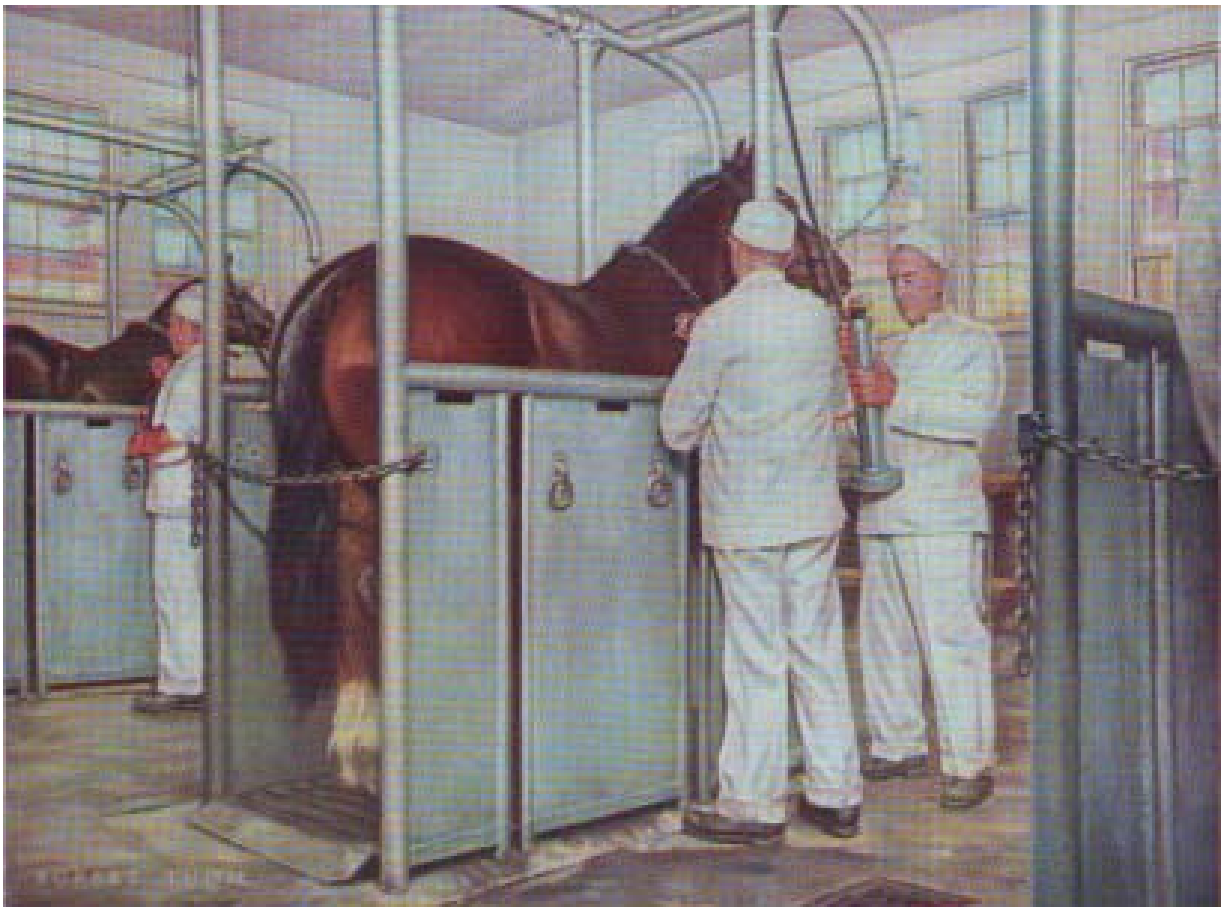
ISSN 1391-0736

The Sri Lanka Prescriber

March 2014; Volume 22, No. 1



CONTENTS

The Sri Lanka Prescriber *is sponsored by the State Pharmaceuticals Corporation of Sri Lanka as a service to the medical profession.*

The Sri Lanka Prescriber

Copies of the *Sri Lanka Prescriber* and inquiries from M. P. Kuruppu, Deputy General Manager, Marketing, and Ms Anusha Gunatilleke, Manager Promotions and Publicity (Telephone 2338102), State Pharmaceuticals Corporation, P. O. Box 1757, 75, Sir Baron Jayathilake Mawatha, Colombo 1.

