

HEALTH SUPPLEMENTS: HOW EFFECTIVE AND HOW SAFE ARE THEY?

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ABSTRACT

About one third of all Singaporeans take health supplements. As health supplements are not subject to the same level of testing as drugs, it is even more important that doctors should be aware of the evidence of their efficacy and safety, particularly as some health supplements interact with drugs. In this paper we review the evidence for some of the more common health supplements found in Singapore and suggest groups of patients that may benefit most from certain health supplements.

SFP 2008; 34(4): 20-23

INTRODUCTION

Based on self-reported intakes from the 2004 National Nutrition Survey, 34.3% of Singaporeans consume health supplements, with females (40.1%) more likely to consume health supplements than males (28.4%). The trend was similar across the three main ethnic groups (Health Promotion Board, 2004). The most commonly consumed health supplements were vitamin C, calcium, multi-vitamin and mineral supplements, botanicals and animal products, and calcium (Health Promotion Board, 2004).

In this paper, we review some of the evidence for the efficacy of various health supplements and provide suggestions on their use in the primary care setting.

EFFICACY OF HEALTH SUPPLEMENTS*Vitamin C*

A meta-analysis of placebo-controlled trials found that prophylactic consumption of 200mg or more vitamin C was not effective in reducing incidence of the common cold in the general population, but was effective among marathon runners and people exposed to extreme cold temperatures (Douglas et al, 2007).

Prophylactic consumption of vitamin C reduced the severity and duration of cold symptoms, but the authors opined that the effect was not clinically significant (Douglas et al, 2007).

High doses of vitamin C (>3g/day) consumed as therapy for cold symptoms had no consistent effect on the duration or severity of symptoms, though more research is required (Douglas et al, 2007).

Implications for Practice

Vitamin C supplements in doses of 200mg or more appear to have little use in preventing or treating cold symptoms. Most patients do not need more than 90mg of vitamin C per day from food or supplements (Health Promotion Board, unpublished), but as health supplements may contain up to 500mg or 1000mg of vitamin C per tablet, a practical limit for intake is no more than 500mg of vitamin C from supplements per day.

Multi-vitamin and mineral supplements

A review of five randomized controlled trials that measured the effect of multi-vitamin and mineral supplements on chronic diseases found that there was no significant effect on the incidence of cancers, cardiovascular disease, hypertension, total mortality rate, cataract and age-related macular degeneration, except for a population of malnourished people in Linxian, China where there was a decreased risk of mortality from cancer and cardiovascular disease (Huang et al, 2006). As the supplement used in the Linxian study was tailor made for the study population, the authors opined that the results could not be extrapolated to the general population consuming those multi-vitamin and mineral supplements available on the market (Huang et al, 2006).

Another meta-analysis of 47 primary and secondary prevention trials of antioxidant supplements and their effect on mortality from all causes with low risk of bias reported that vitamin A, β -Carotene and vitamin E increased overall mortality. Evidence for the effect of vitamin C and selenium on mortality from all causes was inconclusive (Bjelakovic et al, 2007). However, we noted that secondary prevention trials outnumbered primary prevention trials by 2:1, and mortality was not the primary outcome measure for 2/3 of the trials included.

In addition, two large trials have found that β -Carotene increases the risk of developing lung cancer among smokers (Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group, 1994; Omenn et al, 1996), and possibly increases the risk of mortality from cardiovascular disease among women who smoke (Goodman et al, 2004).

Implications for Practice

Although the evidence suggests that certain antioxidant vitamins and minerals increase mortality from all causes, the meta-analysis contains some limitations and it is still unclear if this risk can be applied to the general population. What is more certain is that the evidence does not support the claim that multi-vitamin and mineral supplements are able to reduce the incidence of chronic diseases or reduce the likelihood of death from any cause.

Glucosamine/ Chondroitin sulphate

Earlier studies have suggested that glucosamine and chondroitin preparations were able to treat symptoms of osteoarthritis, but the quality of studies was poor (McAlindon et al, 2000).

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A more recent large randomized controlled trial found that glucosamine and chondroitin sulphate alone or together were not effective in treating pain in the general group of patients, though the two together may provide relief in patients with moderate-to-severe knee pain (Clegg et al, 2006).

Implications for Practice

Glucosamine (500mg) and chondroitin sulphate (400mg) in combination, three times a day may be useful for patients with clinical osteoarthritis and report moderate to severe pain. Clinical osteoarthritis was defined as having knee pain for at least six months and on the majority of days during the preceding month. Pain was defined using the Western Ontario and McMaster Universities Osteoarthritis Index.

Doses of up to 500mg of glucosamine and 400mg of chondroitin sulphate three times a day appear to be safe.

Omega 3 fatty acids (fish oil & α -linolenic acid)

Omega 3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) that are found in fish oil may reduce mortality from cardiac and sudden death, and possibly stroke. Evidence for this effect appears to be stronger for secondary prevention than for primary prevention (Wang et al, 2006), though more recent evidence implies that fish oil may be effective in primary prevention of death from coronary heart disease or sudden cardiac death (Mozaffarian, 2008).

