the technique utilized, for example, hernia and upper abdominal surgery (3), perineal repair (4), and neurosurgical surgery (6). However, it was shown that postoperative sensory recovery in the leg after saphenous vein coronary artery bypass graft was better preserved with the simple interrupted method (10).

Scar complications were comparable in both groups. This showed that the methods of wound closure had no bearing on the long-term scar complaints, either on the 3rd month or 6th month after the surgery.

This study attempted to compare the cosmetic outcome of the wound closure by providing the subjective and objective assessment. The patients were asked to assess their wounds. It was noted that most patients rated their wounds good or fair, and infrequently graded as poor. Overall, there was no difference between the groups on self-assessment. The assessment of cosmetic result with visual analogue scale allowed translation of a complex subjective experience to a visual-spatial display, which involves perceptual judgment and accuracy. Previous work has shown the minimal clinically important difference on the visual analogue cosmesis scale to be 1.5 cm (8). This study had sufficient power (90% with 0.05α-error) to determine a 1.6 cm difference on the visual analogue scale. The objective scoring by the patients utilizing visual analogue scale showed no difference in the perception of the cosmetic result of the wound in between the groups.

Difficulties in understanding the visual analogue scale did occur, especially amongst manual worker and older patients. Much time was devoted to explaining the function and how to use the visual analogue scale correctly.

Clinical scar scoring by the author using the modified clinical scar scoring system (8) showed equal results between two groups. This provides an objective way to assess the subjective parameter.

For both the categorical or visual analogue scale, the subjects were asked to score their wound without comparison. They had no idea except from the limited past experience how well the wound should appear. For this reason, a third assessment method was utilized. Three standardized photographs for each patient were taken and assessed by a panel of three medical personnel who were blind to the study, using visual analogue scale. Analysis of the result further showed no difference existed in between the wound closed by the simple interrupted or subcuticular technique. The result of the cosmetic outcomes is

comparable to the similar design of study in hernia surgery (3) and saphenous vein harvesting in coronary artery bypass surgery (10).

In conclusion, the choice of technique for wound closure did not affect the final outcome of the wound, up to the 6th month after the surgery. Until additional studies are available, the surgeons are free to select the technique of their preference.

References

1. Gabrielli F, Potenza C, Puddu P, *et al*. Suture materials and other factors associated with tissue reactivity, infection, and wound dehiscence among plastic surgery outpatients. Plast Reconstr Surg, 2001; 107:38.
2. McLean NR, Fyfe AHB, Flint EF, *et al*. Comparison of skin closure using continuous and interrupted nylon sutures. Br J Surg, 1980; 67:633-635.
3. Cassie AB, Chatterjee AK, Mehta S, *et al*. Pain quantum and wound healing: a comparison of interrupted inversion PDS and standard nylon sutures in abdominal skin closure. Ann R Coll Surg Engl, 1988; 70(6):339-42.
4. Mahomed K, Grant A, Ashurst H, *et al*. The Southmead perineal suture study. A randomized comparison of suture materials and suturing techniques for repair of perineal trauma. Br J Obstet Gynecol, 1989; 96(11): 1272-80.
5. Shamiyeh A, Schrenk P, Steltzer T, *et al*. Prospective randomized blind controlled trial comparing sutures, tape and octycyanoarylate tissue adhesive for skin closure after phlebectomy. Dermatol Surg, 2001; 27(10):877.
6. Mylonas C, Brocklehurst G. A prospective randomized comparison of continuous Polydioxanone and interrupted Neurilon for neurosurgical wound closure. Br J Neurosurg, 1991; 5:357-360
7. Ouinn JV, Well G. Outcome measures in clinical wound studies: The reliability of cosmesis scales with a determination of a minimal clinically important difference. Acad Emerg Med, 1998; 5:583-586.
8. Dolynchuk KN, Ziesmann M, Serletti JM. Topical Putrescine (Fibrostat) in Treatment of Hypertrophic Scars: Phase II Study. Plast Reconstr Surg, 1996; 97:117.
9. Nichols RL. Surgical infection: Prevention and treatment – 1965 to 1995. Am J Surg, 1996; 172:68.
10. Nair UR, Griffiths G, Lawson RA. Postoperative neuralgia in the leg after saphenous vein coronary artery bypass graft: a prospective study. Thorax, 1988; 43(1):41-3.