Price per copy Rs 50.00 (students Rs 25.00). Personal callers may also obtain copies from the Departments of Pharmacology at the Medical Faculties in Colombo, Galle and Sri Jayewardenepura.

Published by

Department of Pharmacology
Faculty of Medicine
271, Kynsey Road, Colombo 8, Sri Lanka.
Telephone: + 94 11 2695300 Ext 315
E-mail: phrm_cmb@hotmail.com
and
State Pharmaceuticals Corporation
75, Sir Baron Jayathilake Mawatha, Colombo 1.
Telephones + 94 11 2320356-9
Fax: + 94 11 447118
E-mail: prmanager@spc.lk Web site: www.spc.lk

Printed by

Ananda Press
82/5, Sir Ratnajothi Saravanamuttu Mawatha,
Colombo 13.
Telephone: + 94 11 2435975
E-mail: anpress@sltnet.lk

Cover picture

THE ERA OF BIOLOGICALS

Biological products (made from microorganisms) got their start with the discovery of diphtheria antitoxin by the German, Behring, in 1894. Pharmaceutical manufacturers since have improved serums, antitoxins and vaccines, which have saved countless lives.

One of a series: *A History of Pharmacy in Pictures*, presented by Parke, Davis & Company.

George A. Bender, Director © 1957 Robert A. Thom, Artist

The risks and benefits of vitamin E supplementation

Introduction

Vitamin E is the collective name for a group of fat soluble compounds with distinctive antioxidant activities. In addition to being an antioxidant, vitamin E is involved in immune function and, as shown by in vitro studies of cells, cell signalling, regulation of gene expression, and other metabolic processes. Vitamin E is found in vegetable oil, nuts, wheat, green leafy vegetables, and fish. There is no published data on vitamin E intake among Sri Lankan adults. However, typical Sri Lankan dishes are usually full of vitamin E rich foods such as green leafy vegetables, nuts and fish. It can be stored in adipose tissue, liver, and muscle. Recommended intake: recommended daily allowance (RDA) for vitamin E for adults (including 14-18 years) is 15 mg (22 IU). There are no increases for pregnancy, but for lactation the RDA is 19 mg/d. The RDA for children 1 to 3 years is 6 mg; for those 4-8 years, it is 7 mg; and 11 mg for those 9 to 13 years. However a common vitamin E capsule (green colour) has 400mg. Vitamin E is one of the most commonly prescribed over-the-counter antioxidant vitamins in Sri Lanka. Prolonged intake of vitamin E among some population groups such as healthy women (for cosmetic reasons), the elderly and cardiac patients is particularly common. Although observational studies suggested several health benefits of vitamin E intake, intervention studies do not support that. The aim of this article is to discuss the highest quality evidence on vitamin E supplementation on apparently healthy individuals for chronic diseases prevention and treatment.

Cardiovascular diseases

A pool of 84 studies showed that supplements of vitamin E do not affect the outcome of cardiovascular diseases [1]. Heart Outcomes Prevention Evaluation – The Ongoing Outcomes (HOPE-TOO) trial showed that in patients with vascular disease or diabetes mellitus, long term vitamin E supplementation (400 IU/d) does not prevent cancer or major cardiovascular events, and may increase the risk for heart failure [2]. In the Heart Protection Study, a combination of vitamin E (600 IU), vitamin C, and beta-carotene did not affect mortality. However, it did cause a significant, albeit small, increase in total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, as well as a decrease in high-density lipoprotein (HDL) cholesterol [3]. The protective increase in HDL with simvastatin plus niacin was attenuated by concurrent therapy with vitamin E [4]. In a meta-analysis, high-dosage vitamin E (≥400mg/d) supplemented studies (n=11) showed a significant increase in all cause mortality (p=0.035). Furthermore, in dose-response analysis, all cause mortality progressively increased as vitamin E dosage increased by more than 150 IU/d [5].

Vitamin E inhibits platelet aggregation and antagonises vitamin K-dependent clotting factors. As a result, taking large doses with anticoagulant or antiplatelet medications may increase the risk of bleeding, especially in conjunction with low vitamin K intake. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) study reported higher mortality from hemorrhagic stroke among participants receiving vitamin E. Schurks et al. evaluated the effect of vitamin E supplementation on incident total, ischaemic, and haemorrhagic stroke in nine randomised control trials (n=118 765). The meta-analysis revealed that vitamin E increased the risk for haemorrhagic stroke by 22% and reduced the risk of ischaemic stroke by 10% [6].

