



STUDY OF DYSLIPIDEMIA IN POSTMENOPAUSE WITH SPECIAL REFERENCE TO SERUM BUTYRYLCHOLINESTERASE AND LIPOPROTEIN (a) [Lp (a)]

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ABSTRACT

Hyperlipidaemia is one of the important risk factor for the development of coronary heart disease. Butyrylcholinesterase is a serum esterase which is synthesized primarily in the liver, increased serum butyrylcholinesterase activity is found to be associated with altered lipid metabolism such as hyperlipoproteinemia, obesity and diabetes. Epidemiological studies have shown lipoprotein (a) is one of the independent risk factor for atherosclerosis. Postmenopausal women are known to have altered lipid profile; hence the present study is designed to estimate serum lipoprotein (a) [Lp(a)] and serum butyrylcholinesterase and to correlate with dyslipidaemia in post-menopausal women compared to pre-menopausal women. The study was conducted on 60 normal female volunteers with no history of liver disease, alcohol consumption, smoking, hypertension and diabetes, the volunteers were divided into premenopausal (n:30) and postmenopausal (n:30). Serum butyrylcholinesterase was determined on semiautomatic biochemical analyzer using commercial kit with butyryl-thiocholine as a substrate. Serum Lp(a) levels was estimated by a specific and sensitive immunoturbidometric assay. Concentration of serum total cholesterol (TC), Triglyceride (TG), low density lipoprotein (LDL-C), high density lipoproteins (HDL-C) were determined on semi-automatic biochemical analyzer. There was significant increase in serum butyrylcholinesterase, TC, LDL-C, TG (P<0.01), Lp (a) levels (p<0.01) and significant decrease in HDL-C (P<0.01) in postmenopausal women. Serum TC, LDL-C, TG correlated positively with serum butyrylcholinesterase (p<0.01), Lp (a) (p<0.01) and negatively with HDL-C (P<0.01) in postmenopausal women. This suggests that dyslipidaemia associated with increase in serum Lp (a) and increase in pseudo cholinesterase and decrease in the HDL-C in post-menopausal women, possibly because of the estrogen deficiency associated with menopause.

Keywords: Coronary heart disease, Butyrylcholinesterase, Lipoprotein (a) [Lp (a)]

INTRODUCTION

Cardiovascular disease is a leading cause of death among women in the developed world. In the United States, more than 500,000 women die of cardiovascular disease and about half are due to coronary artery disease (CAD)¹. Multiple risk factors have been identified as contributory to the development of CAD. These risk factors are important in both men and women and are present in both Caucasians and Africans. They include cigarette smoking, hypertension, Diabetes mellitus and hypercholesterolemia. Hypercholesterolemia is a key factor in the pathophysiology of arteriosclerosis². Studies have shown that women are at less risk of developing CAD than their male counterparts, but this is abolished after 60 years of age^{3,4}. High levels of LDL and low levels of HDL are strongly associated with the risk of CAD⁵. Smaller LDL particles (LDL-III) are considered more atherogenic than larger more buoyant species because of their increased susceptibility to oxidation⁶ and their increased residence time in plasma⁷. Plasma triglycerides concentration also has a determinative influence on the concentration of small dense LDL particles in normal population⁸. After menopause, there is loss of ovarian function. This results in adverse changes in glucose and insulin metabolism, body fat distribution, coagulation, fibrinolysis and vascular endothelial dysfunction⁹. There is also derangement of lipoprotein profile independent of

age. A number of changes that occur in the lipid profile after menopause are associated with increased cardiovascular disease risk. Lack of estrogen is an essential factor in this mechanism. Apart from maintaining friendly lipid profile, estrogen changes the vascular tone by increasing nitrous oxide production. It stabilizes the endothelial cells, enhances antioxidant effects and alters fibrinolytic protein¹⁰. All these are cardio protective mechanisms, which are lost in menopause. The current study was designed

- To estimate serum Lp(a) and serum butyrylcholinesterase in post menopausal women and
- To correlate Lp(a) and butyrylcholinesterase with dyslipidaemia in post menopausal women.

