ORIGINAL ARTICLE

Correlation Between Dehydroepiandrosterone Sulfate (DHEA-S) and Coronary Artery Disease

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- **Abstract**

Background-Dehydroepiandrosterone (DHEA) or it's sulfate derivative (DHEA-S) is the major C19 steroid hormone secreted by the adrenal cortex. It has been claimed that it has an inverse correlation with atherogenesis through its antiproliferative effect. The aim of this study is to examine the effect of DHEA-S on coronary artery disease(CAD).

Material and Method-In a prospective randomized study 202 patients with possible coronary artery disease who underwent coronary angiography between January 1999 and June 1999 were studied. They were allocated into two groups, group 1 (n=142, female: 39, male: 103) included patients who had more than 75 percent cross sectional area narrowing of at least one coronary artery, and group 2 (n=60, female: 28, male: 32) included patients who had no coronary artery disease. The age range was 18-75 years, and it was matched between the two groups. Level of DHEA-S (measured by two different methods; ELISA and RIA), fasting blood sugar, and full lipid profile (TG, total cholesterol, LDL-C, HDL-C) were measured in both groups. Other major coronary risk factors were also compared between the two groups.

Results-The level of DHEA-S had an inverse linear correlation with age ($r=-0.34$ and $p<0.01$). There was no statistically significant correlation between the level of DHEA-S and coronary artery disease in different age groups in males or females. Likewise, there was no statistically significant correlation between the level of DHEA-S and blood sugar ($p=0.08$), HDL ($p=0.41$), LDL ($p=0.09$), body mass index ($p=0.4$), hypertension and current smoking.

Conclusion-The present study does not confirm an inverse correlation between DHEA-S and coronary artery disease.

Keywords • DHEA-S • coronary artery disease • serum lipid levels

Introduction

Atherogenesis has been shown to be a proliferative process similar to carcinogenesis.[1] Proliferative diseases caused by mononuclear cells are regulated by growth factors.[2] DHEA-S, unlike other androgens is not carcinogenic and has been shown to inhibit the process of atherosclerosis in experimental animal models.[3] The serum level of this hormone increases with age, reaching a maximum at 25 years[5] and subsequently diminishes by aging due to decreased synthesis.[6] Human studies have revealed a relationship between the lipid profile and serum DHEA-S concentration[8], especially a high level of LDL-C, which had an inverse relationship with DHEA-S concentration.[9] Epidemiological surveys have demonstrated that serum DHEA-S level decreases with aging, therefore, DHEA-S is sometimes referred to as an "age discriminator" and plays an important role in the aging process. Studies on experimental animal models, showed that mice fed with DHEA-S not only had a longer life span, but also had improved facial characteristics such as hair thickness and appearance.[10] Biochemically, an important function of DHEA-S is its ability to improve lipid profile in experimentally induced atherosclerosis in animals. Thus when animals with a high total cholesterol and LDL-C were fed with DHEA-S, there was a dramatic decrease in TC, LDL-C and VLDL-C levels, which resulted in reduction of atherosclerosis.[11] Some investigators have reported a link between diabetes and the therapeutic effects of DHEA-S on obesity.[13,14] The inhibition of conversion of fibroblasts to adipocytes by DHEA-S has been demonstrated in cell culture.[15] Many studies have been done to evaluate the relation between DHEA-S level and coronary artery disease. Some studies have confirmed this relation[16,17,18], and others have rejected such a

relationship.[20,21] The present study represents a compendium of measurement of various parameters in relation to different effects of DHEA-S on the lipid profile, blood sugar, aging, obesity, smoking and hypertension in a relatively large number of CAD patients, and angiographically confirmed normal individuals.

Materials and Methods

In a prospective randomized study, 202 patients with possibility of CAD who underwent coronary angiography between January-June 1999 were selected. They were allocated into two groups. Group one consisted of 142 patients (male: 103, female: 39) who had more than 75 percent cross-sectional area narrowing of at least one coronary artery and group two, which consisted of 60 persons (male:32,female:28) with angiographically confirmed normal coronary arteries. The age range was 18-75 years, which was matched between the two groups. Patients receiving digoxin were excluded from the study because of probable interaction between digoxin and DHEA-S assay. DHEA-S level was measured by two different methods, first by RIA (RA-1000 automatic analyzer, Technicon Co, and Kontron gamma counter) and then by the ELISA method. Results of analysis were almost the same for both ELISA and RIA methods, so we considered ELISA values in the following table. Various blood parameters such as fasting blood sugar, TG, total cholesterol, LDL-C, HDL-C were measured and compared between the two groups.