Cancer

In a large cancer prevention trial (SELECT), a total of 35 533 men were supplemented with vitamin E (400 IU/d) and followed up for a minimum of 7 years. Results showed that men with vitamin E supplementation had 17% increased risk for prostate cancers compared with placebo. A systemic review and meta-analysis on antioxidant supplements for preventing gastrointestinal cancers reported that antioxidant vitamins (including vitamin E) seem to increase overall mortality [7]. Antioxidant supplements (including vitamin E) seemed to increase the development of colorectal adenoma in three low-bias risk trials [8]. Oncologists generally advise against the use of

antioxidant supplements during cancer chemotherapy or radiotherapy because they might reduce the effectiveness of these therapies by inhibiting cellular oxidative damage in cancerous cells [9].

Liver diseases

There is no convincing evidence to support or refute vitamin E (with or without other antioxidant vitamins) for patients with liver diseases. The TONIC trial showed that supplementing with vitamin E (800 IU/d) produced no significant improvement for children and adolescents with non-alcoholic fatty liver disease (NAFLD) [10]. Based on available evidence, vitamin E is only recommended in non-alcoholic steato-hepatitis (NASH) adults without diabetes or cirrhosis, and those with aggressive histology [11].

Other diseases

The Women's Health Study, a randomised, double-blind, placebo-controlled trial of vitamin E supplementation in 39 876 healthy US women did not provide evidence of cognitive benefits [12]. A systematic review on randomised control trials (RCTs) showed no improvement in glycaemic control in type 2 diabetes patients with vitamin E supplementation [13]. A systematic review and meta-analysis of randomised controlled trials showed supplementation with vitamins C and E during pregnancy does not prevent pre-eclampsia [14].

Bjelakovic et al. reviewed 46 studies (n= 171 244) on vitamin E supplementation of mortality in healthy participants and patients with various diseases. Low-biased studies showed a 3% significant increase ($p<0.05$) in the total mortality in the supplemented participants [15].

Summary

In summary, current evidence does not support vitamin E supplementation for preventing and treating several chronic diseases, especially cardiovascular diseases. Prescribing a large dose of vitamin E (400mg) for long periods may do more harm than good to patients.

References

1. Shekelle PG, Morton SC, Jungvig LK, et al. Effect of supplemental vitamin E for the prevention and treatment of cardiovascular disease. *Journal of General Internal Medicine* 2004; **19**: 380-9.
2. Lonn E, Bosch J, Yusuf S, et al. Effects of long-term vitamin E supplementation on cardiovascular events and cancer: a randomized controlled trial. *Journal of American Medical Associations* 2005; **293**: 1338-47.
3. Brown BG, Zhao XQ, Chait A, et al. Simvastatin and Niacin, Antioxidant Vitamins, or the Combination for the Prevention of Coronary Disease. *New England Journal of Medicine* 2001; **345**: 1583-92.
4. Cheung MC, Zhao XQ, Chait A, et al. Antioxidant supplements block the response of HDL to simvastatin-niacin therapy in patients with coronary artery disease and low HDL. *Arteriosclerosis, Thrombosis, and Vascular Biology* 2001; **21**: 1320-6.
5. Miller ER 3rd, Pastor-Barriuso R, Dalal D, et al. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Annals of Internal Medicine* 2005; **142**: 37-46.
6. Schurks M, Glynn RJ, Rist PM, et al. Effects of vitamin E on stroke subtypes: meta-analysis of randomised controlled trials. *British Medical Journal* 2010; **341**: c 5702.
7. Bjelakovic G, Nikolova D, Simonetti RG, et al. Systematic review: primary and secondary prevention of gastrointestinal cancers with antioxidant supplements. *Alimentary Pharmacology & Therapeutics* 2008; **28**: 689-703.
8. Bjelakovic G, Nagorni A, Nikolova D, et al. Meta-analysis: antioxidant supplements for primary and secondary prevention of colorectal adenoma. *Alimentary Pharmacology & Therapeutics* 2006; **24**: 281-91.
9. Lawenda BD, Kelly KM, Ladas EJ, et al. Should supplemental antioxidant administration be avoided during chemotherapy and radiation therapy? *Journal of National Cancer Institute* 2008; **100**: 773-83.
10. Lavine JE, Schwimmer JB, Van Natta ML, et al. Effect of vitamin E or metformin for treatment of nonalcoholic fatty liver disease in children and adolescents: the TONIC randomized controlled trial. *Journal of American Medical Association* 2011; **305**: 1659-68.
11. Pacana T and Sanyal AJ. Vitamin E and nonalcoholic fatty liver disease. *Current Opinion in Clinical Nutrition and Metabolic Care* 2012; **15**: 641-8.
12. Kang JH, Cook N, Manson J, et al. A randomized trial of vitamin E supplementation and cognitive function in women. *Archives of Internal Medicine* 2006; **166**: 2462-8.

