Improvement of Arterial Stiffness by Multi-Nutrient Supplementation

PA Öckerman, MD, PhD[1]

1 Professor emeritus in Clinical Biochemistry, University of Lund, Suddeviksvägen 12, S-475 37 Bohus-Björkö, Sweden, email: pa.oeckerman@telia.com

Abstract *Nutrients like amino acids, vitamins, trace elements, minerals and antioxidants have been found to diminish risk factors for cardiovascular disease (CVD).*
Objectives: To determine if multi-nutrient supplementation mitigates CVD risk factors as determined by pulse wave velocity (PWV) and augmentation index (AIX).
Design: Case series involving 85 patients, age 44–91 years, mean age 67.1 years, involving 51 females and 34 males.
Setting: Private medical practice (Bohus-Björkö, Sweden).
Intervention: Multi-nutrient supplementation was taken orally during two months. Included were recommended dietary intakes of all vitamins, minerals and trace elements, except iron, and higher doses of all B vitamins, vitamin C and E, selenium and magnesium. Other nutrients that were taken orally included L-arginine, fish oil, N-acetylcysteine, pollen extract and probiotics.
Main outcome measures: Arterial stiffness before and after two months of treatment, as determined by PWV and AIX.
Results: Improvement was seen for PWV in 87.1 % and for AIX in 88.2 % of patients. Values for AIX decreased from +5.2 to -14.1 and for PWV from 12.0 m/s to 10.0m/s. The values for PWV can be expressed as a decrease of the biological age of the aorta from 92.9 years to 63.2 years, i.e., a decrease of 29.7 years.
Conclusion: In 85 patients, multi-nutrient supplementation produced highly significant improvements in aortic PWV (i.e., aortic artery stiffness) and AIX (i.e., peripheral artery stiffness and function) in two months. This type of study might be preferable to studies using single nutrients.

Background

Nutrients like amino acids,[1] fatty acids,[2] vitamins,[3-6] trace elements,[7] minerals[8] and antioxidants,[9] as well as food extracts,[10] and nutritional[11-14] and life-style interventions[15] have in some studies been found to diminish risk factors for cardiovascular disease. Often a more critical conclusion has been drawn.[16] With the advent of new evaluation methods, such as aortic arterial stiffness and endothelial function, it has become easier to evaluate the potential impacts of specific interventions like broad spectrum nutrients upon cardiovascular disease (CVD) risk factors.

Methods

Patient selection

All patients were thoroughly examined and diagnosed in the ordinary medical system before seeking advice from an integrative medicine out-patient clinic, where they were routinely tested for aortic arterial stiffness (via measuring pulse wave velocity; PWV) and endothelial function (via measuring augmentation index; AIX) by the Arteriograph. Patients had many different diagnoses and were on many different types of medications. Smokers and cancer patients were excluded from participating in this study. Selected patients were offered treatment with multi-

nutrient supplementation if their PWV and AIX values indicated a possible problem. In total, 85 patients participated, age ranged from 44-91 years, with a mean age of 67.1 years. A total of 51 females and 34 males completed treatment for two months.

Analyses

Assays were made of PWV and AIX using the Arteriograph. Assay values were given as a mean of three measurements at pre-treatment time and after two months of treatment. Figures are given for PWV and AIX as determined by the Arteriograph.[17-22]

Treatment

The patients were prescribed the following multi-nutrient interventions:
1. Antioxidants: 6 tablets/day (**Table 1,** below).
2. Pollen extract: 1000 mg/day from 2 g of granulate (see: www.allergon.se).
3. Vitamin C: 2 g/day in tablet form.
4. L-arginine: 2.25 g/day.
5. N-acetylcysteine: 400 mg/day.
6. Fish oil: 2 g/day comprised of 35% omega-3 essential fatty acids.
7. Extra minerals: potassium 367 mg/day, magnesium 167mg/day, and calcium 317 mg/day.
8. Probiotic preparation: 5 mL/day containing lactococcis lactus, lactobacillus rhamnosus, inulin and dried powder of blueberries (see: www.probac.se).

Results

Tables 2 and **3** (opposite) demonstrate a highly significant effect from the multi-nutrient supplementation on the measured variables.

