

Correlation of Platelet Aggregation with Serum Lipids Level in Women Taking Hormonal Contraception

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ABSTRACT

Increased platelet functional activity has been noticed as an initial disorder in women taking hormonal contraception leading to hypercoaguable state in these subjects. This is due to direct effect of estrogen present in oral contraceptive pills on platelet functional activity while progesterone, by changing plasma lipids level has indirect role in the genesis of thromboembolism. Present study was conducted in women taking oral Pills (Group B) and injectable contraceptive preparations (Group C) and their results were compared with Control (Group A). Platelet hyperaggregation was determined by using ADP and collagen as agonist. Serum lipids levels were also measured. A positive correlation between platelet hyperactivity and raised lipids level had been observed. Statistically, p value (< 0.01) was significant in Group B and Group C as compared to Group A.

Key words: Serum lipid level, contraception, platelet aggregation

INTRODUCTION

The most important purpose of recent developments in hormonal contraceptive drugs have been directed towards lowering the dosage of these steroid hormones, in order to minimize their risk potentials like ischemic heart disease stroke, MI, and thromboembolism and changes in blood clotting mechanism¹. Among all these thromboembolism is the most important fatal complication².

The first and most important disorder in the pathogenesis of thromboembolism is increased platelet aggregation³. The hyperactivity of platelet is due to direct effect on estrogen present in hormonal contraceptive drugs on platelet functions. Progesterone on the other hand, by altering serum lipids level enhances platelet aggregation⁴ and hence thrombosis thereby shortening bleeding⁵.

Estrogen and progesterone level present in these drugs have different and some time opposite effect on lipid metabolism e.g., estrogen increase serum level of HDLc while progesterone, in turn reduces HDLc level and increases serum LDLc leading to increase chances of thromboembolism⁶. Estrogenic component of these drugs is responsible for venous thrombosis while arterial complications are due to both estrogen and progesterone⁷. It is the dosage of estrogen which is important in this regard as higher doses lead to ischemic disorder by arterial spasm⁸. Progesterone by changing lipid fractions causes atherosclerosis⁹.

Ratio of total serum cholesterol to HDLc is a better prediction to the extent of atherosclerosis and

thromboembolism. The dynamic balance between proatherogenic and antiatherogenic factors may allow a clear understanding of actual impact of these drugs on thromboembolism¹⁰.

MATERIALS AND METHODS

The present study was conducted on sixty women for a period of six months. These women were taken from different local hospitals of Lahore city. Among these twenty were taking low dose oral contraception pill (Lo-femenal (Group B), twenty women were on injectable preparation (Norigest) (Group C). Twenty normal subjects not taking HRT were considered as control (group A). Platelet aggregation was carried out using different dilution of ADP as primary agonist and collagen as secondary agonist. Serum lipids level were determined and their correlation was calculated. The result of group B and group C were compared with control group (Group A), who had never taken hormonal contraception.

RESULTS

Platelet hyperaggregation response had been seen by with ADP by assessing spontaneous platelet aggregation, percentage aggregation and slope of aggregation. Similarly hyperfunctioning of platelets were determined with collagen by estimating lag phase, percentage aggregation and slope of aggregation. Enhanced platelet activity was found in 90% of Group B and 85% of group C. Statistically this hyperaggregability of platelet was highly significant in group B ($P < 0.001$) and significantly raised in group C ($P < 0.05$) as compared to group A.

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Serum cholesterol triglyceride and LDLc fraction had been estimated. These values were highly significant ($P < 0.001$) in group B and C. A positive correlation between platelet hyperfunctioning and raised serum lipids level had been found.

Statistically correlation of serum lipids like cholesterol triglyceride, HDLc and LDLc with platelet hyperactivity showed a significant value ($P < 0.05$). The ratio between total cholesterol and HDLc had been significant raised group C ($P < 0.001$) as compared to group A and B ($P < 0.05$).

Table Correlation of platelet aggregation with serum cholesterol, triglyceride, HDL-C and LDL-C

	Serum cholesterol	Serum triglyceride	HDLc	LDLc
'r' value	+0.327	+0.347	-0.228	+0.367
'p' value	<0.01	<0.01	<0.01	<0.01s

DISCUSSION

Enhanced platelet aggregation is an initial disorder before any evidence of vascular injury¹¹. It is directly related to the dosage of estrogen and type of progesterone present in these contraceptive drugs¹². Modern contraceptive preparation have less side effects but the risk of hypercoaguable state including decreased antithrombin III and increased production of II, V, VIII, in the body still exist¹³.

Endothelial cells, smooth muscle cells, cardiac myocytes and fibroblasts, the cellular components of blood vessels and the heart, play important roles in cardiovascular health and disease. During the development and progression of cardiovascular disease, changes occur both in the structure and function of these cells, resulting in a wide range of abnormalities, which affect growth, death and physiological function¹⁴.

Present study observed a significant correlation of platelet aggregation with serum cholesterol and triglycerides level in women taking HRT. A number of studies agreed with our study. A group of workers¹⁵ found a correlation was found between increased estrogen level and decreased total cholesterol, triglyceride, and LDL-C levels; HDL-C levels remained unchanged. There was a positive correlation between the estradiol levels and free fatty acid elevation. It is reported that the oxidation of low-density lipoprotein (LDL) might play an important role in the development of atherosclerosis¹⁶. Estradiol has a protective effect against LDL oxidation, although only at pharmacological dosages. Progesterone or medroxyprogesterone acetate did not limit the E(2) action. The size of the LDL particles remained unaltered after each E(2) dose, but MPA, and not P, was associated with a diminution¹⁷. Studies reporting that endogenous human estrogens could be rendered fat-soluble by esterification with fatty acids in vivo, and the subsequent detection of such esters in blood and fat tissue suggested a possible mechanism explaining how estrogens might protect LDL. Because of their lipophilicity, esterified estrogens may become incorporated in the

lipoprotein structure, providing antioxidant potential for the particles¹⁸.

A study reported that a positive correlation between platelet hyper functioning and raised lipid level gives a guideline as follow up investigation in the subjects especially those who gave the family history of thrombolism¹⁹. Another study proposed that the sex steroid hormones, including estrogen, progesterone, and androgen, mediate their biological effects on cell proliferation, differentiation, and homeostasis through their respective nuclear receptors. Their study observed that there is a rapid non-genomic signaling action of sex steroids, including novel membrane receptors and interactions of nuclear steroid receptors with membrane and cytoplasmic signaling molecules such as adapter proteins, G proteins, ion channels, and protein kinases²⁰. This study is promoted by a group of workers. They confirmed that prototypical non-genomic actions of sex steroids at this level include the induction of rapid vasodilatation as well as anti-inflammatory and antiatherogenic actions²¹.

Another study stated that cardiovascular diseases (CVDs) may have their origin before birth: the combination of being small at birth and having an overly rich post-natal diet increases the likelihood of obesity and of acquiring a specific metabolic syndrome in adulthood that carries an increased risk of CVD²².

Platelet hyperaggregation is more commonly seen in oral contraceptive pill user due to direct effect of estrogen on them as compared to subjects on injectable preparations²³. Thrombosis of microvessels of vital organs like brain and heart lead to fatal is ischemic complications²⁴.

CONCLUSION

- Platelet aggregation study should be done routinely in subject taking hormonal contraception.
- Platelet aggregation should be conducted in subject with family history of thrombophilic

disorders the lack of protein C and S, antithrombin III and factor V mutation. Other family member should also be screened.

- Serum cholesterol, triglyceride, LDLc and HDLc should regularly be done.

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