RECENT ADVANCES IN GERIATRIC MEDICINE - A REVIEW

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ABSTRACT: The rapid aging of populations worldwide demands major changes across all aspects of health care for older persons. Geriatric medicine which is that branch of of medicine which is concerned with the clinical, preventive and rehabilitative aspects of care of older persons, has much to offer in relieving the suffering and increasing the disability free years they can enjoy. Recent advances in Geriatric Medicine based on well designed randomised trials and meta-analysis that are clinically significant to the practicing physician are reviewed in this article. *(JUMMEC 1999; 2: 67-73)*

KEYWORDS: Recent advances, Geriatric Medicine, Older persons.

Introduction

Geriatric Medicine is that branch of Medicine concerned with the clinical, preventive and rehabilitative aspects of care of older persons. According to the United Nations estimates, the population of the elderly in the world will reach 590 million by the year 2000 of which 60 % will be residing in developing countries. In Malaysia, of the estimated population of about 18 million in the year 2000, approximately 10.3% or 1.84 million would be older persons aged 60 years or older. Physicians in managing older persons with illnesses strive to relieve their suffering, increase their disability free years they can enjoy and hence improving their overall quality of life. In recent years there has been many methodologically rigorous studies relevant to the medical care of older persons have been published. A review of the clinically significant recent advances in geriatric medicine is presented.

Ageing and oxidative stress

Oxidative stress is one of the mechanisms of aging and it has been shown that aging involves defects in the mitochondrial DNA which promote oxidative stress mediated cell damage (1). In recent years numerous trials have been completed involving the use of antioxidants like Vitamin E, Selenium, β-carotene and Vitamin C in the management of Alzheimer's disease, heart disease and in reduction of incidence of cancer. In a 2 year randomised placebo controlled trial, 2000 IU of Vitamin E per day given to patients with moderate Alzheimer's disease delayed 50% the combined endpoint of death, admission to an institution, inability to perform the activities of daily living, or severe dementia (2).

In the Cambridge heart antioxidant study, the active treatment group receiving Vitamin E 400-800 IU per day death from cardiovascular causes or non-fatal myocardial infarction was significantly reduced (3). However a similar Finnish study found no significant changes in the rates of coronary events and a significantly higher rate of coronary events in those participants randomised to receive β-carotene (4). An observational study reported a followup of 7 years of over 34486 post menopausal women who had a high dietary intake of Vitamin E who showed a significantly reduced risk of death from coronary disease (5). The clinical trial data for the regular use Vitamin C, Selenium and β-carotene in the prevention of cancer or reduction in risk of coronary events is less favourable.

Importance of inflammation and role of NSAID in the elderly

Inflammation has a major role in many of the disease processes that affect the physical function and cause disability in the elderly. Investigators in the SOLVD study (6) and other studies (7) have shown the association of proinflammatory cytokines such as tumour necrosis factor a and interleukin 6 with poor prognosis and increased severity of heart failiure. Cardiac cachexia causing wasting of skeletal muscle often seen in older people with cardiac failure is associated with excess of cytokine production. Aspirin through its anti-platelet effects has been proven of benefit in cardiovascular disease in the elderly and there is now increasing data that aspirin may inhibit inflammation in atherosclerosis. In the Physicians health study (8), the reduction in the risk of acute myocardial infarction associated with taking aspirin was greater in people with high concentrations of C-reactive protein than those with low values. The

protective effect of NSAID use on the cognitive decline in older persons and the reduction of risk of Alzheimer's disease was highlighted in 2 studies (9,10). However more definitive studies need to be done in this area before recommending the use of NSAID in the prevention of dementia. For Alzheimer's disease, the commonest cause of dementia, two cholinesterase inhibitors, donepezil (Aricept) and rivastigmine (Exelon), are now licensed for the symptomatic treatment of mild to moderate cognitive impairment [minimental state examination score of 10-26]. Trials (11,12) suggest that in some patients these agents improve cognition, global function, and behavioural function, but there are as yet no data as to whether they delay deterioration or improve outcome.

