

ORIGINAL ARTICLE

Total Count of Platelet to Assess the Correlation between Hypercoagulability and Long time Use of Oral Contraceptive Pill

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DOI : <https://doi.org/10.47648/jmsr.2024.v3702.02>

Abstract:

It is necessary to assess the hypercoagulability and the risk of thromboembolism in women taking oral contraceptive pill (OCP) for prolonged period of time. So, we need to know the hemostatic changes that are occurring in Bangladeshi women taking OCP for prolonged period of time. This cross sectional study was done in the department of Physiology, Dhaka Medical College, Dhaka from Jan 2012 to Dec 2012. Ninety female subjects with the age range from 25-45 years, were taken as a study population. Among them, 60 women taking oral contraceptives for prolonged period of time (>1 years) were included for the study group and age matched 30 women of OCP nonusers were taken as a control. Study subjects were divided into two groups according to their duration of oral pill use: group B-1 (1 to 5 years users) were 30 women and group B-2 (>5 to 10 years users) were 30 women. For assessment of hypercoagulable state total counts of platelet levels were estimated in all groups. Statistical analysis was done by unpaired Student's 't' test and Pearson's Correlation Coefficient test. In this study the mean ($\pm$ SD) total count of platelet level was higher in study group (who were taking OCPs) than control group (OCP nonusers) which was statistically highly significant ($P < 0.001$). Total count of platelet levels were positively correlated ($r = +0.155$) with the 1 to 5 years user group and negatively correlated ($r = -0.019$) with the >5 to 10 years user group. But all the relationships were statistically non-significant. My present study revealed that prolonged duration of OCP use (at least 5 years) may increase the risk of thromboembolic effects. This study concludes that OCP users had more tendency of hypercoagulability and therefore these women are at higher risk of thromboembolic effects.

Key words: Hypercoagulability, Oral Contraceptive Pill, Total Count of Platelet.

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Introduction:

It is estimated that more than 100 million women worldwide use the oral contraceptive pill (OCP)¹. OCPs are the combination of progestin & synthetic estrogen. They are widely used & effective for women but a number of side effects may be present in the users, one of which is the

changes in intrinsic & extrinsic blood coagulation pathway. This change is important because of its involvement in the development of thrombosis^{2,3}. Some studies indicate that newer low-dose oral contraceptives are clearly associated with a 3 to 6 fold increased risk of venous thrombosis and pulmonary thromboembolism⁴. Hepatic synthesis of coagulation factors are increased in the OCP

users that may produce hypercoagulability^{1,3}. There may be a procoagulatory changes occur due to a hypercoagulable state caused by oral contraceptives. These changes can be observed by some coagulation tests⁵. Hypercoagulable state was indicated by the significant elevation of the total count of platelet in women taking OCP for prolonged period of time^{6,7}.

OCP containing 30 µg of EE (ethinyloestradiol) enhanced platelet activity, increased levels of factor II, VII, VIII, IX and X, fibrinogen and soluble fibrin and decreased levels of antithrombin (AT) and vessel wall fibrinolytic activator were observed^{8,9,10}.

According to the duration of OCP use, women taking oral contraceptives for 5 years & compared them with another group of women who were taking pills for 1 year. Here, total platelet counts were affected by the duration of use. There were significant decrease in platelet count in women of 5 years users as compared with 1 year users. But the findings were not similar to my present study⁷. Some researchers observed platelet counts remain unchanged after one year of OCP use¹¹.

Several studies have been done abroad to observe the thromboembolic effects & hypercoagulable state in women who are taking oral contraceptives for prolonged period of time at least 5 years. But a few published data has been available in our country regarding the hypercoagulability in OCP users. Therefore, the present study has been undertaken to estimate total count of platelet in women of OCP users in different period of time that will help us to detect the risk for future thromboembolism. It is expected that findings of this study would give a guideline to the physician for better management of women who were taking oral contraceptives for prolonged period of time. Again this study will also help to build awareness about thromboembolism which is now-a-days an utmost importance worldwide. Moreover early detection & prevention of it can reduce morbidity & mortality and thus reduce burden on our health budget.

Materials and method:

This cross sectional study was carried out in the Department of Physiology, Dhaka Medical College, Dhaka between January 2012 and December 2012. The protocol of this study was approved by the Ethical Review Committee of Dhaka Medical College, Dhaka. Sixty apparently healthy women taking hormonal oral contraceptives (Shukhi) for 1 to 10 years with age range between 25 to 45 years were taken as study group (group B). Study group was further divided into 1 to 5 years user group (group B-1, n=30) and >5 to 10 years user group (group B-2, n=30). In addition, 30 apparently healthy women of OCP nonusers aged 25 to 45 years were included as control group (group A). All the study subjects and controls were selected from family planning clinics of NariMaitree (Second urban primary health care project, P.A-6, Dhaka city corporation & from personal contact in different area of Dhaka city.

