

Combined Oral Contraceptive Pills Produce Fewer Changes in Platelet Count

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ABSTRACT

Objective: to determine whether low dose combined oral contraceptive pills affect platelet count

Methodology: The study was conducted at Family Planning Centers at social obstetrical unit Baqai Medical University and Reproductive and Health Sciences (RHS) Institute, a family planning unit, at Jinnah Post Graduate Medical Center Karachi, from November 2010 to April 2011. Fifty healthy non smoking women were administered combined oral contraceptive pills (COCPs) containing Ethinylloestradiol: 0.03mg, Levonorgestrel: 0.15mg, ferrous fumarate 75.0mg for six months.

Results: At 6 months, no significant rise in the Platelet count which could be due to the low dose of estrogen used in combination.

Conclusions: Low-dose 30mcg ethinylestradiol in COCPs produced fewer changes in platelet count.

Key Words: Low dose Combined oral contraceptive pills, platelet count.

INTRODUCTION

Platelets or thrombocytes are small, irregularly-shaped, anuclear cells with a diameter of 2-3 micrometer (μm).¹ Normal platelet count in a healthy individual is between 150,000 and 450,000 per microlitre (μl) or ($150\text{--}450 \times 10^9/\text{L}$) of blood². The average life span of a platelet is normally 5 to 9 days¹. Old platelets are destroyed by phagocytosis in the spleen and by Kupffer cells in the liver. The principal function of platelets is to prevent bleeding by forming platelet plug at the site of injury³. In addition to being the chief cellular effector of hemostasis, platelets are rapidly deployed to sites of injury or infection, and potentially modulate inflammatory processes by interacting with leukocytes and by secreting cytokines, chemokines, and other inflammatory mediators^{4,5}. An abnormality or disease of the platelets is called a Thrombocytopathy. Which could be either a low number of platelets termed Thrombocytopenia, an increase in the number of platelets called Thrombocytosis or a decrease in function of platelets known as Thrombasthenia.

Thrombocytosis is the presence of high platelet counts in the blood above 10, 00,000 per microliter⁶. It can predispose to thrombosis. Living in high altitudes, strenuous exercise, and being post partum may cause increased platelet levels. Drugs that may cause increased platelet levels include estrogen^{7,8}. COCPs increase the risk of venous thromboembolism including deep vein thrombosis

(DVT) and pulmonary embolism (PE). Thromboembolism is an important cause of morbidity and mortality, especially in adults. Contraceptive steroids increase the concentrations of many coagulation factors^{9,10}. increase platelet adhesiveness¹¹ and reduce venous flow velocity by increasing venous distensibility and whole-blood viscosity⁸. All of these effects increase the risk of thromboembolism. The association between arteriovenous thromboembolism and use of oral contraceptives is well established^{12,13}. The risk in users of combined oral contraceptives depends on the dose of oestrogen, type of progestogen, and length of use. Pills containing the lowest doses of oestrogen (20 micrograms ethinylloestradiol) have shown the least changes in haemostatic factors thus decrease risk of venous thromboembolism^{14,13}. The progesteron component of the pill modifies the effect of estrogen on the haemostatic system¹⁴.

Despite the general acceptability, and the obvious advantages that have been attributed to oral contraceptive use, some serious side effects have been reported in women taking the pills. Epidemiologic studies have indicated a relationship between oral contraceptive use, platelet changes and thromboembolic phenomenon¹⁵. These associations have been identified and extensively documented among Caucasians. Furthermore, the possible danger of intravascular coagulation resulting from the use of oral contraceptive pill had been extensively studied among the Caucasian women by laboratory measurements of coagulation and platelet changes taking the combined oestrogen-progestogen combined oral contraceptive pill¹⁶. Oral contraceptives have been reported to increase platelet

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count^{8,15}. Closely linked with these changes are the risks of thromboembolism, myocardial infarction and other cardiovascular diseases which have been reported to be higher in young women on oral contraceptive pills compared to non-users¹⁷. However, the use of oral contraceptives is still being strongly undertaken and promoted in our environment. We have therefore, in this study examined the effects of a low dose combined oral contraceptive (COCP) pill on platelet count of healthy women over a six month period. It was hypothesized to detect changes in platelet count in women taking the contraceptive pills.