Discussion

Most studies that have evaluated nutrients in the prevention and treatment of CVD have used single nutrient interventions. The results of such studies have most often been negative. The background for the approach in the present study was that multi-nutrient supplementation might afford synergistic effects, and therefore prevent negative results due to incipient nutrient deficiencies. This philosophy was derived from the fact that

Table 1. Oral Mixture of Broad Spectrum Nutrients (6 tablets)[1]

Vitamins: A 2.4 mg; B_1 20 mg; B_2 20 mg; B_3 40 mg; B_5 48 mg; B_6 24 mg; B_{12} 0.04 mg; C 480 mg; D 0.02 mg; E 200 mg; K 0.12 mg; folic acid 0.4 mg

Minerals and trace elements: Calcium 320 mg; potassium 600 mg; magnesium 200 mg; phosphorus 240 mg; iodine 0.06 mg; copper 2 mg; chromium 0.16 mg; manganese 20 mg; molybdenum 0.06 mg; selenium 0.2 mg; zinc 20 mg

Antioxidants: Lycopene 12 mg; beta-carotene 12 mg; citrus flavonoids 100 mg

Other components: Biotin 0.6 mg; inositol 20 mg; choline 120 mg

[1]Ingredients: Dicalcium phosphate, potassium chloride, ascorbic acid, d-alpha-tocopherol acetate, magnesium oxide, citrus extract, manganese gluconate, extract of tomatoes/lycopene, choline-L-bitartrate, selenomethionine, zink lactate, beta-carotene, calcium-d-pantothenate, nicotinamide, potassium molybdate, pyridoxine hydrochloride, inositol, riboflavine,thiaminehydrochloride, retinyl acetate, copper gluconate, chromium sulphate, cholecalcipherol, d-biotin, folic acid, phyllokinone, iodine, cyanocobalamine.
Also: Microcrystalline cellulose, isomaltose, magnesium stearate, stearinic acid, silicium dioxide, mannitol
Surface treatment: Shellac and talcum

Table 2. Pulse Wave Velocity (PWV, aortic arterial stiffness) expressed as m/sec and as biological age in 85 patients treated with multi-nutrient supplementation

Pre-treatment mean value (reference value: <10.0 m/sec)	Post-treatment mean value (reference value: <10.0 m/sec)	p-value) (p<0.001)
12.0	10.0	<0.001
Pre-treatment biological age (years)	**Post-treatment biological age (years)**	**p-value (p<0.001)**
92.9	63.2	<0.001

Percentage of patients that improved: 87.1%
Mean decrease in biological age among all patients: 29.7 years
Mean decrease in biological age among only the improved patients: 35.8 years

Table 3. Augmentation Index (AIX) in 85 patients treated with multi-nutrient supplementation

Pre-treatment mean value*	Post-treatment mean value*	p-value (p<0.01)
+5.2	-14.1	<0.001

*value calculated from quotient between the pressure peak of the initial and the reflected wave.
Percentage of patients that improved: 88.2%

a diet rich in antioxidants counteracts oxidative stress, but single antioxidants might not. Also, it is general knowledge that antioxidants in combination possess synergistic effects while single antioxidants might not.

The mechanisms behind the therapeutic effects induced by multiple nutrients are most certainly complex. The addition of essential nutrients, that might be wanting, would help to restore adequate or "healthy" endothelial function. Vitamin C and other antioxidants counteract oxidation of cholesterol moieties (e.g., low-density lipoprotein cholesterol), but also diminish free radical activity, since oxidative stress is a well-known CVD risk factor. Chronic low-grade inflammation, common to CVD, rheumatoid arthritis and other degenerative diseases, might also be counteracted by judicious nutritional supplementation. Since multiple nutrient preparations appear to diminish inflammation, they might be of value in other diseases, such as rheumatoid arthritis, in which an increased risk of CVD has been demonstrated.[23]

Conclusion

In 85 patients, multi-nutrient supplementation produced highly significant improvements in aortic PWV (i.e., aortic artery stiffness) and AIX (i.e., peripheral artery stiffness and function) in two months. This type of study might be preferable to studies using single nutrients. Future research is needed and should be performed to find simpler nutritional treatment protocols, assess long-term results, and to determine how diet and specific nutrient preparations influence morbidity and mortality.

Statement of Informed Consent

Informed consent was obtained from all patients who underwent treatment with the prescribed nutrients.

Competing Interests

The author declares that he has no competing interests.

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