Antioxidant Status In Periodontitis In Asymptomatic Hypercholsterolemic Subjects

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Citation

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Abstract

An imbalance between antioxidant and oxidant-generating systems leading to an oxidative stress has already been proposed in the pathogenesis of atherosclerosis. In the present study, the antioxidant status in 20 men with periodontitis and asymptomatic hypercholesterolemic (HC) was compared with 16 periodontitis normocholesterolemic (NC) men. HC had significantly lower vitamin E, superoxide dismutase and glutathione levels as compared to NC. Serum lipid peroxidation product, malonaldehyde (MDA) levels were significantly higher in HC as compared to NC. These observations demonstrate altered antioxidant status in asymptomatic HC and low vitamin E detected in HC supports the hypothesis that vitamin E deficiency manifests in the early stage of atherosclerosis and might be the most sensitive parameter for this.

INTRODUCTION

Accumulating evidence suggests that alterations or disturbances in defensive antioxidant system may contribute to or exacerbate the development of atherosclerosis.[1,2] The so-called “oxidation hypothesis” states that the oxidative modification of LDL (or other lipoproteins) is import ant and possibly obligatory in the pathogenesis of the atherosclerotic lesions.[3,4] The antioxidant defenses that prevent oxidation of LDL need to be defined. The antioxidant content of the LDL particle is critical for its protection[5] and the most abundant natural antioxidant in LDL is alpha-tocopherol.[6] The potential antiatherogenic role of vitamin E has been evaluated from epidemiological studies.[7] It has been reported that in hypercholesterolemia, erythrocyte vitamin E content was decreased although their plasma vitamin E concentration was unchanged compared with normocholesterolemic men.[8] Also, erythrocyte enzymes superoxide dismutase (SOD) and glutathione peroxidase (GPx) contribute to the cell antioxidant defense mechanisms. Decrease in SOD and/or GPx activities has been described in stable angina and coronary heart disease.[8] While increased SOD was found in unstable angina reflecting an adaptive induction of the enzyme in order to limit the excess free radical production.[9] All these results are available for subjects with symptomatic cardiovascular diseases, but few subjects investigated the antioxidant status in a stage of preclinical disease.

The present study was planned to investigate the antioxidant status in subjects free from any symptomatic cardiovascular diseases, but with a well-established cardiovascular risk factor, hypercholesterolemia (HC), compared with periodontitis with normocholesterolemic subjects (NC).

MATERIAL AND METHODS

The study was carried out in 20 subjects with a total cholesterol level > 240 mg/dl (Periodontitis with hypercholesterolemic HC) and they were compared with 16 Periodontitis with NC subjects. All the subjects were free of secondary hypercholesterolemia, hypertriglyceridemia (TG > 175 mg/dl), renal failure, diabetes mellitus or history of myocardial infarction, stroke or intermittent claudication and were not taking any vitamin supplements or lipid-lowering drugs.

Overnight fasting venous samples were drawn. Serum total cholesterol and triglycerides were determined enzymatically. Also, serum malonaldehyde $(MDA)_{10}$, vitamin E_{11} were analyzed. SOD activities were measured by Misra and Fridovich method.[12] Glutathione levels were analyzed by Beutler's method.[13] The vitamin E total lipid ratio was calculated. Data is obtained was analyzed statistically using student's t-test.

RESULTS

Serum lipid peroxidation product MDA levels were significantly higher in HC as compared to NC (Table I, p <

0.05). On the other hand, antioxidant defenses: vitamin E, SOD and GSH were significantly lower in HC compared with NC. Vitamin E: total lipids ratio was lower in HC as compared to NC.

Figure 1

Table 1: Parameters of oxidative stress (mean + SD)

	HC (n=20)	NC (n=16)
Vitamin E (umol/L)	19.93 ± 2.53	25.75 ± 2.84
SOD (EU/L)	183 ± 2.51	266.12 ± 6.09
MDA (nmol/ml)	0.97 ± 0.27	0.76 ± 0.02
GSH (mg/dl)	45.5 ± 6.8	40.3 ± 11.6*
Vitamin E/Total lipids (umol/mmol)	5.84 ± 0.17	7.57 ± 6.26

Values are significant at all levels ($p<0.05$) except*

DISCUSSION

The present study was designed to assess antioxidant status in subjects free from asymptomatic cardiovascular disease, but with a well established cardiovascular risk factor, hypercholesterolemia (HC), compared with normocholesterolemic (NC) subjects. The vitamin E concentrations, expressed as umol per mmol of cholesterol plus triglyceride, were significantly lower in HC compared with NC. Our findings arte consistent with those reported in literature.[8] Vitamin E localizes mainly to lipoproteins and membranes, where it serves to scavenge lipid peroxyl radicals.[6] Despite this activity, atherosclerosis is characterized by lipid peroxidation within the vascular wall even in the presence of alpha-tocopherol independent of its effect to inhibit lipid peroxidation. This is shown in a report, where depleting the diet of total tocopherols in rabbits resulted in a dose-dependent impairment of NO-mediated relaxation upon exposure to OX-LDL.[15] In contrast, vessels containing abundant alpha-tocopherol content were markedly resistant this effect OX-LDL.[15]One hallmark of the atherosclerotic plaque is proliferation of vascular smooth muscle. Patients who demonstrate rapid lesion progression also exhibit excess cardiovascular events.[15]Considerable in-vitro data indicate that vitamin E inhibits the proliferation of smooth muscle cells.[16] And reports suggest that alpha-tocopherol inhibits smooth muscle cell proliferation principally as a consequence of protein kinase C inhibition.[16] In the setting of atherosclerosis, inhibition of protein kinase C by vitamin E would be expected to maintain normal vascular homeostatis and thus reduce the clinical incidence of cardiovascular disease.

Also, SOD activities were significantly lower in HC compared with NC and GSH content was lower in HC, but, it was statistically insignificant. Several studies have indicated that superoxide production is elevated in atherosclerotic vessels.[17]This increased production of superoxide has been shown to interfere with EDRF-dependent relaxations of vessels.[17]Intriguingly, administration of CuZn-SOD encapsulated in liposomes results in an increased level of SOD activity in the extracellular matrix.[17]This elevation in SOD activity augments EDRF-dependent relaxation in atherotic vessels. Finding of low GSH levels in HC in addition to elevated lipid peroxidation products suggest existence of oxidative stress in HC subjects.

These results demonstrate altered antioxidant status in Periodontitis with asymptomatic HC. The decreased vitamin E detected in HC supports the hypothesis that low vitamin E manifests in the early stage of atherosclerosis. Measures that decrease pro-oxidant stimuli or enhancement of antioxidant defenses may reduce risk of clinical events from atherosclerosis, however, interventional trials only support a role for vitamin E in this regard.

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