MATERIALS AND METHODS

Two hundred & thirty women were attended in the hospital but only Sixty two met the inclusion criteria, out of which only 50 were followed till six months. Six of them were dropped from the study due to change of contraceptive method, four due to improper use of combined oral contraceptive pills (COCPs) like missing one or more pills and two of them got pregnant so COCPs were discontinued. Women were enrolled consecutively from patients presenting for regular gynecologic check-ups. All participants signed informed consent. Twenty eight women had never used COCP's before. The remaining women had previously used oral contraceptives but discontinued treatment at least 2 years before enrollment in our study. Participants were considered healthy on the basis of medical history and physical examination and vital signs.

Inclusion Criteria:

- Women aged 20-40 years who were interested in contraception not desiring pregnancy for the duration of the study.
- Women with history of any or active uterine bleeding disorder like menorrhagia or polymenorrhea, to which other methods of contraception were not preferred.
- Carefully evaluated by clinical examination to be labeled as normal & healthy before starting the COCPs.
- Written or verbal consent was taken before enrolment in the study.

Exclusion criteria:

- Patients with hypertension & heart disease.
- Renal and hepatic dysfunction
- Diabetes mellitus
- The women not willing to take the COCPs.
- Patients who were already on COCPs.
- Post menopausal women.
- Women having Depot medroxyprogesterone acetate (DMPA) hormonal contraceptive injection in the past 90 days.

Obstetrical history was taken. General and systemic examination including Gyneacological examination was performed. A COCP with Ethinyloestradiol: 0.03mg, Levonorgestrel: 0.15mg was prescribed. Blood was drawn from a large vein, from the median cubital vein or superficial veins on the dorsum of the hand and sent to Auto hematology analyzer, Mindray BC- 2800 for count Platelets. Automated cell counters sample the blood, and quantify, classify, and describe cell populations. The subjects were divided into four categories, Control (category 0) i.e. before the start of COCPs, after 1 month (category 1), 3 months (category 2) and 6 months (category 3). Blood was taken once at the beginning of the study for calculating platelet count. Later, sample was collected after 1 month, 3 months and 6 months between 9–12a.m.

Comparison of platelet count was done before and after the treatment by finding the means, calculating the standard deviation and standard error of mean. Student T- test was applied to check the difference between control and different categories platelet count. Data has been analyzed using SPSS (version 10) level of significance P<0.05.

RESULTS

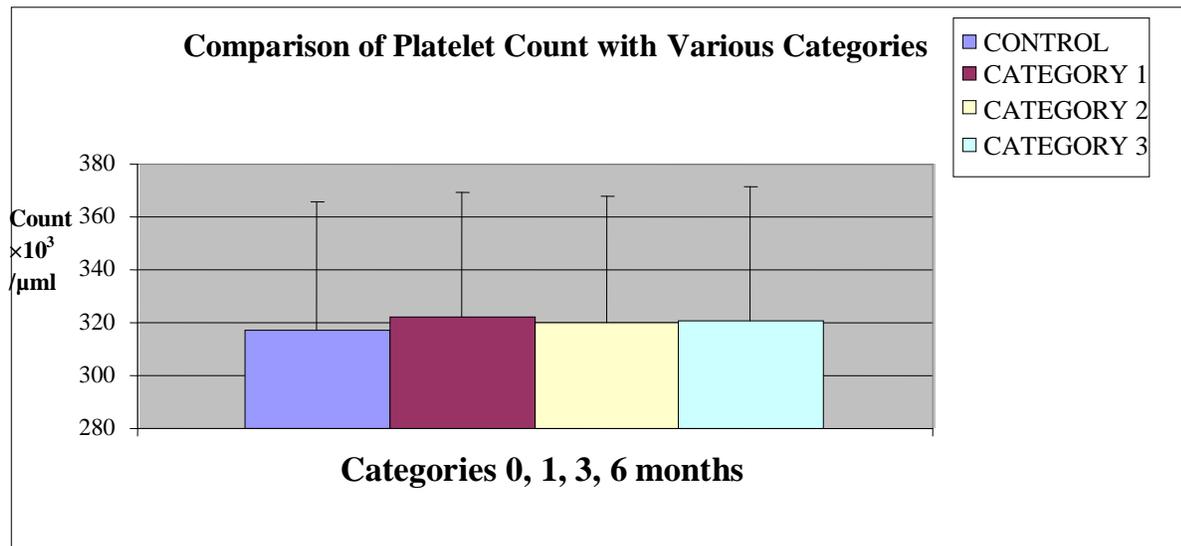
Mean platelet count of control was found to be 316.88±6.87. Category 1 showed mean platelet count of 321.94±6.65. On comparing control with category 1 non significant correlation (P>0.05) was observed. The mean platelet count of category 2 was 319.68±6.85. Non significant (P>0.05) correlation was observed on comparison of control with category 2. While comparing control with category 3, still non significant (P>0.05) correlation was observed. It was due to very little rise in mean platelet count in category 3 subjects which was 320.9±7.19.