13. Suksomboon N, Poolsup N, Sinprasert S. Effects of vitamin E supplementation on glycaemic control in type 2 diabetes: systematic review of randomized controlled trials. *Journal of Clinical Pharmacology and Therapeutics* 2011; **36**: 53-63.

14. Conde-Agudelo A, Romero R, Kusanovic JP, et al. Supplementation with vitamins C and E during pregnancy for the prevention of preeclampsia and other adverse maternal and perinatal outcomes: a systematic review and metaanalysis. *American Journal of Obstetrics & Gynecology* 2011; **204**: 503 e1-12.

15. Bjelakovic G, Nikolova D, Gluud LL, et al. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. *Cochrane Database of Systematic Reviews* 2012; **3**: CD 007176.

Dr. Ranil Jayawardena MBBS (Colombo), MSc (Glasgow), PhD (Queensland), RNutr (SL), ARNutr (UK), ARNutr (Australia).
Clinical Nutritionist.
Email <ranil7@gmail.com>.
I have no conflicts of interest regarding this article.

Cardiovascular drugs in older people

Summary

Cardiovascular drugs are the most frequently prescribed medicines for older people. However, it can be difficult to find a regimen that does more good than harm, especially if the patient is frail.

Prescribers should determine the goals of treatment, understand the limitations of the evidence and be vigilant for the adverse effects of cardiovascular drugs.

Regimens for common cardiovascular diseases, such as hypertension, chronic heart failure and chronic atrial fibrillation, need to be tailored to the individual patient, taking into account factors such as comorbidity and life expectancy.

Key words: aged 80 and over, atrial fibrillation, heart failure, hypertension

(Aust Prescr 2013; 36: 190-4)

Introduction

The prevalence of diseases such as hypertension, coronary heart disease, chronic heart failure and chronic atrial fibrillation increases with age, so cardiovascular drugs are the most frequently prescribed treatments for older people. These drugs are also responsible for a large proportion of the adverse drug reactions suffered by older people.

Important considerations when prescribing

There are some general principles to apply when prescribing cardiovascular drugs to older people (Box). It is important to tailor a regimen for each individual patient.

Determine the goals of treatment

Prescribers should ask themselves, 'What outcome do I hope to achieve for this patient?' The prescriber should also consider what their patient hopes to achieve by following the treatment regimen. In general, cardiovascular drugs are helpful for symptom control, prevention of cardiovascular events or life extension. In a healthy 80-year-old person all three goals may be applicable. In contrast, symptom control may be the only goal for an 80-year-old with severe dementia.

Box

Guidelines for prescribing cardiovascular drugs to older people

1. Take into account all the information obtained from a comprehensive assessment (e.g. postural hypotension, cognitive status, life expectancy)
2. Set goals of treatment – symptom control vs life prolongation
3. Understand and apply the evidence appropriately
4. Avoid under-prescribing drugs that are likely to have symptomatic and functional benefits (e.g. diuretics for chronic heart failure)
5. Be vigilant for adverse effects (see Table 2)
6. Specifically look for drug-drug and drug-disease interactions
7. Discuss the potential benefits and harms with patient, family and carers
8. Choose drugs wisely, start at a low dose and then increase the dose slowly
9. Try to avoid starting several drugs simultaneously
10. Conduct regular drug reviews
11. Stop drugs that are unlikely to be of benefit or are likely to result in more harm than good
12. Take a multidisciplinary approach to achieving optimal regimens (e.g. pharmacists can advise on simplifying the regimen and the best delivery system)

In frail older people with multiple comorbidities and functional limitations, it is important to prioritise the goals of treatment. These priorities should guide prescribing. A common dilemma faced by clinicians is the combination of supine hypertension and

symptomatic postural hypotension in a frail older person. In this situation, if the hypotension results in falls, dizziness and impairment of everyday function then avoiding postural hypotension should be the priority even at the expense of less than ideal control of blood pressure. High blood pressure may have to be accepted as long as it is not causing symptoms. The consequences of a fractured hip as a result of a fall due to postural hypotension can be more devastating than the vascular events one was aiming to prevent by lowering blood pressure.