Inclusion criteria:

For all groups:

- Women with age ranging from 25-45 years.
- For study groups -women with the history of taking OCP for 1 to 5 years were included in group B₁ & women who were taking OCP for >5 to 10 years included in group B₂.
- For control group-women with no history of taking oral or hormonal contraceptives were included in group A.

Exclusion criteria:

For all groups:

- Women with age more than 45 years & less than 25 years.
- Women with heart, liver, kidney & any endocrine disease like thyroid disease, TB & malignancy.
- Women with taking hormone replacement therapy, steroid, aspirin & anti platelet aggregator.

Data were collected through written questionnaire, clinical examination and relevant investigation. Total count of platelet - Was analyzed on Sysmex Automated Hematology Analyzer, XT - 1800

I. Statistical analysis was done by Unpaired Student's 't' test and Pearson's Correlation Coefficient tests as applicable and p value <0.05 was considered as level of significant.

Results:

The mean ($\pm$ SD) total count of platelet level in group B₁ was higher than that of group A & the result was statistically significant ($P < 0.01$). The mean ($\pm$ SD) total count of platelet level in group B₂ was higher than that of group A which was also statistically highly significant ($P < 0.001$). Within the study groups, Total count of platelet levels were positively correlated ($r = +0.155$) with the group B-1 and negatively correlated ($r = -0.019$) with the group B-2. But both the relationships were statistically non-significant. (Table I, II and Figure I).

Table 1: Total count of platelet in different groups (n=90)

Groups	N	total count of platelet ($\times 10^3/\mu\text{L}$)	P value for total count of platelet
A	30	272.57 $\pm$ 36.48	(A vs B ₁) 0.001** (A vs B ₂) 0.8001***
B ₁	30	316.57 $\pm$ 61.87	
B ₂	30	320.83 $\pm$ 42.32	

Group A: OCP nonusers

n=Number of subjects

Group B₁: OCP users 1-5 years

ns=Not significant

Group B₂: OCP users >5-10 years

* =Significant at $P < 0.05$ ***=Significant at $P < 0.001$

Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated and p values <0.05 was accepted as level of significance.

Table 2: Correlations of duration of OCP use with total count of platelet in different study groups (n=60)

Parameter	Group B ₁ (n=30)		Group B ₂ (n=30)	
	r	p	r	p
Total count of Platelet	+0.155	0.415 ^{ns}	0.019	0.922 ^{ns}

Pearson's correlation coefficient (r) test was performed to compare relationship between duration of OCP use and total count of platelet. The test of significance was calculated and p value <0.05 was accepted as level of significance.