MATERIALS AND METHODS

The study was conducted on 60 normal female volunteers with no history of hypertension and diabetes. The volunteers were divided into premenopausal (n: 30) and "post-menopausal" (n: 30). Under aseptic conditions blood samples (5 ml) were drawn into plain vacutainers from ante-cubital veins. The collected blood was allowed to clot for 30 minutes, and then centrifuged at 2000 g for 15 minutes for clear separation of serum. All assays were performed immediately after serum was separated. Serum butyrylcholinesterase was determined on



semiautomatic biochemical analyser using commercial kit with butyrylcholine as a substrate (Agappe system reagent cholinesterase). Serum Lp(a) levels was estimated by a specific and sensitive immunoturbidimetric assay and concentrations of serum TC, TG, LDL-C, HDL-C, were determined on semiautomatic biochemical analyser using enzymatic colorimetric kit (Agappe diagnostic kit).

Statistical analysis

All the values are expressed as mean \pm SEM. A p value less than 0.05 was considered as significant. Statistical analysis was done using SPSS (statistical package for social sciences, SPSS-17, Chicago, USA). Independent sample t test was used to compare mean values. Pearson's correlation was used to correlate between the parameters.

RESULTS

There was significant increase in Serum butyrylcholinesterase, Lp(a), TC, LDL-C, TG, ($p < 0.01$) and significant decrease in HDL-C ($P < 0.01$) in postmenopausal women compared to premenopausal women. Serum TC (Fig-1) ($r = 0.466$, $p < 0.05$), TG (Fig-2) ($r = 0.478$, $p < 0.001$) correlated positively with serum butyrylcholinesterase and Lp (a) (Fig-3) ($r = 0.436$, $p < 0.001$) and negatively with HDL-C (Fig-4) ($r = -0.336$, $p < 0.05$) in "post-menopausal" women.