Table 1 gives examples of how priorities may differ between a well older person and a frail older person for the treatment of specific cardiovascular diseases. Avoiding adverse effects is important in both groups, but the risk of harm is greater in frail older people. In addition, mortality benefits are less likely to be seen in frail older people.

Be aware of the limited evidence

Older people are poorly represented in clinical trials,[1] so there are limited data about the benefit and harm of giving cardiovascular drugs to frail older patients. Clinical guidelines for cardiovascular diseases rarely provide any details on how they should apply to older frail people with multiple comorbidities. Given these limitations, prescribers should choose a regimen which is appropriate for the individual patient and minimises the risk of harm. Prescribing purely on evidence from younger patients or disease-specific guidelines leads to polypharmacy, pill burden and often harm. However, the lack of direct evidence should not be a reason to deny older people treatments that have the potential to improve their quality of life. For example, treatment to minimise the breathlessness of heart failure can have a big impact on the everyday function and overall quality of life of an older person.

Be vigilant for adverse effects

Over the past 20 years there has been an increase in hospital admissions due to adverse drug reactions particularly in people over 80 years old.[2] Cardiovascular drugs are responsible for about 20% of these reactions in this age group. Adverse drug reactions can occur even at recommended adult doses. As people become frailer and acquire new diseases a previously safe and tolerated regimen may result in harm. Age-related changes in drug receptors, impairments in homeostatic mechanisms and postural autonomic function are just some of the reasons why older people are more sensitive to the hypotensive effects of many cardiovascular drugs.

Older people are likely to have diseases that result in disease-drug interactions. For example, people with

Table 1. Priorities of treatment for cardiovasclar diseases in healthy and frail older people

Disease	Healthy older person	Frail older person
Hypertension	Decrease risk of vascular events Decrease mortality	Avoid symptoms of hypertension and hypotension
Chronic heart failure	Symptomatic relief Decrease admissions to hospital for decompensated acute heart failure Potential mortality benefit	Symptomatic relief Decrease admissions to hospital for decompensated acute heart failure Avoid symptomatic hypotension and other adverse effects
Anticoagulation for chronic atrial fibrillation	Harm-benefit ratio usually favours anticoagulation	Harm-benefit ratio may favour amtiplatelet drug over anticoagulant
Dyslipidaemia	Decrease risk of vascular events	Maintaining nutition and treating malutrition takes priority over dyslipidaemia

dementia may become more confused if they are prescribed drugs that can cause confusion such as beta blockers. Frail older people with Parkinson's disease often have orthostatic hypotension due to disease-related autonomic dysfunction. They are therefore more likely to come to harm from hypotension when prescribed cardiovascular drugs which lower blood pressure. This problem can be exacerbated by the blood pressure lowering effects of drugs for Parkinson's disease.

In addition, older people on many different drugs (polypharmacy) are at increased risk of adverse events, in part because of the increased likelihood of drug-drug interactions.

To minimise the possibility of adverse drug reactions it is a good idea to take a 'start low, go slow' approach when prescribing. If possible, start only one new drug at a time, at the lowest dose possible and increase the dose slowly while being vigilant for possible adverse effects.

It is important to question and examine older people for possible adverse drug reactions. Often the symptoms can be non-specific such as falls, tiredness or confusion. An adverse drug reaction such as postural hypotension can easily be missed if not looked for. It is important to be aware of the common problems that could be the adverse effects of cardiovascular drugs (see Table 2). Ask specifically about, and look for, these adverse effects. Be particularly aware of drugs that have a narrow therapeutic window or a long half-life such as digoxin and warfarin.

The drug regimen should be easy to follow and, with the help of pharmacists, have packaging, labels and dose administration aids that are easy to use. A general practitioner can order a home medicine review for people living in the community. A similar scheme is funded to encourage a medication management review for patients in residential aged-care facilities.