Heart disease, dyslipidaemia, hypertension and stroke in older people

Coronary Heart disease (CHD) is the most important part of the broad spectrum of disease conditions affecting the heart and circulation that progresses dramatically as the age advances. CHD contributes heavily to the disability and death especially in the elderly persons. A systemic evaluation of risk associations, focussing on the initial development of CHD in subjects aged 65-94 years in Framingham and other studies, showed that the majority of risk factors established in middle age also maintained significant associations with CHD in older persons, but with some differences related to sex. Hypertension particularly elevated systolic blood pressure, emerged as the dominant risk factor for CHD irrespective of sex. Serum total cholesterol alone lost statistical power as a predictor for CHD, particularly in older men, but predictive strength for serum lipids was restored when high density lipoproteins were considered in the analysis. Cigarette smoking was not associated with risk of overall CHD incidence but remained a risk factor for coronary death. ECG left ventricular hypertrophy and non-specific repolarisation abnormalities were related to enhanced CHD risk. Glucose intolerance and diabetes mellitus made independent contributions to CHD risk particularly in older women.

Systolic hypertension

Data from the systolic hypertension in the elderly program has shown that treating isolated systolic hypertension with diuretic drugs can reduce the risk of heart failiure over time (13). The reduction in congestive heart failiure events is greatest in patients with a history of myocardial infarction or electrocardiograhic evidence of this. Results from the same group has shown that diuretic drug treatment of isolated systolic hypertension in patient's with moderate type II diabetes was at least as effective as treatment with other types of hypertensive drugs in reducing stroke, non-fatal myocardial infarction and coronary heart disease and all other major cardiovascular events. Data from another large trial the Syst-Eur trial (14) showed that among elderly patients with isolated systolic hypertension, antihypertensive drug treatment starting with nitrendipine reduces the rate of cardiovascular complications. Treatment of 1000 patients for 5 years with this type of regimen may prevent 29 strokes or 53 major cardiovascular endpoints. The same group in a related analysis found that that the calcium channel blocker nitrendipine, given as a single antihypertensive medication, prevents cardiovascular complications in older patients with isolated systolic hypertension. A meta analysis of trials of antihypertensive therapies has shown that treatment with diuretics given in low doses to older adults was associated with reduced risks of stroke, coronary heart diseas,congestive heart failiure and total mortaility (15). The Hypertension in the Very Elderly Trial (HYVET) is an ongoing multicentre, open, randomised, controlled trial(16). The aim of this trial is to investigate the effect of active treatment on stroke incidence in hypertensive patients over the age of 80 years. Secondary end-points include total cardiovascular mortality and morbidity. Patients are to be randomised to 3 groups-(i) no treatment; (ii) treatment with a diuretic (bendrofluazide); or (iii) treatment with an angiotensin converting enzyme (ACE) inhibitor. It is expected that this trial will provide with the answers whether to treat hypertensives above the age of 80 years with mild to moderate hypertension. Many other trials are also in progress in the U.S. and Europe to determine which hypertensive agents are better at preventing major complications of hypertension. The effect of anti-hypertensive treatment on cognitive function is still uncertain. Although the MRC trial (17) and the SHEP trial (13) showed no impact on cognitive function the data from the Kungsholmen project (18) and the Syst-Eur Trial (14) are more promising. Extrapolating from the results of Syst-Eur Trial, treatment of 1,000 hypertensive patients for 5 years could prevent 19 cases of dementia. More large scale and definitive studies are needed to answer the question of the prevention of cognitive decline with antihypertensive treatment.

Dyslipidaemia

The predictability of CAD by serum cholesterol appears to decline with advancing age. In an ongoing longitudinal community study of cardiovascular disease in Australian elderly, 60 years or older [The Dubbo Study] (19), hypercholestroleamia due to elevated LDL cholesterol was predictive of initial and recurrent CAD in men and women 60-69 years, but not predictive in older subjects. Hypertriglcerideamia was predictive of initial and recurrent CAD in men 60-69 years only, and in all women 60 years and older Controlled trials of lipid

therapy have not been conducted specifically in the elderly. However in men and women aged 60-69 with established CAD in the 4S (20) study achieved similar CAD prevention to younger subjects. In the WOCSOPS trial (21) demonstrated benefit from pravastatin in hypercholestroleamic men up to the age of 65 years but evidence of similar benefit above the age or in women is lacking. Hence although the case for lipid intervention in still older subjects with established CAD is justified on empirical grounds, the available evidence leads to the conclusion that dyslipideamia should not be treated in asymptomatic, elderly free clinical CAD of above the age of 70 years.

