ASSOCIATION OF SERUM ANTIOXIDANTS AND RISK OF CORONARY HEART DISEASE IN SOUTH INDIAN POPULATION

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ABSTRACT

BACKGROUND AND AIM: Higher prevalence of coronary heart disease (CHD) has been reported in south Indian population, which cannot be accounted for by the traditional risk factors like hyperlipidemia. Identification of new risk factors may help in treatment and prevention of CHD in this part of the world. In an attempt to investigate the causes of increased incidence of CHD in this part of the world, we intended to look for oxidative stress in our patients as a possible risk factor. As an initial step in this perspective, a case-control study was conducted to find out the serum antioxidant levels and their association with CHD in south Indian population. SETTING AND DESIGN: A tertiary care hospital; Case-control study. MATERIALS AND METHODS: One hundred thirty nine angiographically proven CHD patients (aged 29-75 years) were studied against 59 population based healthy controls (aged 29-72 years) free of CHD. Fasting serum cholesterol, triglycerides, HDL cholesterol, erythrocyte and plasma glutathione peroxidase and superoxide dismutase were estimated on automated clinical chemistry analyzer. LDL cholesterol and VLDL cholesterol were calculated. Vitamins A and E were estimated using high performance liquid chromatography (HPLC). STATISTICAL ANALYSIS: Unpaired t test was used to compare means. Binary logistic regression was done to find out the association between dependent and independent variables. RESULTS: Significantly higher levels of Total Cholesterol/HDL cholesterol and LDL cholesterol/HDL cholesterol ratio and lower HDL cholesterol levels were observed in patients when compared to controls. No significant difference of plasma and erythrocyte glutathione peroxidase and superoxide dismutase activities was observed between patients and controls. Significantly lower levels of vitamin E in patients than in controls was observed (P<0.001). Serum vitamin E was inversely associated with coronary heart disease even after controlling for age and other coronary risk factors (Odds ratio 0.898, 95% CI 0.826-0.976 P=0.01). CONCLUSIONS: The results of present study suggest that deficiency of vitamin E may be an independent risk factor of CHD. This study brings out the need for long-term monitoring of vitamin E supplementation as a preventative measure for CHD in the population studied.

KEY WORDS: Coronary heart disease, Lipids, Lipoproteins, Antioxidants, South India.

INTRODUCTION

Coronary heart disease (CHD) is a leading cause of morbidity and mortality in developed countries and is emerging as an epidemic in developing countries. It is predicted that there will be an increase of 111% in cardiovascular deaths in India by the year 2020 when compared to the year 1990. This is much higher than that predicted to any other region both in Asia as well as outside Asia. In India, the prevalence of CHD is much higher in south when compared to north India. This high prevalence warrants probing into the presence of various risk factors and their association with CHD. Traditional risk factors like serum cholesterol, blood pressure and smoking account for not more than 50% difference in mortality of CHD. This led to studies on newer risk factors like fibrinogen, Lp(a), plasminogen activator, antioxidants etc. Harman first suggested oxidation of biopolymers as etiology in aging. Oxidative modification hypothesis of atherosclerosis originated with the observation of Goldstein et al. Oxidized LDL has been identified in atherosclerotic lesions. This has prompted the study of antioxidants in the prevention of the initiation and progression of cardiovascular disease. Descriptive, case-control and prospective cohort studies have found inverse associations between the frequency of coronary heart disease and dietary intake of antioxidant vitamins. Case-control studies have shown low levels of serum antioxidants in CHD patients when compared to controls and suggested the role of Vitamin E in prevention of CHD.

In India Dube et al (Jaipur), Nand et al (Haryana) and Singh et al (Moradabad) have reported deficiency of serum vitamin E levels in CHD patients. In one study efficacy of antioxidant vitamins was tested on serum lipid profile and lipid peroxide levels in a clinical trial which lasted for 30 days. Decreased lipid peroxide levels were observed in supplemented group as compared to placebo group.

But the results of the prospective studies have been equivocal. As a result some considered this as a set back for antioxidant therapy as a preventive measure for CHD in the population studied. But the results of the prospective studies have been equivocal. As a result some considered this as a set back for antioxidant therapy as a preventive measure for CHD in the population studied. Deakin et al have also confirmed that antioxidant intake did not influence the risk of myocardial infarction in patients undergoing coronary artery surgery.

In an attempt to investigate the causes of increased incidence of CHD in this part of the world, we intended to look for oxidative stress in our patients as a possible risk factor. As an initial step in this perspective, a case-control study was conducted to find out the serum antioxidant levels and their association with CHD in south Indian population.
this part of world.

**MATERIALS AND METHODS**

One hundred thirty nine consecutive patients attending cardiology clinic from November, 2000 to November, 2002 and willing to get enrolled in the study formed the patient group. Coronary heart disease status was confirmed by angiographic evidence. The patient group included 79 smokers, 66 diabetics and 51 hypertensives. Fifty patients had a family history of CHD. Age of the patients ranged from 29-75 years. Patients with pancreatic insufficiency, cystic fibrosis, betalipoproteinemia or small intestinal resection were excluded. Fifty nine population-based controls free of clinical CHD (substantiated by 12 lead rest ECG and history) were included in the study. Their age ranged from 29-72 years. An ethics committee of our Institute cleared the protocol for execution of the study. Informed consent of the subjects was taken for participation in the study.