α -linolenic acid (ALA) is found in plant foods (e.g. canola oil, soy foods, linseed oil) and can be converted by the body to EPA and DHA, but the rate of conversion is generally poor at around 5% (Brenna, 2002; Williams & Burdge, 2006). Evidence seems to indicate that ALA supplements are not effective for reducing cardiovascular disease (Hooper et al, 2004; Wang et al, 2006; Wendland et al, 2006).

Implications for Practice

As evidence seems to imply a protective effect of EPA and DHA against heart disease, all patients without heart disease should aim to consume a variety of fish and include a serving of oily fish (e.g. tuna, salmon, mackerel or sardines) twice a week, especially if they have cardiovascular disease risk factors (e.g. high blood cholesterol, hypertension, BMI >27.5, diabetes, etc.). One serving of fish is a palm-sized portion (about 90g). Depending on type, 1 serving of oily fish contains between 0.5-1.5g of EPA and DHA (Kris-Etherton et al, 2002).

Patients who have heart disease should consume 1g EPA + DHA per day, preferably from oily fish, but fish oil supplements can be considered. Fish oil supplements appear to be safe at doses up to 4.8g per day (Kris-Etherton et al, 2002).

For vegetarians, it is suggested that they switch their cooking oils to soybean or canola oil, and have 1 serving of soy products every day to increase intake of ALA and possibly increase synthesis of EPA and DHA (Williams & Burdge, 2006). One serving of soy products is 150g of tofu or similar products.

Ginkgo biloba

Meta-analysis of 29 trials found that Ginkgo biloba was safe

for use, but there was no consistent evidence that administering Ginkgo biloba had any clinically significant effect on people with dementia or cognitive impairment (Birks & Grimley, 2007). Studies included in the meta-analysis did not report significantly higher adverse events from the intervention groups compared to placebo (Birks & Grimley, 2007).

Studies on the effects of Ginkgo biloba on memory and cognitive performance in healthy, young people are mixed. The most recent evidence suggests that acute doses of 120mg of Ginkgo biloba extract can modestly improved memory performance, but have a detrimental effect on the speed of attention task performance (Kennedy et al, 2007). Other recent studies have found Ginkgo biloba extract to be ineffective in young people (Burns et al, 2006) or have raised questions over whether Ginkgo biloba extract can sustain its effect over the longer term (Elsabagh et al, 2005).

A separate meta-analysis found that trials of sufficient quality did not provide enough evidence to support the use of Ginkgo biloba to promote recovery among stroke survivors. Large, high-quality trials are required (Zeng et al, 2005).

Implications for Practice

Evidence does not support the use of Ginkgo biloba to treat dementia or cognitive impairment, to aid in stroke recovery, or to improve memory in younger people. Ginkgo biloba leaf extract of up to 300mg per day appears to be safe for use.

There is some evidence to suggest that ginkgo biloba extract can increase bleeding risk. Caution may be required for patients on anticoagulant drugs (e.g. warfarin), with bleeding disorders, or who are planning surgery or dental work. Ginkgo nuts are toxic when raw and it is suggested that patients limit their consumption even when cooked (Kajiyama et al, 2002).

Garlic

Garlic may have beneficial effect in patients with hypertension and hypercholesterolaemia. Meta-analysis of 11 randomized controlled trials using placebo found that garlic was able to reduce both systolic (-8.4 mmHg) and diastolic (-7.3 mmHg) blood pressure in people with hypertension (Ried et al, 2008). Another meta-analysis of randomized controlled trials with placebo found that garlic could reduce cholesterol levels in people with hypercholesterolaemia, but when limiting analysis to high-quality trials, the reduction was small (-0.11 mmol/L) and not statistically significant (Stevinson et al, 2000). Both sets of authors were of the opinion that more research was required to confirm their findings.

For cancers, increasing intake of garlic by about 16g per week (5-6 cloves) appears to protect against stomach and colorectal cancers, but quality of the data analysed was poor and the result may be confounded (Fleischauer et al, 2000).

Implications for Practice

Current evidence does not support the use of garlic supplements. Garlic appears to be safe for most adults, but as garlic reduces the ability of blood to clot in a manner similar to aspirin. Caution may be required for patients on anticoagulant drugs (e.g. warfarin), with bleeding disorders, or who are planning surgery or dental work.

Soy isoflavones

The American Heart Association review of soy protein and isoflavones (phytoestrogens) found that evidence from 22 randomized trials indicates that isolated soy protein with soy isoflavones, was responsible for a decreased LDL cholesterol, though the effect was small – approximately 3% for an average intake of 50g of soy protein (about 5 servings or 750g of tofu). There were no significant effects on HDL cholesterol, triglycerides, lipoprotein (a), or blood pressure. Nineteen studies of soy isoflavones had no effect on LDL cholesterol and other lipid risk factors (Sacks et al, 2006).