Stroke

Recently published large clinical trials (22) of heparin and aspirin in acute stroke - the International Stroke Trial, Chinese Acute Stroke Trial, and Trial of ORG 10172 in Acute Stroke Treatment - fail to show a net benefit from heparin. The rates of recurrent ischemic stroke in the control groups of these trials were low, ranging from 0.6 to 2.2% per week. The low rates of recurrent stroke observed in these groups, coupled with the morbidity and mortality associated with i.v. heparin in this patient population, argue against routine use of i.v. heparin in the acute stroke period. Aspirin's benefit in preventing vascular outcomes is well established (23). It reduces the relative risk for stroke, myocardial infarction, and vascular death by about 25% compared with placebo. Almost 10 years ago we learned that ticlopidine is more effective than aspirin (about 12% relative risk reduction for stroke or death). However, ticlopidine has important adverse effects. In 1996, the Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) trial showed that clopidogrel, a new thienopyridine similar to ticlopidine, is also more effective than aspirin (by a similar amount) and is as safe as aspirin. Also in 1996, the European Stroke Prevention Study 2(ESPS-2) showed that dipyridamole alone prevents stroke and that when combined with aspirin it is more effective, probably comparable to ticlopidine and clopidogrel. Dipyridamole combined with aspirin reduced the relative risk for stroke or death by about 13% compared with aspirin alone. Both clopidogrel and dipyridamole are safe but will cost more than aspirin. Aspirin also appears beneficial for acute stroke treatment. The Chinese Acute Stroke Trial (CAST) (24) and the International Stroke Trial (IST) (25) demonstrated that aspirin given at the time of an acute ischemic stroke reduces the risk for early death (about 5 less/1,000 treated), recurrence or death (about 10 less/1,000 treated), and dependence (about 5 less/1,000 treated). Overall, the benefits of aspirin in acute stroke treatment and stroke prevention are definite but modest. Combination therapy with antiplatelet agents that act through different mechanisms is a promising way to maximize the benefits of antiplatelet treatment. All the randomised controlled trials comparing the outcome of patients with stroke cared for in a specialist stroke unit with the outcome of those cared for in general medical wards were examined and showed that stroke units reduce the risk of death or living in an institution at a median of 12 months afterstroke (26). However there is some evidence that elderly patient's with stroke may benefit from care in geriatric assessment or rehabilitation units as much as care from stroke units (27). However the most important factors contributing to the effectiveness of the stroke or rehabilitation units will be their organisation and the presence of a multidisciplinary team that is knowlegeable and enthusiastic about treating stroke. Rudd *et al* showed that in a randomised controlled trial (28) early discharge from the hospital after stroke with specialist rehabilitation at home is feasible without an increase in readmission rates or stress to carers. This study has shown that considerable reductions in the use of hospital beds are achievable with the development of an effective rehabilitation team in the community and may provide an opportunity to cut costs.

Interventions to improve healthy ageing

Cardiovascular disease is still the most important cause of morbidity and mortality in older persons and interventions to reduce blood pressure by 6mmHg and blood cholesterol by 10 % will reduce the risk of heart attack or coronary artery disease by 15% and 30% respectively. Diets high in fruit, vegetable intake, high complex carbohydrates, non-starch polysaccarides and reduced saturated fat and total fat intake has been found to be especially protective for cardiovascular disease in older people. Similiarly the risk of fractures can be reduced by ensuring that older people have adequate dietary intake of calcium and vitamin D. Physical activity has been shown to protect against cardiovascular disease, osteoporosis and fractures, diabetes, breast and colon cancer. Exercise programmes in the elderly can not only improve their balance but resistance exercises for the legs are especially useful in helping them rise from the chair and increase their walking speed. A combination of upper body resistance exercises which can increase the range of activities of daily living and flexibility exercises that protect against falls are important interventions in the elderly. In a randomised controlled trial (29) of general practice programme of home based exercises showed that strength and balance retraining exercise improved the physical function and was effective in reducing falls and injuries in women 80 years and older. Exercise also provides some performance improvement and pain relief in patients with knee osteoarthritis. In a 18 month randomised controlled trial (30) of 463 community dwelling older persons mean age 68 years old, with pain and functional limitation from knee osteoarthritis, both aerobic and resistance exercise

training improved performance and diminished pain in these patients with knee osteoarthritis. These exercise regimens were well tolerated with 2 % adverse effects (falls and fractures).