Fasting blood samples were drawn from subjects who were on 12 hour fasting. Triglycerides, total cholesterol (total-C) and high density lipoprotein cholesterol (HDL-C) were estimated using commercial kits on the synchro cx4 analyzer from Beckman Instruments Inc., California, USA. Erythrocyte and plasma glutathione peroxidase and superoxide dismutase activities were measured using Ransel and Ransod kits (Randox Laboratories Limited Crumlin, UK) on the same analyzer. Low density cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) were calculated using Friedewald’s formula. Total-C/HDL-C and LDL-C/HDL-C ratios were calculated. Serum Vitamin A and E were measured simultaneously by high performance liquid chromatography. Hemoglobin was estimated by the cyanomethemoglobin method using commercial kits.

**Statistical Analysis**

II continuous variables except superoxide dismutase, plasma glutathione peroxidase showed skewness and hence a non-parametric test, Mann-Whitney U test, was used to compare means. Logistic regression analysis was done to find out the association of dependent variable (CHD) and independent variables using the forward stepwise likelihood ratio method. All statistical analysis were done using windows based SPSS version 11.5.

**RESULTS**

Mean ± S.D values of demographic, lipid and lipoprotein parameters are factors presented in Table 1; serum antioxidant levels in patients and controls are shown in Table 2.

Total-C/HDL-C and LDL-C/HDL-C ratio (P<0.001) were significantly higher and HDL-C (P<0.002) levels were lower in patients when compared to controls.

Significantly lower levels of vitamin E in patients than in controls (P<0.001) were observed. No significant difference of serum and erythrocyte glutathione peroxidase activity and superoxide dismutase activity and serum levels of vitamin A were observed between patients and controls.

**DISCUSSION**

An important implication of oxidative modification hypothesis of atherosclerosis is that antioxidants may inhibit atherogenesis, through mechanisms like protection of LDL against oxidative modification. Antioxidant enzymes are present in small amounts only in plasma and other external fluids. Besides these, antioxidants like Vitamin E are of major importance.

Increased prevalence of coronary heart disease necessitated the intervention that can reduce the risk of CHD. Hence, correspondingly greater attention is being focused on prevention of CHD. In this area antioxidants may serve an important role.

Activity of glutathione peroxidase was shown to be increased in blood and decreased in erythrocyte, whereas decreased or no change in super oxide dismutase was reported in patients than in controls in earlier studies. Our study did not reveal any change in the antioxidant enzymes of blood in patients with CHD when compared to the control group. Also, administration of antioxidant enzymes to improve the antioxidant defense has its own practical implications. Hence the attention logically gets diverted towards the antioxidant vitamins. Decrease or no change in concentration of vitamin A was observed in
Increased serum vitamin E levels may be due to the reduced intake or smoking. Reduced levels of vitamin E may also be due to the increased requirement of vitamin E in pro-oxidant milieu with enhanced free radical status, leading to the increased lipid peroxidation, a resultant depletion of free radical scavenger and antioxidant reserves of the body. Esterbauer et al. have reported that endogenous antioxidants, mainly tocopherol, contained in LDL particles are rapidly consumed after induced oxidation and propagation of the oxidative process doesn’t begin until antioxidant molecules are largely exhausted. Low levels of vitamin E was associated with increased risk of CHD.

Significant inverse association of vitamin E and CHD was observed in studies conducted in India and abroad. In our study also we have observed significant inverse relation of serum vitamin E with CHD after adjustment for age, sex, smoking, diabetes, hypertension, family history of CHD, lipids and lipoproteins (Odds ratio 0.898, 95 CI% 0.826-0.976 P<0.01).

Diabetes, hypertension and smoking, which are known to produce oxidative stress are present in the patients studied and might have contributed to the low levels of vitamin E observed in our study. However, the significant association observed between vitamin E levels and CHD even after correcting for these factors points towards a greater attention to this and treat this as an independent risk factor.

Further efforts are on to identify the local causes of low vitamin E levels and the effects of vitamin supplementation on the CHD incidence.

REFERENCES

IMMUNOGENICITY AND SAFETY OF HEPATITIS B VACCINE (SHANVAC-B) USING A NOVEL PRE-FILLED SINGLE USE INJECTION DEVICE UNIJECT IN INDIAN SUBJECTS

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ABSTRACT

BACKGROUND: Hepatitis B is a major public health problem, which has now been controlled to some extent by vaccination especially with the recombinant hepatitis B vaccine, which has been proven to be safe and efficacious since its introduction in the 1990s. But problems of unsafe injection practices still persist. Newer delivery devices like uniject are available for making vaccination very safe.

OBJECTIVE: To evaluate the immunogenicity and safety of the Hepatitis-B (Shanvac-B) vaccine in Uniject pre-filled device administered to healthy adults and infants at 0, 1, 2 months schedule.

METHODS: A total of 122 healthy subjects (62 adults and 60 infants) were administered three doses of the recombinant Hepatitis-B vaccine using Uniject pre-filled device. Blood samples for antibody titer estimation were taken before vaccination and 4-6 weeks after third dose. Subjects, parents or guardians were given diary cards to record any adverse reactions.

RESULTS: Protective immune responses to the vaccine were seen in 96.4% of adults and 100% of infants who completed the study. The Geometric Mean Titers (GMT) in adults and infants were 518.5 and 385.41 mIU/ml respectively. Mild fever, itching, and swelling at injection site were the most common side effects observed.

CONCLUSION: The safety and immunogenicity of the Hepatitis B Vaccine in the novel pre-filled device Uniject was effectively demonstrated in the present study.

Key Words: Hepatitis B vaccine, Uniject, Pre – filled device.

INTRODUCTION

Hepatitis B virus (HBV) infection is an important public health problem worldwide with over 350 million carriers of the virus worldwide, of these 25-30% will die as a consequence of the infection. India is in the intermediate zone of endemicity with a prevalence of 4.7% and contributing 10-15% of the total infected population worldwide. In...