Other major coronary risk factors such as smoking, hypertension (systolic or diastolic), and obesity (body mass index) were also compared between the two groups. Data were analyzed by student t-test, chi-square test, correlation coefficient and analysis of variance (ANOVA) through SPSS software.

Results

The average age was 54.9 years in group one and 53.2 in group two without statistically significant differences (t=-1.69, p=0.27).

As shown in Table 1, coronary disease cases had significantly higher mean values of LDL-C, total cholesterol, FBS, TG, and lower levels of HDL. BMI was not significantly different between CAD cases and controls.

Sex and age adjusted mean DHEA-S levels measured by the ELISA method did not differ significantly between coronary artery disease cases and controls when compared in each age group and each sex (Table 2). There was no significant correlation between the level of DHEA-S and the number of involved coronary vessels (F=0.451, p=0.7). Rechecking the DHEA-S values by the RIA method and statistical analysis again showed no statistically significant difference between DHEA-S in CAD cases and controls.

Among the patients with angiographically proven CAD, there was no statistically significant difference in the mean DHEA-S level between high (FBS = 126) and normal (FBS < 126) fasting blood sugar groups.

There was no significant relationship between smoking, history of hypertension and serum DHEA-S level, in different age groups in either males or females with the exception of a significantly higher DHEA-S level in smokers aged 31-40 years Regression analysis showed an inverse linear correlation between the level of DHEA-S and age (r = -0.34, p<0.01), but there is no correlation between DHEA-S level and serum lipoproteins or body mass index.

Discussion

In the present study there was no association between DHEA-S and presence of coronary artery

disease. No association was found between the levels of DHEA-S and extent of coronary artery disease defined by coronary arteriography.

Considering other coronary risk factors such as serum lipoproteins, fasting blood sugar, body mass index, smoking and hypertension, no correlation was found between these risk factors and DHEA-S levels. The only coronary risk factor that had an inverse correlation with DHEA-S was age.

Earlier reports relating DHEA S and urinary 17-ketosteroids (a strong correlate of DHEA-S) to history of myocardial infarction and fatal coronary heart disease are inconsistent. Some studies have shown lower DHEA-S levels in patients with coronary artery disease[7,16-18], whereas other studies did not show such a relationship when adjustment was made for other coronary risk factors.[20,21] Even a unique study by Lacroix et al. showed no relation between DHEA-S level prior to death and the extent of atherosclerosis at autopsy.[4]

In our study there was no association between fasting blood sugar and DHEA-S. An inverse association of plasma DHEA-S with fasting plasma glucose was observed among men in Barrett-Connor et al's prospective study, but the association was weak and not statistically significant.[19]

A Japanese study[8] however, showed an inverse correlation between DHEA-S level and LDL-C, and a linear relation with HDL-C. Our study and Lacroix et al study[4] failed to show such a relationship.

The present study is in agreement with several past studies that have documented a marked decrease in DHEA-S level with advancing age.

There are several reports, which show higher levels of DHEA-S among current smokers.[19] Our study however, did not show such a relation except in males aged 31-40 years

In our study, there was no prospective role for DHEA-S in hypertension. Although a Japanese study showed an antihypertensive effect for DHEA-S in rats[22], no human study showed such a relationship.

The antihypertensive effect of DHEA-S has been reported in rats[22], but this effect has not been configured in human studies. Our study also failed to show any correlation between hypertension and DHEA-S.

In conclusion, in the present study, lower DHEA-S levels were not significantly related to the incidence of coronary artery disease, nor with the extent of coronary involvement. Among the coronary risk factors only age was inversely related with this weak androgen. The present findings argue against an important role for DHEA-S in coronary disease pathology or prevention.

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