In a randomised controlled trial of prevention of falls in the elderly (PROFET) (31), Close J *et al* assesed the benefit of a structured interdisciplinary assessment of people who have fallen in terms of further falls. The study shows that an detailed medical and occupational-therapy assessment of this high-risk population with referral to relevant services if indicated; can significantly decrease the risk of further falls and limit functional impairment. External hip protectors or safety pants have been shown in open randomised nursing home study (32) to reduce the rate of hip fractures by 50 %. The risk of fracture in older people can be reduced by increasing their low bone mass by ensuring adequate intake of Vitamin D and calcium. Alendronate-α biphosphonate has emerged as alternative to hormone replacement for women who are unable or unwilling to take the drug and it has been shown to reduce risk of vertebral fracture and preserves bone mass at all sites of major osteporotic fracture. In a randomized double blind placebo controlled trial (33) of 2027 post menopausal women with osteoporosis taking 5-10 mg/day of a biphosphonate-alendronate, treating 35 (95%CI:22-85) women with alendronate for three years prevented 1 clinical vertebral fracture; treating 52 (95% CI:28-234) women prevented one wrist fracture.

Hence healthy life expectancy is often influenced by chronic disabling conditions like cardiovascular disease, osteoporosis, or serious injuries associated with falls which can be prevented or postponed by appropriate interventions throughout life.

Hazards of hospitalisation in older persons

Functional decline is a common problem during and after acute hospitalization in older adults. Sager *et al* (34) showed that one third of older adults lose the ability to perform at least one ADL after acute medical hospitalisation and 40% had of these patients had not regained preadmission ADL/IADL function 3 months later. Patients with hospital acquired ADL declines were more likely to be re-hospitalized or newly institutionalized at 3 month followup. In another study of hospitalized patients (35) researchers found that 15-18% of patients developed delirium during the first 9 hospital days. Use of physical restraints, malnutrition(albumin<3.0 gm/dl), more than 3 medications added in 24 hours, use of a bladder catheter, and iatrogenic events were identified as independent risk factors for the precipitation of delirium in the hospitalized older adults. Falls by inpatients are associated with increased duration of stay in hospital and a greater chance of unplanned readmission or discharge to residential or nursing home care. Oliver *et al* (36) by identifying five factors significantly associated with falls have devised a simple risk assessment tool (STRATIFY) to predict which high risk elderly patients will fall and hence target prevention programmes towards this group.