1. Hypertension

The Hypertension in the Very Elderly Trial (HYVET) found that treating hypertension (systolic blood pressure above 160 mmHg) in patients over 80 years old is beneficial in terms of all-cause mortality, episodes of heart failure and deaths from strokes.[3] However, it is important to be aware that participants

Table 2. Problems with cardiovascular drugs

Problem	Drug
Confusion	beta blockers digoxin HMGCoA reductase inhibitors (statins)*
Cough	ACE inhibitors less common with angiotensin receptor antagonists
Gout	thiazide diuretics loop diuretics
Headache/ flushing	calcium channel blockers
Hyperkalaemia	ACE inhibitors angitensin receptor antagonists aldosterone antagonists
Hypokalaemia	thiazide diuretics loop diuretics
Hyponatraemia	ACE inhibitors thiazide diuretics loop diuretics
Lethargy	beta blockers
Oedema	calcium channel blockers
Postural hypotension	antihypertensive drugs diuretics nitrates
Bleeding	antiplatelet drugs e.g. aspirin, clopidogrel anticoagulants e.g. warfarin, dabigatran and rivaroxaban
Renal	diuretics ACE inhibitors angiotensin receptor antagonists
Myalgia and myopthy	statins
Constipation	calcium channel blockers

* based on case reports

were screened carefully for comorbidity including postural hypotension (systolic blood pressure less than 140mmHg after two minutes of standing was an exclusion criteria). Although patients in the trial were healthier than the general population of the same age, antihypertensive therapy should be considered in this age group if their life expectancy is more than one or two years. However, there will be a proportion of patients, particularly the frail, who will not tolerate treatment or in whom a decision will be made not to treat after weighing up the harms and benefits.

The current National Heart Foundation hypertension guidelines[4] recommend treating patients with grade 2 and 3 hypertension (systolic >160 mmHg or diastolic >100 mmHg). For patients aged 80 and over, the results from HYVET would support this recommendation. However, it is not clear if antihypertensive therapy should be prescribed to patients with grade 1 hypertension (systolic 140-159 mmHg or diastolic 90-99 mmHg). There is no direct clinical trial evidence in people aged 80 and over showing a benefit for treating this range of blood pressure.

The guidelines also recommend antihypertensive treatment regardless of blood pressure in patients with associated conditions such as diabetes, strokes and chronic kidney disease, or evidence of end-organ damage such as proteinuria from chronic kidney disease. It may be reasonable to follow this recommendation, but it is based on extrapolating the evidence from trials in much younger patients. Clinical judgement and common sense are required. For example, most patients over 80 years old will not live long enough for proteinuria to ever progress to clinically significant renal failure.

The National Heart Foundation correctly says that all patients aged 75 years and over can be assumed to have a high absolute cardiovascular risk (more than 15% probability of a cardiovascular event within the next five years) without needing to use a cardiovascular risk calculator. This could be interpreted as a recommendation that all patients aged over 75 years should be prescribed antihypertensives, but there is no direct evidence to support treatment regardless of blood pressure. There is also little evidence that treating hypertension in old age prevents dementia or slows progression in patients with dementia.

Target blood pressure

HYVET had a target blood pressure of 150/80 mmHg. The National Heart Foundation recommends less than140/90 mmHg and less than130/80 mmHg in patients with associated conditions or end-organ damage. 'Lower is better' may not apply to blood pressure in the very old. There is evidence from epidemiological studies in older people that low blood pressure is associated with poorer survival. These studies suggest there is a threshold blood pressure, which varied by study, below which mortality increases.

Choice of drug

Coexisting conditions, tolerability and the potential for adverse effects should guide the choice of antihypertensive drug. In many patients other conditions such as ischaemic heart disease or chronic heart failure will determine what is prescribed. Avoiding the adverse effects of high doses of a single drug is a reasonable rationale for adding a second drug. However, there is no evidence that combination antihypertensive drugs are more effective or safer in older people.

2. Chronic heart failure

A study in the USA suggests that many older patients would have been excluded from clinical trials in heart failure.[5] Only 18%, 13% and 25% of more than 20 000 patients aged over 65 years from a heart failure cohort would have met the enrolment criteria of three major trials in heart failure – SOLVD (ACE inhibitor),[6] MERIT-HF (beta blocker)[7] and RALES (aldosterone antagonist).[8] For example, impaired systolic function was an entry criterion for these trials. However, a large proportion of older people have heart failure with preserved systolic function for which there is little evidence that 'standard' treatments are of benefit.