Group B₁ : OCP users 1-5 years

n = Number of subjects

Group B₂ : OCP users >5-10 years

ns = Not significant

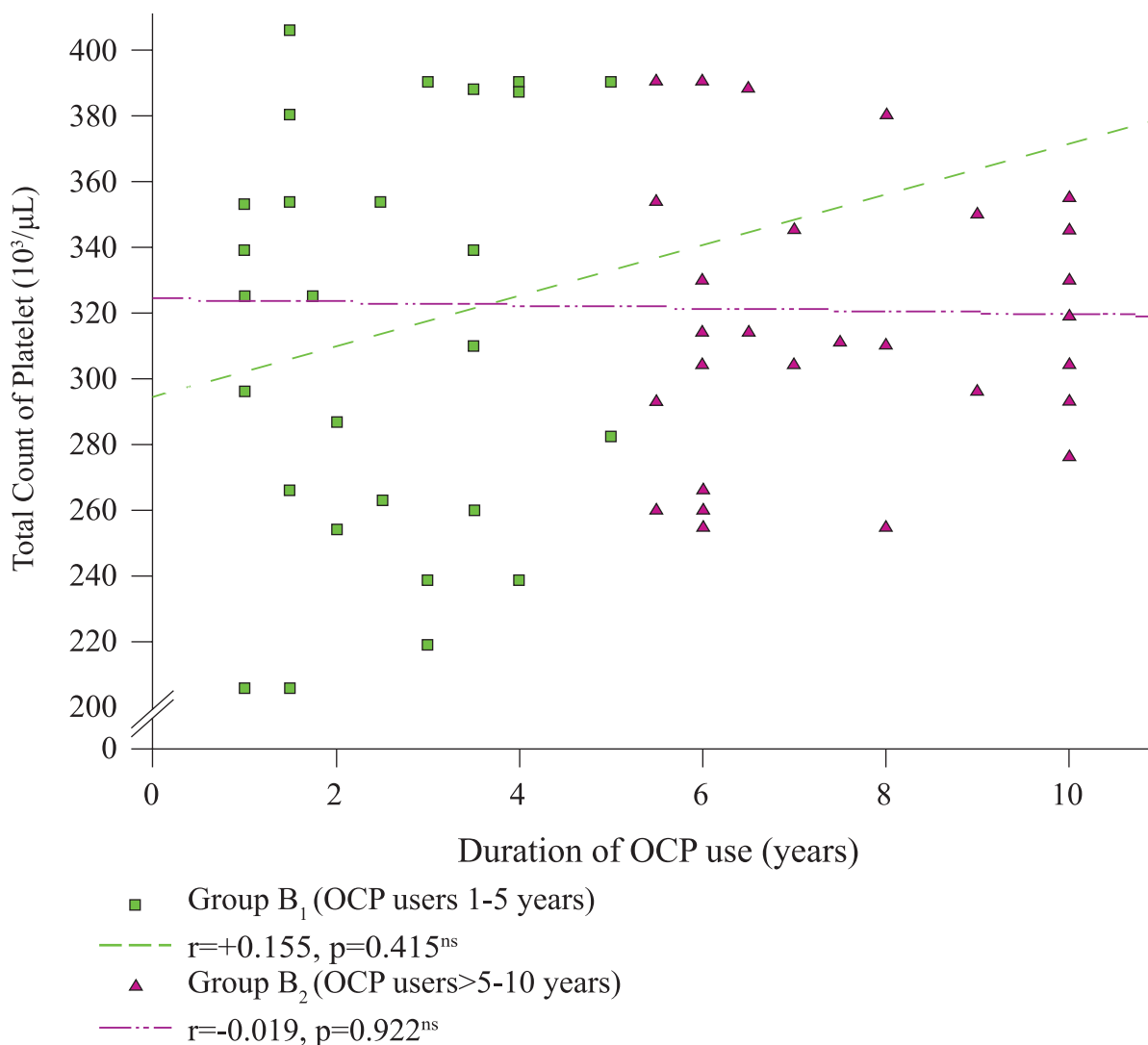


Fig-1: Correlation between duration of OCP use and total count of platelet

Discussion:

In the present study, the mean value of total counts of platelet was higher in >5 to 10 year users than 1 to 5 year users. But the result was not statistically significant. Almost similar type of result was observed by some researchers⁷.

In between study groups, total counts of platelet were positively ($r = +0.155$) correlated with the group B₁ and negatively ($r = -0.019$) correlated with the group B₂. But all these relationships were statistically non-significant. Similar types of observations were reported by the different researchers of different countries^{6,11}.

Above findings of correlations showed that the duration of OCP use among 1-5 years and >5-10 years did not show any statistically significant difference on study parameters such as total count of platelet. Smaller sample size of the present study may be the cause of these above findings.

It has been suggested that estrogen present in combined oral contraceptive pills acts as a contributory factor for significant elevation of total count of platelet. These might play an important role in development of thromboembolism⁶.

Clinical & epidemiological studies indicate that use of OCP is associated with an increased risk of thrombotic disorders³. The pathogenesis underlying

this apparent prothrombotic state is not clear. It has been suggested that plasma concentration of several markers of coagulation have been found higher in prolonged OCP user group compared with nonusers.

Many explanations are suggested by different investigators for the higher mean value of total count of platelet in women taking oral contraceptive for longer duration of time but the exact mechanism is not yet clear.

Any hormonal therapy, including oral contraception may increase the risk for venous thromboembolism. Careful and individual risk-to-benefit analysis is needed in any woman taking oral contraceptives. But the factors and mechanism by which prolonged use of oral contraceptive leads to a prothrombotic state are complex and cannot be found out from this present study.

Limitations of the study:

The study was conducted in a single family planning clinic with a small sample size. So, the results may not represent the whole community. There was also time and financial constraints. To establish the findings of our study, further studies with involvement of larger population are needed for clarification.

Conclusion:

From this study, it can be concluded that the longer duration of OCP use causes non-significant increase of total count of platelet among >5 to 10 years OCP users than 1 to 5 years user group. This altered results of above parameter was more profound with advanced age specially after 30 years of women taking oral pills for prolonged period of time. Thus it may be stated that prolonged duration of OCP users are susceptible to develop hypercoagulability and increased risk of thromboembolism.

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