

Ascorbic acid inhibits the increase in low-density lipoprotein (LDL) susceptibility to oxidation and the proportion of electronegative LDL induced by intense aerobic exercise

BACKGROUND: We have previously reported the finding of an acute increment in the susceptibility of low-density lipoprotein (LDL) to oxidation and in the proportion of electronegative LDL [LDL(-)] after intense exercise. We have now studied the effect of oral supplementation with 1 g ascorbic acid, immediately before a 4-h athletic race, on the susceptibility of LDL to oxidation, the proportion of LDL(-), and the alpha-tocopherol and lipid peroxides content in LDL, in order to inhibit such deleterious changes, and to confirm the oxidative nature of modifications of LDL induced by exercise. **METHODS:** We studied seven highly trained runners who received a supplement of 1 g ascorbic acid and a control group of seven who did not receive the supplement. The susceptibility of LDL to oxidation was assessed by measurement of conjugated dienes after CuSO₄-induced oxidation, the proportion of LDL(-) was determined by anion exchange chromatography, alpha-tocopherol was quantified by reverse-phase high performance liquid chromatography, and lipid peroxides were measured by the thiobarbituric acid-reactive substances (TBARS) method. **RESULTS:** After exercise, in the control group there was an increase in both the susceptibility of LDL to oxidation (change in lag phase from 51.4 +/- 4.7 min to 47.0 +/- 4.6 min, P < 0.05) and the proportion of LDL(-) (from 11.1 +/- 1.4% to 13.0 +/- 2.2%, P < 0.05), but these did not occur in the ascorbic acid group (change in lag phase from 49.7 +/- 2.3 min to 50.4 +/- 4.2 min, and in LDL(-) from 9.7 +/- 1.7% to 10.1 +/- 1.7%). No significant changes in the absolute amount of LDL alpha-tocopherol were observed after exercise (ascorbic acid group: 6.65 +/- 0.94 mol/mol apoB before the race, 7.13 +/- 0.88 mol/mol apoB after the race; control group: 7.34 +/- 0.69 mol/mol apoB before the race, 7.06 +/- 0.69 mol/mol apoB after the race), but significant differences were found when increments or decrements of alpha-tocopherol were tested (alpha-tocopherol increased 9.9 +/- 11.5% in the ascorbic acid group, and decreased 0.6 +/- 7.3% in the control group; P < 0.018). TBARS did not change after exercise. **CONCLUSIONS:** We conclude that 1 g ascorbic acid inhibits the increase in LDL susceptibility to oxidation after exercise, preventing this acute pro-atherogenic effect. In addition, the observation that LDL(-) enhancement is prevented by ascorbic acid supports the hypothesis that at least some of the circulating LDL(-) originates from oxidative processes. Sanchez-Quesada JL et al. *Coron Artery Dis* 1998;9(5):249-55.

Immune function in aged women is improved by ingestion of vitamins C and E

We have investigated the effects of supplementation of the diet with the antioxidant vitamins C and E on several functions of the immune response of aged women. Ten healthy women and 20 women (72 +/- 6 years old) suffering two diseases often associated with age (10 with major depression disorders, MDD, and 10 with coronary heart disease, CHD) were administered 1 g of vitamin C and 200 mg of vitamin E daily for 16 weeks. Blood samples were collected before and after treatment for measurement of several immunological functions, namely proliferative response of lymphocytes to the mitogen phytohemagglutinin (20 mg/L) and phagocytic functions of polymorphonuclear (PMN) neutrophils, i.e., adherence to vascular endothelium, chemotaxis, phagocytosis of latex beads, and superoxide anion production. In addition, we also determined the levels of serum cortisol and lipid peroxides. Intake of vitamins resulted in a significant increase in the lymphoproliferative capacity and in the phagocytic functions of PMN neutrophils as well as in a significant decrease of serum levels of lipid peroxides and cortisol, both in the healthy aged women and in the aged women with MDD or CHD. These findings suggest an important role of antioxidant supplementation in the improvement of immune function in aged females as well as in the prevention and treatment of specific diseases associated with age that are quite prevalent in the developed countries. de la Fuente M, Ferrandez MD, Burgos MS, Soler A, Prieto A, Miquel J. *Can J Physiol Pharmacol* 1998 Apr;76(4):373-80.

