

Are multivitamins safe? March 2009

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We have known for centuries that a diet rich in micronutrients, specifically vitamins, minerals and antioxidants is helpful in preventing a range of diseases, and slowing down the ageing process. It has not been clear however whether extracting those nutrients, concentrating them, and taking them in supplement form has any benefits. Like essential fatty acids, many of these compounds cannot be made in the body and must be ingested in the diet.

Eating a diet rich in vegetables, fruit, nuts, seeds and grains ensures a potent dietary mixture of these essential substances. It also ensures that they are in their natural state, balanced with other food factors essential for their optimal function. The question is should we take vitamin and mineral supplements instead of, or in addition to getting them through our food. There has until recently been very little evidence, despite much interest and research in the area, that these compounds taken as supplements make any difference at all to health. It was assumed that, even if they had no benefit, at least they were doing no harm, and so could be taken almost as a form of insurance against an unhealthy lifestyle.

Several major well-conducted studies published in the early 2000s have cast serious doubt over this assumption, raising the likelihood that taking some antioxidant and multivitamin supplements probably does very real harm.¹⁻⁷ These studies were systematic reviews or meta-analyses of all the published randomised controlled trials (RCTs) on multivitamins and antioxidant supplements in various diseases, and their effect on overall mortality. Meta-analysis is considered the highest form of medical evidence. Researchers analyse pooled data from all comparable trials. This means large patient numbers and greater likelihood of finding real effects rather than those caused by chance.

Vivekananthan's study from the Cleveland Clinic Foundation looked at seven RCTs of vitamin E and eight of beta-carotene supplementation versus placebo or no intervention in heart disease.¹ These studies involved around 220,000 patients. There was no effect from vitamin E supplementation, but rather alarmingly, they found that beta-carotene supplementation resulted in a 7% increase ($p=0.003$) in deaths overall, and a 10% increase ($p=0.003$) in death from heart disease.

Bjelakovic's group from Copenhagen looked at various supplements in the prevention of cancers of the digestive system.^{2,3} They examined trials involving over 170,000 people, and found no benefit of beta-carotene, vitamin A or vitamin E in reducing the incidence of these cancers. However, again, they found an increase in the overall death rate of the people who took these supplements versus those taking placebo. For beta-carotene and vitamin A combination supplements there was a 29% increase in mortality, and for beta-carotene together with vitamin E there was

a 10% increase.

Miller and colleagues from the Johns Hopkins School of Medicine examined nearly 136,000 people in 19 clinical trials, taking either vitamin E alone or in combination with other supplements.⁴ They found an alarming increase in the overall death rate of those taking high dose vitamin E (400IU or more per day), with a clear dose-response relationship, that is, the higher the dose, the more likely that death was the outcome. The size of the increase in risk was alarming, with an extra 39 deaths per 10 000 people ($p=0.035$) taking the high dose supplements compared with those not taking vitamin E.

Lawson from the National Cancer Institute, Bethesda looked at the relationship between multivitamin use and the five year risk of prostate cancer in over 295 000 men in the National Institutes of Health Diet and Health Study who were cancer free at enrolment in 1995 and 1996.⁵ Alarmingly, they found a 32% increased risk of advanced prostate cancer, and a massive 98% increased risk of death in those men taking multivitamin supplements more than seven times a week. Because the study was very large, and was prospective, thus reducing bias from hindsight, the results were very likely to be accurate.

The risk of taking antioxidant vitamin supplements was characterized further by Bjelakovic's group from Copenhagen in 2007.⁶ This major meta-analysis looked at death rate from all causes for people taking antioxidant supplements versus no treatment in 68 trials with nearly a quarter of a million participants. They separated the trials into those of high and low quality. The high quality trials showed a clear increase in risk for those taking the supplements, with a 4% increase in death rate for those taking vitamin E alone, 7% increase for those taking beta-carotene, and 16% increase for those taking vitamin A.

Of the other vitamins, many people in Western countries are deficient in vitamin D as a result of lack of sunlight, as shown on blood testing in several populations. Supplementation according to current evidence is very safe and effective. The levels for the B group of vitamins can be low and special care needs to be taken with B12 levels on a vegetarian diet. Supplementation of the B vitamins is regarded as safe. Vitamin C also is considered to be safe as a supplement according to available evidence. Amongst the minerals and trace elements, many have a relatively small safety margin, that is deficiency is a problem and too much is a problem - as in the notable case of selenium. On a vegetarian diet, iron and zinc levels may be low and warrant monitoring. Australasian soils are notoriously low in selenium and iodine and supplementation may be warranted. In general, modest supplementation with mineral and trace elements appears on the evidence to be relatively safe and may be worth considering if the diet is inadequate.

Overall, the evidence now appears clear. Taking some multivitamins, in particular those containing the antioxidants vitamin E and A (and its precursor beta-carotene), may be problematic and should be avoided by people eating a healthy diet. We

therefore caution against taking regular, long term supplementation with the antioxidant vitamins E and A or any mixture containing them. Supplementation with the other vitamins and with minerals is a complex question for people with major illness, but may be useful in certain circumstances.

Conclusions

1. Food is the best source of human nutrition.
2. People who are actually eating a truly healthy diet and living a healthy lifestyle may not need nutritional supplements.
3. There is strong evidence that taking supplements of vitamins E and A shortens life.
4. More research is needed in this field.
5. There may be a case for a multivitamin/mineral supplement that does not contain vitamins E or A.

References

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