Choice of drug

In a robust older person with systolic heart failure it is reasonable to try to achieve optimal doses of ACE inhibitors and betablockers, but start at low doses and watch for adverse effects. In frail patients with systolic heart failure the best approach is to try one drug at a time, starting at a low dose, and observe closely for benefit and harm. In many cases, the recommended doses will not be achievable and measured renal function may decline. If the patient's function and health improves, the uncertainty about whether there are mortality benefits at lower doses

is less important. In addition, the decline in measured renal function may not be clinically significant.

In patients with preserved left systolic function, the regimen should focus on minimising the symptoms and signs of heart failure. Diuretics are the mainstay of treatment for relieving symptoms of fluid retention. Age-related decreases in renal function may reduce the efficacy of conventional doses of diuretics so careful upward titration of the dose may be needed. This needs to be balanced with the fact that older people are more at risk of electrolyte disturbances and volume depletion from diuretics. Older people and their carers can sometimes learn to self-adjust the dose of diuretic using weight as a guideline.

3. Atrial fibrillation

Atrial flutter or fibrillation can occur in older people as the result of a transient condition such as an infection. This is important to recognise, as a long-term antiarrhythmic drug may not be required. Chronic atrial fibrillation usually, but not always, requires rate control. Symptomatic improvement should be the goal rather than a specific heart rate. Digoxin and beta blockers are commonly used for rate control in atrial fibrillation.

Digoxin

Digoxin has a narrow therapeutic window. Reduced renal function and a lower lean body mass increase serum digoxin concentrations. A number of commonly used drugs, such as verapamil, amiodarone and diltiazem, can also increase serum digoxin. Electrolyte abnormalities such as hypokalaemia, hypomagnesaemia, hypercalcaemia as well as conditions such as hypothyroidism and myocardial ischaemia can aggravate digoxin toxicity. Health professionals need to be aware that symptoms of digoxin toxicity can occur in the target range. The prescriber should therefore be vigilant in checking for adverse effects such as anorexia, nausea, vomiting, visual disturbances, depression and confusion.

Beta blockers

In patients with renal impairment, use beta blockers with predominantly hepatic elimination (for example metoprolol). For patients with hepatic impairment, use beta blockers with predominantly renal elimination (for example atenolol). Even if liver function tests are normal, there is an age-related decrease in liver blood flow. So if adverse effects such as confusion are thought to be possibly due to a predominantly hepatically eliminated beta blocker, it may be worth a trial of changing to a renally eliminated beta blocker. Less lipid soluble beta blockers (atenolol and bisoprolol) may be less likely to enter the brain so may cause fewer sleep disturbances and nightmares.

Anticoagulation

In carefully selected older patients with non-valvular atrial fibrillation, there is good evidence that oral anticoagulation is better than antiplatelet therapy in reducing the risk of stroke. The clinical dilemma is that older people are at a higher risk of bleeding during anticoagulation. The decision on anticoagulation versus antiplatelet therapy is best made by a doctor who has a comprehensive understanding of the whole patient and is able to take into account factors such as falls risk, bleeding history, potential drug interactions and likely compliance with dose adjustments and INR monitoring. There are a number of bleeding risk scoring systems,[9] but they are not used much in everyday practice. There is no evidence that a lower target INR (<2) is effective or has a lower risk of bleeding than a target of 2-3.

The newer oral anticoagulants, such as dabigatran, may seem to be an attractive alternative to warfarin in older people as regular blood tests are not required. However, there is no antidote or reversal drug if bleeding occurs. In addition, severe renal impairment is a contraindication and any decrease in renal function can increase the risk of bleeding.

Conclusion

Appropriate and safe prescribing of cardiovascular drugs for older people can be challenging. There are many things to take into account when prescribing for older people, especially if they are frail. Tailoring treatment to the individual patient with the aim of doing more good than harm, should be the guiding principle when prescribing cardiovascular drugs to older people.

References

1. Nair BR. Evidence based medicine for older people: available, accessible, acceptable, adaptable? *Australas J Ageing* 2002; **21**: 58-60.

