Vitamins, Supplements and Heart Disease

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JACC 2005;46:184-221
Scope of Use

• In 1997, ~15 million adults took prescription medications + vitamins and herbal remedies.

• In 2000, 50% of Americans sought help from an alternative health care provider → ~600 million visits + ~$30 billion.

• In 2004, 36% of Americans used some form of alternative medicine.
Identifying and Understanding the Issues

• No formal training in medical school or residency

• Little solid research has been published in peer-reviewed journals

• Vitamins and herbal supplements are considered “foods” and therefore, there is no regulation of the manufacturing and selling of these therapies.

• No monitoring and evaluation of product and ingredient safety or assurance of product quality.

• Little, yet growing, understanding of the interactions of therapies with traditional cardiovascular medicines.
Traditional Medications

• FDA Process
  – Pre-clinical testing (animals)
  – Phases I (<100 patients)
  – Phase II (100-300 patients)
  – Phase III-IV (hundreds to thousands)

• Post marketing surveillance

• Time to market ~7-10 years with patent protection for 15 years from onset of drug research.

• Average cost per marketed drug ~$10 to 200 million

• 1 in 10 drugs make it to market
Ultimate Goal

• The integration of alternative therapies into traditional medicine must be guided by:
  A. Compassion
  B. Sound scientific evidence
  C. Patient safety
Nutrition

• Diet is the major determinant of cardiovascular health.

• General nutrition affects:
  - Body weight
  - Lipoproteins
  - Blood pressure
  - Blood glucose
  - Endothelial function
  - Inflammation
  - Coagulation
Nutritional Recommendations

• Achieve and maintain ideal body weight by limiting foods high in calories.

• Eat a variety of fruits, vegetables, nuts, soy products, low fat dairy products and whole grain breads, cereals, and pastas.

• Eat baked or broiled fish at least twice a week.

• Choose oils and margarines low in saturated and trans fat and high in omega-3 fat (canola, soybean, walnut and flaxseed oils including those fortified with stanols and sterols).

• Be physically active – exercise 30 minutes daily.

• Minimize salt intake to <2,400 mg per day.
Alcohol

- Epidemiologic studies show a reduction in heart attacks, cardiac events, and coronary-related deaths in patients who drink 2 or fewer drinks daily.

- Mechanisms include HDL raising, changes in inflammatory markers and improvement in insulin resistances.

- At levels of consumption of greater than two drinks/day for men and one drink/day for women all-cause mortality overwhelms the cardioprotective effect.

*Lancet* 2001; 357 (9258): 763-7
Fish Oil
Omega-3 Fatty Acids

• Epidemiologic data suggests improved outcomes in patients who eat fish.

• Four prospective, controlled trials with either fish or omega-3 fatty acid capsules have demonstrated reduced cardiovascular events.

• GISSI study showed that total mortality was reduced by 20% due to a reduction in sudden cardiac death.

Lancet 1989; 2 (8666) : 757-61
Lancet 1999; 354 (9177) : 447-55
Cardiovasc Drugs Ther 1997;11:485-491
Ann Intern Med 1999;130:554-562
Stanol and Sterol Esters

• Consumption of ~2 grams per day of commercially available margarines lower LDL by 9-20%.

• No trials have studied the effects of stanol/sterol esters on cardiovascular risk.

Circulation 2001;103:1177-1179
Miscellaneous

- **Garlic** – 13 randomized, placebo controlled trials showed no significant benefit.

- **Soy** – 38 trials showed reduction in LDL (12.9%) and TG (10.5%), with an increase in HDL of 2.5%

- **Nuts** – Large epidemiologic studies found that eating 5 ounces of nuts per week resulted in a 34% reduction in heart disease.