ANTICHOLINERGIC EXACERBATION OF PSYCHOTIC SYMPTOMS: A CASE REPORT

Gill JS, Jambunathan ST, Muhsin M, Abdul Rashid R
Department of Psychological Medicine, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur

ABSTRACT: A common practice in psychiatry when treating patients is the concurrent administration of anticholinergics along with antipsychotics, either to prevent or treat extrapyramidal syndrome reactions from occurring. However, most antipsychotics have inherent anticholinergic properties themselves. Therefore, this subtype of these patients have a higher than usual risk of developing anticholinergic side-effects, of which the central nervous manifestations can mimic psychosis, and may cloud judgement on patients' progress towards their treatment. ***(JUMMEC 2003-2005; 8: 61-62)***

KEYWORDS: Anticholinergics, anticholinergig toxicity, antipsychotics

Introduction

Since the introduction of Chlorpromazine in the 1950's, antipsychotics have been the mainstay of treatment for psychosis. They have complex central nervous system actions with effects on numerous receptors such as dopaminergic, serotogenic muscarinic (cholinergic), alpha1-adrenergic and H1-histaminergic receptors, giving rise to numerous possible side-effects (1). A common practice when prescribing antipsychotics is the concurrent administration of anticholinergics, either to prevent or treat extrapyramidal syndrome (EPS) reactions from occurring. This addition of anticholinergics to a patient on antipsychotics, particularly, those with significant inherent anticholinergic properties, would theoretically increase the risk of anticholinergic side-effects occurring. One of the side-effects that is rarely recognized or reported is exacerbation of the positive symptoms of schizophrenia, which if unrecognized, may cloud the physician's judgement on the patient's progress. This phenomenon of psychosis exacerbation, though replicated from several sources has failed to gain the recognition in clinical practice that its potential significance would justify (2). We present a case of a patient whose psychotic symptoms apparently worsened after he was commenced on anticholinergics, to illustrate this important point.

Case Report

A 22-year old single man was admitted to the psychiatric ward with aggressive and abnormal behaviour for one day. He believed that everyone was watching him, that the contents of television had significant importance to him, and admitted to hearing voices. He was physically aggressive towards his family members and destroyed things in the house. The only significant stressor elicited was that he had broken off with his girlfriend two months before, and had since established another relationship with another girl despite his father's strong objections. Physical examination, lab investigations and a CT brain scan revealed no abnormal findings. He was started on Risperidone, an atypical antipsychotic at a dose of 2 mg twice a day after a provisional diagnosis of Brief Psychotic Disorder was made. His agitation and psychotic symptoms improved gradually over six days of treatment. He then developed severe dystonia, which was attributed on the antipsychotic he was on. The dystonia soon resolved after Benzhexol, an anticholinergic agent was added at a dose of 2 mg three times a day. However, on the 8th day of admission, he became verbally abusive, agitated and aggressive again. Auditory hallucination reappeared, and at times he appeared confused and disinhibited. As repeat physical examination and lab investigations were normal, anticholinergic psychosis was suspected and Benzhexol was tapered down over three days. His condition then improved dramatically and he was discharged well on day 13 of admission.

Correspondence:
Dr Jesjeet Singh Gill
Department of Psychological Medicine
Faculty of Medicine
University of Malaya
50603 Kuala Lumpur

Discussion

The patient discussed above was on high doses of an anticholinergic, in addition to a high dose of an antipsychotic which by itself has anticholinergic properties, therefore increasing the risk of him developing anticholinergic side effects. Peripheral muscarinic receptors may result in dilated pupils, warm, dry and flushed skin, decreased secretions of the mouth, pharynx, nose, and bronchi; fever, tachycardia, hypertension, hyperreflexia, constipation and urinary retention. On the other hand, central nervous system manifestations may result in signs that mimic functional psychosis such as hallucinations, delusions, agitation, anxiety and paranoia (3). However, rarely in clinical practice do all of these signs manifest together. In milder forms, patients may only present with peripheral signs, and central signs may only be apparent in severe cases. However, it is important to note that some patients may present only with a few central signs, without any peripheral anticholinergic manifestations. It has been shown that addition of anticholinergic agents in acutely ill patients treated with antipsychotics can result in a small but definite exacerbation of positive (hallucinations and delusions) symptoms without any other anticholinergic signs (4). However, this unique situation is rarely recognized in patients that are psychotic to begin with. Clinicians should be aware of this possibility, especially in psychotic patients who are not improving, or appear to be resistant despite adequate antipsychotic treatment. Failure to do so would lead to these patients being given increasing doses of antipsychotics to control the so-called escalating psychosis, and exposing them to potentially more side-effects, or being labeled as treatment resistant.

References

1. Stahl SM. Essential Psychopharmacology: Neuroscientific Basis and Practical Applications. 2000; 2nd Edition, Cambridge University Press. pg 401-458.
2. Owens DGC. Guide to the Extrapyramidal Side-Effects of Antipsychotic Drugs. 1999; Cambridge University Press. pg 18-31.
3. Porteus HB, Ross DN. Mental Symptoms in Parkinsonism following Benzhexol Hydrochloride Therapy. Br Med J 1956; 2:138-140.
4. Johnstone E, Crow T, Ferrier N. Adverse Effects of Anticholinergic Medication on Positive Schizophrenic Symptoms. Psychol Med 1983; 13:513-527.