2. Burgess CL, Holman CD, Satti AG. Adverse drug reactions in older Australians, 1981-2002. *Med J Aust* 2005; **182**: 267-70.

3. Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, et al. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 2008; **358**: 1887-98.

4. National Heart Foundation of Australia (National Blood Pressure and Vascular Disease Advisory Committee). Guide to management of hypertension 2008. Updated December 2010. National Heart Foundation; 2010.

5. Masoudi FA, Havranek EP, Wolfe P, Gross CP, Rathore SS, Steiner JF, et al. Most hospitalized older persons do not meet the enrollment criteria for clinical trials in heart failure. *Am Heart J* 2003; **146**: 250-7.

6. SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med* 1991; **325**: 293-302.

7. MERIT-HF Investigators. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF). *Lancet* 1999; **353**: 2001-7.

8. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, et al; Randomized Aldactone Evaluation Study Investigators. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. *N Engl J Med* 1999; **341**: 709-17.

9. NPS MedicineWise. Good anticoagulant practice. Medicinewise News 2013 Feb 4. www.nps.org.au/publications/health-professional/medicinewise-news/2013/good-anticoagulant-practice [cited 2013 Nov 7]

Further reading

1. Hilmer S, Gnjidic D. Statins in older adults. *Aust Prescr* 2013; **36**: 79-82

Vasi Naganathan, *Associate Professor, Centre for Education and Research on Ageing, Sydney Medical School, University of Sydney and Consultant Geriatrician, Concord Hospital, Sydney, Australia.*

Conflict of interest: none declared

This article is reproduced from the *Australian Prescriber* 2013; **36**: 190-194 by prior arrangement, courtesy of *Australian Prescriber.*

Self-assessment questions

Select the **best** response in each question

Question 1

A 38 - year old male wants your opinion regarding regular vitamin E supplementation. He has read that taking high doses of vitamin E can improve cardiovascular health and slow the ageing process. You explain to him that these claims are not based on good evidence. What potential side-effect should this patient be told?

A. Deep venous thrombosis.
B. Hemorrhagic stroke.
C. Night blindness.
D. Peripheral neuropathy.
E. Retinopathy.

Question 2

The benefits of long-term vitamin E supplementation include.

A. Reduced risk of cardiovascular disease.
B. Reduced risk of malignancy.
C. Improved glycaemic control in patients with type-2 diabetes.
D. Reduced risk of pre-eclampsia in pregnancy.
E. None of the above.

Question 3

A 79-year old male with type-2 diabetes has been started on captopril 12.5mg tds for hypertension 4 weeks earlier. His blood reports show that his creatinine has increased from 100 µmol/l (initial visit) to 128 µmol/l (this visit). His blood pressure remains elevated at 150/98 mmHg. Which of the following is the most appropriate course of action?

A. Add amlodipine 5mg once daily and review renal tests in 1 week.
B. Add spironolactone 25mg once daily.
C. Change from captopril to losartan.
D. Stop captopril and initiate amlodipine 5mg once daily.
E. Add amlodipine 5mg once daily and review serum creatinine in 3 months.

Answers to self-assessment questions

Question 1. The best response is **B.** Vitamin E can inhibit platelet aggregation and antagonise vitamin K-dependent clotting factors. Studies have shown that vitamin E supplementation increases the risk for haemorrhagic stroke by 22%.

Question 2. The best response is **E.** Current evidence is not supportive of supplementing vitamin E for preventing and treating several chronic diseases especially cardiovascular diseases. So, prescribing a large dose of vitamin E (400mg) for a longer period may do more harm than good for your patients.

Question 3. The best response is **A.** It is common to see a slight increase in serum creatinine following initiation of an angiotensin converting enzyme inhibitor (ACEI). NICE guidelines recommend that if there is a fall in eGFR of 25% or less and/or there is a rise in serum creatinine of 30% or less, the renal profile can be reviewed in a week with continuation of therapy. However, if hyperkalaemia develops or if the GFR change is greater, the angiotensin converting enzyme inhibitor (ACEI) should be withdrawn.

Dr. Priyanga Ranasinghe MBBS. *Lecturer, Department of Pharmacology, Faculty of Medicine, University of Colombo, Sri Lanka.*

Email: priyanga.ranasinghe@gmail.com

I have no conflicts of interest regarding the above questions and answers.

ISSN 1391-0736

Printed by Ananda Press, Colombo.