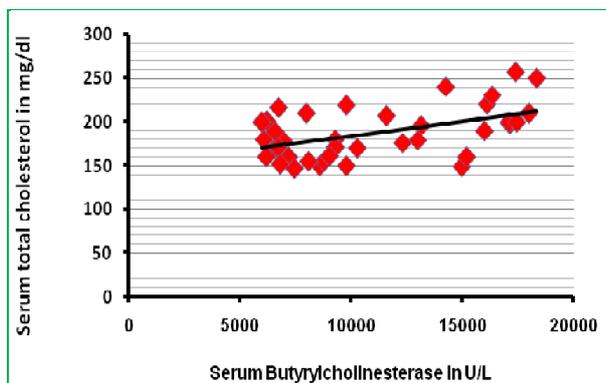


Figure 1: Correlation between serum total cholesterol and butyrylcholinesterase

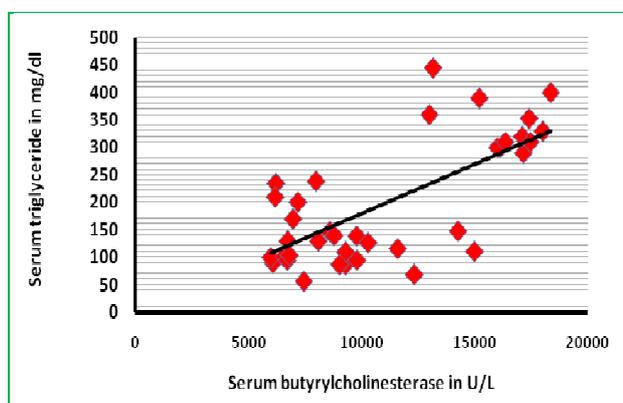


Figure 2: Correlation between serum triglyceride and butyrylcholinesterase

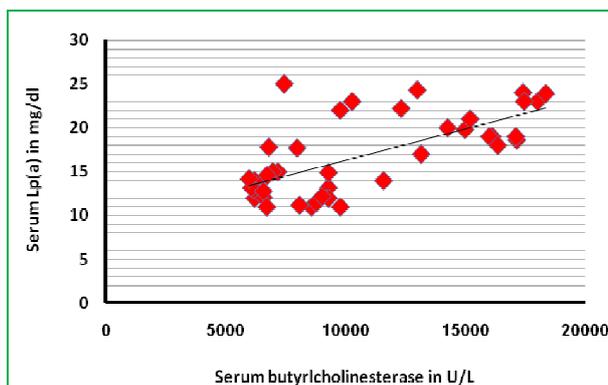


Figure 3: Correlation between serum Lp(a) and butyrylcholinesterase

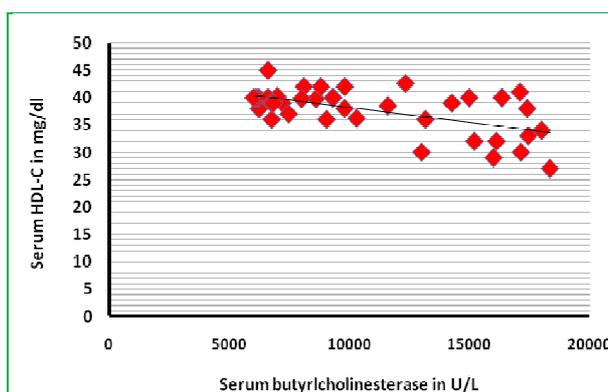


Figure 4: Correlation between serum HDL-C and butyrylcholinesterase

DISCUSSION AND CONCLUSION

The results presented in this study demonstrates that serum total cholesterol, LDL cholesterol, triglyceride were markedly increased and HDL cholesterol was markedly decreased in "post-menopausal" women compared to premenopausal women, which is in accordance with the previous study¹¹. The marked increase in serum butyrylcholinesterase in our study in "post-menopausal" women compared to "pre-menopausal" women is also in line with a previous study¹². But there is paucity in the literature regarding the correlation of serum butyrylcholinesterase and serum Lp (a) levels with lipid profile in pre and "post-menopausal" women. In our study we found a significant positive correlation of serum total cholesterol and triglyceride and negative correlation of HDL-C with serum butyrylcholinesterase and Lp (a) in "post-menopausal" women compared to "pre-menopausal" women. Hypercholesterolemia is a key factor in the pathophysiology of atherosclerosis¹³. Studies have shown that women are at less risk of developing CAD than their male counterparts but this gets abolished after 60 years of age^{14,15}. After menopause, there is loss of ovarian function, metabolism, body fat distribution, coagulation, fibrinolysis and vascular endothelial dysfunction¹⁶. Lipoprotein (a) [Lp(a)] is a circulating particle closely related to low density lipoprotein (LDL). It is a genetic variant of LDL and consists of covalent association of the unique and enigmatic apolipoprotein (a) to apolipoprotein B-100 by a single disulphide

bridge¹⁷. It has been reported that raised Lp (a) concentrations have relation with genesis, progression and complication of both atherosclerosis and thrombosis¹⁸. All these changes that occur in the lipid profile after menopause are associated with increased cardiovascular disease risk.

Estrogen is a female sex hormone that has plasma cholesterol lowering action. It also produces vasodilatation¹⁹. Apart from maintaining friendly lipid profile, estrogen changes the vascular tone by increasing nitrous oxide production. It stabilizes the endothelial cells, enhances antioxidant effects and alters fibrinolytic protein. These actions reduce atherogenesis; decrease the incidence of myocardial infarction and other complications of atherosclerotic valvular disease in premenopausal women. All these cardio protective mechanisms are lost in menopause. The circulating levels of estrogen are considerably lower in "post-menopausal" women along with increase in serum total cholesterol, triglycerides, LDL cholesterol and decrease in HDL cholesterol^{20,21}. As estrogen levels are low in "post-menopausal" women, the lipid lowering action as well as the decreased hepatic synthesis of butyrylcholinesterase is lost, thus leading to increased serum lipids along with increase serum Lp (a) levels and serum butyrylcholinesterase. There is no doubt from this study that the changes that occur in the lipid profile along with serum Lp (a) and butyrylcholinesterase after menopause is not friendly for the cardiovascular health of women. Hence "post-menopausal" women with dyslipidaemia along with increased serum butyrylcholinesterase and Lp(a) could be more prone for coronary artery disease compared to "pre-menopausal" women.

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