Since soy isoflavones mimic the action of oestrogen in the human body, it has been suggested that soy isoflavones might be able to reduce the risk of breast cancer. Some observational evidence suggests that intake of soy foods, possibly from a young age and at levels usually found in Asian diets, are able to reduce the risk of breast cancer in women (Qin et al, 2006; Wu et al, 2008), but evidence is still mixed (Sacks et al, 2006; Messina & Wood, 2008). There is also no evidence to support a beneficial effect of soy isoflavones for breast cancer patients (Messina & Wood, 2008). Intake of soy isoflavone supplements of <100mg/day does not appear to elicit adverse effects in women or breast cancer survivors not undergoing active treatment (Messina & Wood, 2008).

Implications for Practice

Evidence suggests that soy isoflavone supplements would have little effect on reducing cardiovascular disease risk. There is currently insufficient evidence to make recommendations on soy isoflavone supplements and cancer, though intakes of <100mg/day appear to be safe.

Patients seeking to reduce their risk of cardiovascular disease or breast cancer should be recommended to consume soy products rather than soy isoflavone supplements. One serving of soy products (e.g. 150g of tofu) can safely replace a serving of meat (about 90g) in the daily diet.

WHO SHOULD CONSUME HEALTH SUPPLEMENTS?

Vitamin and mineral supplements should not be used to replace a healthy and varied diet. It is possible to get all nutrients that the body requires from food alone and, in the case of vitamin D, exposing arms and legs to the sun for 5-30 minutes (depending on time of day and skin pigmentation) between 10:00 AM and 3:00 PM twice a week without sunscreen (Holick, 2007).

Figure 1: Groups That May Require Health Supplements

| Group | Supplement | Rationale |
|----------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| Women who plan to conceive | Folic acid (200µg) | Reduces the risk of neural tube defects in the foetus (Pitkin, 2007) |
| Older Adults (≥51 years of age) Older adults who tend to eat less | Calcium (1000mg) Multi-vitamin and mineral supplement | Reduce rate of bone loss (Tang et al, 2007) Such persons may not be able to get enough micronutrients from diet alone |
| People on very-low-calorie diets (<1200 kcal/day) | Multi-vitamin and mineral supplement | Such persons may not be able to get enough micronutrients from diet alone |
| People with heart disease | Fish Oil supplements (1g EPA + DHA) | Reduce recurrence of heart disease (Kris-Etherton et al, 2002) |

Doctors should examine the evidence for efficacy of health supplements and consider factors, such as interaction with other drugs or whether the patient can afford the supplements, before advising patients to begin, continue, or cease intake of health supplements.

Certain groups of patients may benefit from health supplements. A list of such groups is listed in Figure 1.

OTHER SOURCES OF INFORMATION

There are too many health supplements available in the market today for all to be covered in this paper. To find out more about the various types of health supplements, you may wish to visit the following websites:

- NIH Office of Dietary Supplements (<http://ods.od.nih.gov>)
- NIH National Centre for Complementary & Alternative Medicine (<http://nccam.nih.gov>)
- Medline Plus – National Library of Medicine & NIH (<http://www.nlm.nih.gov/medlineplus>)
- US Food and Drug Administration Center for Food Safety and Applied Nutrition (<http://www.cfsan.fda.gov/%7Edms/supplmnt.html>)
- Natural Medicines Comprehensive Database (<http://www.naturaldatabase.com/>)

CONCLUSIONS

This brief review shows that the existing evidence regarding the efficacy and safety of health supplements is still evolving and varies with each supplement. Considering that a third of the population in Singapore take health supplements, it is crucial that doctors keep abreast of the latest research and studies. While it is generally recommended that most healthy people should derive their nutrients from foods and not from health supplements, it is also recognised that health supplements may provide benefits to certain groups of people.

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LEARNING POINTS

- **Unlike medicines, health supplements are subject to industry-driven regulation. Sellers/manufacturers of health supplements take responsibility for the safety and quality of their health supplements.**
 - **Where possible, a person should derive both nutrients and non-nutritive substances from foods and not health supplements. Doctors should advise patients to modify their diets to include food sources containing the required nutrients (e.g. oily fish for EPA and DHA, soy foods for soy protein and isoflavones, milk and dairy products for calcium) before recommending any health supplement.**
 - **Groups that may require vitamin and mineral supplements include pregnant women and women who plan to conceive (folic acid – 200µg), and adults >50 years of age (calcium – 1000mg). Multi-vitamin and mineral supplements may be required for older adults who tend to eat less and people on very-low-caloric diets (<1200 kcal/day).**
 - **Specific botanicals and animal products that may be helpful include glucosamine (500mg) and chondroitin sulphate (400mg) in combination, three times a day for patients with clinical osteoarthritis and who report moderate to severe joint pain. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) may be effective for primary and secondary prevention of heart disease. People with heart disease may benefit from fish oil supplements (EPA + DHA – 1g/day).**
 - **It is important to know where to find information on different health supplements as the amount of evidence available on their efficacy and safety varies with each supplement.**
 - **Doctors should examine the evidence for efficacy and safety of health supplements and consider factors, such as interaction with other drugs or whether the patient can afford the health supplements, before advising patients to begin, continue, or cease intake of any health supplement.**
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