Comparison of Platelet Count of Control with Various Categories (n=50)

Categories	Platelet Count (x103/µL) Mean ± SEM	P Values <0.05
Control (0 month)	316.88 ± 6.87	
Category 1 (1 month)	321.94 ± 6.65	P>0.05 ^Δ
Category 2 (3 month)	319.68 ± 6.85	P>0.05 ^Δ
Category 3 (6 month)	320.9 ± 7.19	P>0.05 ^Δ

*P <0.05 S (Significant)
 **P <0.001 H.S (Highly significant)
 Δ P >0.05 N.S. (Non significant)

Comparison of Platelet Count of Control with various Categories



DISCUSSION

Oral contraceptive use is known to cause changes in the haemostatic system. Since the introduction of combined oral contraceptives (COCPs) in the 1960's, it had been known that their use is associated with an increased risk of venous and arterial thromboembolism¹⁸. COCPs with low oestrogen content are being recommended to minimize the side effects.¹⁹ In spite of the various side effects, and the more serious complications that have been associated with the use of COCPs, estrogen-progestogen combined pill is still regarded as a safe and highly effective method of contraception.¹⁹ The estrogen component of the combined OC pill has been implicated as being responsible for most of the adverse effects attributed to the combined pill.²⁰ In our study we used low dose estrogen containing COCPs (Ethinylloestradiol: 0.03mg, Levonorgestrel: 0.15mg, ferrous fumarate: 75.0mg).

Our study have shown results in agreement to number of studies in past. These researches demonstrated that subsequent reductions in the dosages of the estrogen component have lowered the risk of thromboembolism.^{21,22} Throughout the study period, none of the subjects developed any clinical side effects e.g amenorrhea, leukorrhea, headache or depression that could warrant discontinuation of treatment. Similar observation had been made in a multicentre clinical trial carried out in Nigeria with a low dose combined oral contraceptive pills which reported no significant side effects in their patients²³.

Studies of the COCPs in current users showed no significant rise in the Platelet count which could be

due to the low dose of estrogen used in combination. In this respect, the new low-dose formulations are a major step forward and may reduce the risk of vascular thrombotic complications²⁴.

However some studies have shown the opposite results. A study was carried in Nigeria to determine the effect of low-dose combined oral contraceptive pill on platelet count (PC) of apparently healthy women over a period of three months. The mean value of platelet count was significantly increased after three months of contraceptive use⁸. In Lagos, a study conducted on forty Nigerian women taking the COCP found their mean platelet count to be slightly higher than for the control group, but the increase was not statistically significant. The increase may be a reflection of an acute phase response that could pursue minimal vascular tissue damage secondary to estrogen use²⁵. Another research showed the haemorrhological profile of the women who had been taking oral contraceptives for the last six months. The result obtained was significantly higher mean platelet count in oral contraceptive users²⁶.

We settled for the reason of normal platelet count in the patients using COCPs because of low dose estrogen content. This can be explained by the fact that the platelets have estrogen beta receptors (ER β).²⁷ This finding implies that platelet function may be modulated by sex hormone levels.²⁸ Estrogens have a weak anabolic effect.²⁹ So when low dose estrogen COCPs is given it suppresses the actions of other reproductive hormones like Luteinizing Hormon (LH) and Follicle Stimulating Hormone (FSH) and prevents Ovulation.³⁰ It is

assumed that in our study estrogen may not have produced an anabolic effect on platelets so the count did not increase.

We are of the view that low-dose formulations are a major step forward and should reduce the risk of vascular thrombotic complications. Since the low-dose 30 mcg ethinyl estradiol in COCPs produced fewer changes in platelet count, therefore it may be recommended for women with risk factors for thromboembolic disease.

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