The clinical effects of vitamin C supplementation in elderly hospitalised patients with acute respiratory infections

A randomised double-blind trial involving vitamin C/placebo supplementation was conducted on 57 elderly patients admitted to hospital with acute respiratory infections (bronchitis and bronchopneumonia). Patients were assessed clinically and biochemically on admission and again at 2 and 4 weeks after admission having received either 200 mg vitamin C per day, or placebo. This relatively modest oral dose led to a significant increase in plasma and white cell vitamin C concentration even in the presence of acute respiratory infection. Using a clinical scoring system based on major symptoms of the respiratory condition, patients supplemented with the vitamin fared significantly better than those on placebo. This was particularly the case for those commencing the trial most severely ill, many of whom had very low plasma and white cell vitamin C concentrations on admission. Various mechanisms by which vitamin C could assist this type of patient are discussed. Hunt C, Chakravorty NK, Annan G, Habibzadeh N, Schorah CJ. *Int J Vitam Nutr Res* 1994;64(3):212-9.

Ascorbic acid: effect on ongoing iron absorption and status in iron-depleted young women

The effect of ascorbic acid on iron retention from a diet with predicted low iron bioavailability (containing minimal meat and ascorbic acid) was investigated in iron-depleted premenopausal women. Eleven women were depleted of storage iron (indicated by serum ferritin) through a combination of diet (5.0 mg Fe/2000 kcal for 67-88 d) and phlebotomy. They then consumed a diet containing 13.7 mg Fe/2000 kcal, supplemented with placebo or ascorbic acid three times daily (1500 mg total) with meals for 5.5 wk. Ascorbic acid improved apparent iron absorption (balance method) [38 +/- 2% (means +/- SEM) vs 27 +/- 2%]. Ascorbic acid also improved hemoglobin, erythrocyte protoporphyrins, and serum iron but not hematocrit, serum ferritin, iron-binding capacity, or transferrin saturation. In iron-depleted women consuming a diet with predicted poor iron availability, ascorbic acid supplementation enhanced body iron retention for 5.5 wk. Hunt JR, Mullen LM, Lykken GI, Gallagher SK, Nielsen FH. *Am J Clin Nutr* 1990 Apr;51(4):649-655.

The effect of controlled ascorbic acid depletion and supplementation on periodontal health

To determine if systemic levels of vitamin C influence periodontal health, changes in plaque accumulation, gingival health and periodontal probing depth were measured in healthy subjects housed for 3 months in a nutrition suite that provided controlled periods of ascorbic acid depletion and supplementation. Eleven healthy, nonsmoking men, aged 19 to 28 years, ate a rotating 7-day diet adequate in all nutrients except ascorbic acid. This basal diet, which contained less than 5 mg/day ascorbic acid, was supplemented with 60 mg/day ascorbic acid for 2 weeks, 0 mg/day ascorbic acid for 4 weeks, 600 mg/day ascorbic acid for 3 weeks and 0 mg/day ascorbic acid for 4 weeks. Plasma, urine and leukocyte ascorbate levels, Plaque Index, Gingival Index, Bleeding Index and probing depths were monitored throughout the study. A uniform oral hygiene program was maintained in which oral hygiene instructions were reinforced bi-weekly. Ascorbate concentrations in body fluids and leukocytes responded rapidly to changes in ascorbic acid intake. No mucosal pathoses or changes in plaque accumulation or probing depths were noted during any of the periods of depletion or supplementation. However, measures of gingival inflammation were directly related to the ascorbic acid status. The results suggest that ascorbic acid may influence early stages of gingivitis, particularly crevicular bleeding. Leggott PJ, Robertson PB, Rothman DL, Murray PA, Jacob RA. *J Periodontol* 1986 Aug;57(8):480-5.

Oral vitamin C reduces arterial stiffness and platelet aggregation in humans

Atherosclerosis is associated with stiffening of conduit arteries and increased platelet activation, partly as a result of reduced bioavailability of nitric oxide (NO), a mediator that normally has a variety of protective effects on blood vessels and platelets. Increased levels of oxygen free radicals are a feature of atherosclerosis that contributes to reduced NO bioavailability and might lead to increased arterial stiffness and platelet activation. Vitamin C is a dietary antioxidant that inactivates oxygen free radicals. This placebo-controlled, double-blind, randomized study was designed to establish whether acute oral administration of vitamin C (2 g), would reduce arterial stiffness and in vitro platelet aggregation in healthy male volunteers. Plasma vitamin C concentrations increased from 42 +/- 8 to 104 +/- 8 microM at 6 h after oral administration, and were associated with a significant reduction in augmentation index, a measure of arterial stiffness (by 9.6 +/- 3.0%; p = 0.016), and ADP-induced appears to have beneficial effects, even in healthy subjects. The mechanism responsible is likely to involve protection of NO from inactivation by oxygen free radicals, but this requires confirmation. If similar effects are observed in patients with atherosclerosis or risk factors, vitamin C supplementation might prove an effective therapy in cardiovascular disease. appears to have beneficial effects, even in healthy subjects. The mechanism responsible is likely to involve protection of NO platelet aggregation (by 35 +/- 13%; p = 0.046). There was no change in these parameters after placebo. Vitamin C, therefore,

from inactivation by oxygen free radicals, but this requires confirmation. If similar effects are observed in patients with atherosclerosis or risk factors, vitamin C supplementation might prove an effective therapy in cardiovascular disease. Wilkinson IB, Megson IL, MacCallum H, Sogo N, Cockcroft JR, Webb DJ. *J Cardiovasc Pharmacol* 1999 Nov;34(5):690-3.