Ann Intern Med 2000;133:420-429
Archives Internal Medicine 2002; 162: 1382-87
Vitamin E
Proposed Mechanisms of Action

• Improves endothelial function

• Decreases oxidation of LDL

• Inhibits smooth muscle cell growth

• Inhibits platelet adhesion

Clinical Cardiology 1993: 16: 116-118
Vitamin E

- Deficiency is rare

- Natural sources include vegetables, nuts and nut oils
Vitamin E
Primary Prevention Studies

• 2 large epidemiologic studies:
  – Lower cardiac event rates in patients who took vitamin E 100 u per day

• Pooled analysis of 9 studies (293,172 patients):
  – High dietary vitamin E intake was assoc’d with lower CAD risk
  – Supplemental vitamin E did NOT reduce risk of heart disease

NEJM 1993: 328): 1450-1460
NEJM 1993: 328): 1444-1449
Am J Clin Nutr 2004;80:1508-1520
Vitamin E
Secondary Prevention Studies

• **HOPE & GISSI** – no benefit

• **Meta-analysis of 7 studies**
  – 81,788 patients
  – Vitamin E 50 units to 800 units
  – No reduction in mortality or stroke

*NEJM 2000;342:154-160*
*Lancet 1999;354:447-455*
*Lancet 2003;361:2017-2023*
Vitamin C

• Most observational and prospective cohort studies do NOT demonstrate a relationship between vitamin C intake and heart disease.

• No RCTs have specifically examined the effects of vitamin C supplementation on cardiovascular end points.

• Vitamin C supplementation is NOT recommended to prevent heart disease.
Vitamin C and E Heart Protection Study

- 20,536 subjects at high risk for heart disease
- Simvastatin 40 mg +
  - Vitamin E 600 units
  - Vitamin C (250 mg)
  - Beta carotene 20 mg
  - Placebo
- 5.5 years follow-up
- No benefit from combination vitamin therapy

Lancet 2002;360:23-33
Folic Acid, Vitamin B6 & Vitamin B12

• Meta-analysis of 30 trials
  – Elevated homocysteine is less strongly related to ischemic heart disease and stroke risk in a healthy population than has been previously suggested.

• Several trials assessing the benefit of B vitamins are ongoing:

  WACS          SEARCH
  PACIFIC       NORVIT
  CHAOS-2

JAMA 2002; 288:2015-2022
Coenzyme Q10

- Involved in oxidative phosphorylation and the generation of ATP
- Acts as a free radical scavenger and membrane stabilizer

- Two placebo controlled trials
  - Coenzyme Q10 100 mg to 200 mg daily + conventional therapy

- No significant improvement in
  - Left ventricular function
  - Peak oxygen consumption
  - Exercise performance
  - Quality of life in patients with advanced heart failure

JACC 1999;33:1549-1552
Ann Intern Med 2000;132;636-640
Coenzyme Q10

- No mortality benefit has been established
- **Caution advised**
  - CoQ10 + coumadin
  - CoQ10 + statins
Herbal Preparations

• **Hawthorn**
  – Heart Failure
  – Mechanism: positive inotrope + vasodilator
  – Trials underway

• **Ginkgo biloba**
  – Intermittent claudication
  – Mechanism: unknown
  – 8 trials (415 subjects) showed improved pain free walking distance by 34 meters
Summary

• Recommended:

1. Omega-3 supplements
   1-2 grams per day if insufficient from intake from fish

2. Stanol and sterol ester margarine
   2 grams per day

3. Soy foods and protein
   25 grams of soy protein per day
Summary

• Possibly useful:

  Moderate alcohol intake
  • 5 ounces of wine
  • 12 ounces of beer
  • 1.5 ounces of 80 proof whiskey

Folic acid supplementation

  *if homocysteine elevated*
Summary

• Cannot Recommend – *Probably NOT* harmful:

  Folic acid *if homocysteine is not elevated*

  Garlic for lipid lowering

  Soy for lipid lowering

  L-arginine for nutritional support

  CoQ10 for nutritional support

  Hawthorn for mild heart failure

  Ginkgo biloba for peripheral vascular disease
Summary

• Cannot Recommend – *Possibly harmful*:
  
  - Excess doses of Vitamin C  >2,000 mg/day
  - Excess doses of Vitamin E  >1,000 mg/day
  - Beta carotene

• **Take Home Message:**
  Vitamins are best obtained from food sources
Websites

• [http://www.clevelandclinic.org/heartcenter/pub/guide/disease/cad/vitamin_e.htm](http://www.clevelandclinic.org/heartcenter/pub/guide/disease/cad/vitamin_e.htm)


## Diets

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<th>Plan</th>
<th>Fat</th>
<th>Carbohydrate</th>
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<td>High</td>
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<td>Low</td>
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<tr>
<td>Atkins</td>
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*Postgraduate Medicine 2002; 112 (2) : 34-44*