NSAID usage and its complications in older persons

Estimates of attributable risk suggest that non-steroidal anti-inflammatory drugs are responsible for between one quarter and one third of hospital admissions for upper gastrointestinal bleeding in older people (37) In U.K. it is estimated that NSAID inclusive of aspirin cause about 5000 upper gastrointestinal bleeding episodes needing admission with about 800 deaths per year. A result of meta-analysis(38) showed that compared with 11 other NSAID's, ibuprofen at doses<2400mg/d has the lowest risk for serious gastrointestinal complications requiring hospitalization. However the risk of hospitalization increases with higher doses. Another meta-analysis (39) showed that treating eight (95%CI:4-112) short term NSAID users or 12 (95%CI:6-100) long term users with misoprostol will prevent one endoscopic gastric ulcer in each group. Usual doses of H^2 blockers were ineffective in preventing NSAID-associated gastric ulcers. In a double blind placebo controlled RCT (40) famotidine at doses of 20 mg po bid, did not prevent NSAID associated gastric ulcers, but high dose famotidine (40 mg bid) prevented NSAID-induced endoscopic ulcers in arthritis patients. Treating 10 (CI:5-143) patients for 24 weeks with famotidine 40 mg bid, prevents one NSAID-associated gastric endoscopic ulcer. Cyclooxygenase-2 (COX-2) inhibitors are being evaluated in clinical trials or are in development. These agents appear to inhibit only the COX-2 isoenzyme, which is produced largely during inflammation and is responsible for the biosynthesis of prostaglandins and other mediators of inflammation as well as sensitizers to pain. Because COX-2 inhibitors do not inhibit COX-1 isoenzyme activity at pharmacologic concentrations, they are devoid of many of the toxicities that are typical side effects of NSAID. Short term studies in dental pain, osteoarthritis, and rheumatoid arthritis found that the COX-2 inhibitor celecoxib was an effective analgesic (41) but did not cause gastroduodenal erosions. It has the potential to provide analgesia and antiinflammatory action in patients with arthritis without the side effects of NSAID. Further studies are in progress to substantiate these findings. With these results in mind older patients with painful arthritis should be treated initially with acetaminophen or a nonacetylated salicylate. If this is not effective the lowest effective dose of ibuprofen should be started with adequate prophylaxis with either misoprostol or high dose famotidine in high risk patients. The newer COX-2 inhibitors would be a

more suitable and safer alternative in many older patients with arthritis in the future.

Comprehensive geriatric assessment

Comprehensive geriatric assessment is a multidimensional, interdisciplinary diagnostic process intended to determine an elderly person's medical, psychosocial, functional capabilities and problems. Controlled trials in a number of countries have documented benefits from different types of in-home assessment and treatment programs for various subgroups of elderly persons. The concepts of in-home comprehensive geriatric assessment (CGA) consists of a regular follow-up, health education, and preventive care in a community. The intervention includes yearly in-home CGA by geriatric nurse practitioners (GNPs), who provide, following discussions with physician geriatricians, lists of specific recommendations for health and well-being enhancement. The GNPs provide follow-up visits quarterly and regular telephone contacts to improve compliance. In 3-year randomised trial involving 202 older people enrolled in an in-home comprehensive geriatric assessment (CGA) and preventive care program, Cho *et al* (42) found that although functional status was similar at baseline, the presence of certain target conditions in this sample was associated significantly with functional decline in (IADL) instrumental activities of daily living and (BADL) basic activities of daily living during the 3-year period. Four conditions (gait/balance disorders, depression, unsafe home environment, and coronary artery disease) were associated with significant declines in IADL, and four conditions (gait/balance disorders, depression, hypertension, and urinary incontinence) were associated with significant declines in BADL. These findings may help identify older persons at risk for greatest functional decline despite participation in CGA and may also suggest the need for more effective intervention strategies in these individuals. Secondary analysis of the same randomised trial (43) showed that preventive in-home geriatric assessment in well functioning community dwelling older people delayed the onset of disability in them. The effectiveness of outpatient CGA consultation coupled with an adherence intervention on 15-month health outcome was tested in a randomized controlled trial by Reuben *et al* (44). This study showed that a combined approach in an outpatient setting can prevent functional and health-related quality-of-life decline among community-dwelling older persons who have specific geriatric conditions.

Conclusion

Practising clinicians should be aware of the recent advances of geriatric medicine highlighted above as important studies have shown that chronic inflammation has an important role in the abnormal processes related to aging, including changes in body composition, congestive heart failiure, and possibly dementia. Increasing oxidative stress is a key aspect of aging as studies suggest that Vitamin E supplementation reduces coronary events associated with atherosclerosis and may slow the processes underlying Alzheimer's disease. John Glenn's (aged 77 years) recent nine day journey to space aboard the space shuttle Discovery (45) promises to expand human knowledge about the aging process. Many of the biological changes that occur in the weightless environment of space are similiar to those that occur on earth as one ages. Research about the changes in the physiological systems in the ageing body in space will help us learn more about aging-related frailties and conditions, such as osteoporosis, cardiovascular deconditioning, and sleep disorders in older persons. Increasing research into the clinical interventions of common geriatric syndromes by way of methodologically rigorous studies will provide the evidence base that will relieve suffering in old people and increase the number of disability-free years they can enjoy.

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