The effectiveness of vitamin C in preventing and relieving the symptoms of virus-induced respiratory infections

BACKGROUND: An ever increasing demand to evaluate the effect of dietary supplements on specific health conditions by use of a "significant scientific" standard has prompted the publication of this study. **OBJECTIVE:** To study the effect of megadose Vitamin C in preventing and relieving cold and flu symptoms in a test group compared with a control group. **DESIGN:** Prospective, controlled study of students in a technical training facility. **SUBJECTS:** A total of 463 students ranging in age from 18 to 32 years made up the control group. A total of 252 students ranging in age from 18 to 30 years made up the experimental or test group. **METHOD:** Investigators tracked the number of reports of cold and flu symptoms among the 1991 test population of the facility compared with the reports of like symptoms among the 1990 control population. Those in the control population reporting symptoms were treated with pain relievers and decongestants, whereas those in the test population reporting symptoms were treated with hourly doses of 1000 mg of Vitamin C for the first 6 hours and then 3 times daily thereafter. Those not reporting symptoms in the test group were also administered 1000-mg doses 3 times daily. **RESULTS:** Overall, reported flu and cold symptoms in the test group decreased 85% compared with the control group after the administration of megadose Vitamin C. **CONCLUSION:** Vitamin C in megadoses administered before or after the appearance of cold and flu symptoms relieved and prevented the symptoms in the test population compared with the control group. Gorton HC, Jarvis K. *J Manipulative Physiol Ther* 1999 Oct;22(8):530-3.

Vitamin C improves endothelium-dependent vasodilation by restoring nitric oxide activity in essential hypertension

BACKGROUND: Essential hypertension is associated with impaired endothelium-dependent vasodilation. Inactivation of endothelium-derived nitric oxide by oxygen free radicals participates in endothelial dysfunction in experimental hypertension. To test this hypothesis in humans, we evaluated the effect of antioxidant vitamin C on endothelium-dependent responses in essential hypertensive patients. **METHODS AND RESULTS:** In 14 healthy subjects (47.1±4.8 years; blood pressure, 120.6±4.5/80.9±3.5 mm Hg) and 14 essential hypertensive patients (47.3±5.1 years; blood pressure, 153.9±7.1/102.3±4.1 mm Hg), we studied forearm blood flow (strain-gauge plethysmography) modifications induced by intrabrachial acetylcholine (0.15, 0.45, 1.5, 4.5, and 15 microg x 100 mL(-1) x min(-1)) or sodium nitroprusside (1, 2, and 4 microg/100 mL forearm tissue per minute), an endothelium-dependent and -independent vasodilator, respectively, in basal conditions and during infusion of intrabrachial vitamin C (2.4 mg/100 mL forearm tissue per minute). In hypertensive patients but not in control subjects, vitamin C increased (P<0.01) the impaired vasodilation to acetylcholine, whereas the response to sodium nitroprusside was unaffected. Moreover, in another 14 hypertensive patients (47.1±5.2 years; blood pressure, 155.2±6.9/103.7±4.5 mm Hg), the facilitating effect of vitamin C on vasodilation to acetylcholine was reversed by N(G)-monomethyl-L-arginine (100 microg/100 mL forearm tissue per minute), a nitric oxide synthase inhibitor, suggesting that in essential hypertension superoxide anions impair endothelium-dependent vasodilation by nitric oxide breakdown. Finally, because in adjunctive 7 hypertensive patients (47.8±6.1 years; blood pressure, 155.3±6.8/103.5±4.3 mm Hg), indomethacin (50 microg/100 mL forearm tissue per minute), a cyclooxygenase inhibitor, prevented the potentiating effect of vitamin C on vasodilation to acetylcholine, it is possible that in essential hypertension a main source of superoxide anions could be the cyclooxygenase pathway. **CONCLUSIONS:** In essential hypertensive patients, impaired endothelial vasodilation can be improved by the antioxidant vitamin C, an effect that can be reversed by the nitric oxide synthase inhibitor N(G)-monomethyl-L-arginine. These findings support the hypothesis that nitric oxide inactivation by oxygen free radicals contributes to endothelial dysfunction in essential hypertension. Taddei S, Viridis A, Ghiadoni L, Magagna A, Salvetti A. *Circulation* 1998 Jun 9;97(22):2222-9.