

Haematologic Variations Associated With the Long Term Use of Contraceptives in Young Females

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ABSTRACT

Objective: The purpose of the present study was to compare the extent of variation in haematologic parameter associated with the long term use of hormonal and non hormonal contraceptives in urban population of low socio-economic group. **Type of Study:** Cross sectional study. **Setting:** Clinical setting. **Patients and Methods:** Fifty-four young females of age ranging from 26-32 years maintained on Oral contraceptives (OC), Depo-medroxy progesterone (DMPA), Norethisterone (NET-EN), Implant and non hormonal intrauterine contraceptive device (IUCD) for at least one year were invited. Fasting blood samples were collected for the analysis of haematologic parameters. All the results were entered in MS-Excel and mean \pm standard deviation was calculated for each frequency.

Results: Comparison among different groups was done by calculating percentile differences among groups. Though the result of the study does not showed the significant differences in various indices but the hemoglobin levels in IUCD group was found to be significantly low as compared to hormonal contraceptives. Use of hormonal contraceptives was associated with better haematologic profile whereas IUCDs were found to pose risk of anemia in already anemic population of low socio economic group. **Conclusion:** Though the risk in this group of young females maintained on contraceptives was found to be minimized because of good monitoring but continuation of IUCDs might cause this slight predisposition of sub clinical anemia into a well defined anemic disease later in their lives. It is therefore recommended to use intrauterine contraceptive devices with caution in anemic women and such methods should be used under close monitoring.

Keywords: Contraceptives, Hematologic parameters, Hormonal contraceptives, Intrauterine contraceptive devices.

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INTRODUCTION

The present study had compared the haematologic parameters of hormonal contraceptives versus non hormonal intrauterine contraceptive devices. Following study is the continuation of the previous work done in this regard in a new population of low socio economic status.

The use of low dose combined oral contraceptive is associated with the reduction in dysfunctional uterine bleeding¹ furthermore its use had also showed decline in amount of menstrual blood and thus useful in females with anemia and responsible for increase concentration of hemoglobin in such anemic females².

The non contraceptive health benefits of hormonal contraceptives also includes treatment of Dysmenorrhea, irregular or excessive bleeding.³

Progesterone only contraceptives has the advantages of its effectiveness and ease of use, it can be safely used by lactating mothers as they do not contain estrogen so supply and quality of milk remains unaffected, it does not cause serious heart and blood clotting effects as with estrogen containing contraceptives furthermore it is beneficial in the areas where anemia is endemic as it decreases the menstrual loss⁴.

On the other hand the major disadvantages of IUCDs which is non-hormonal contraceptive which restrict its use in certain users are bleeding irregularities, pain at the time of insertion and afterwards, vaginal discharges, spontaneous expulsion during menstruation which is 2%-10% in the first year of use⁵, trauma to the cervix during insertion, introduction or aggravation of infection and perforation of the uterine wall. There is an inverse correlation among chances of infection and time since insertion; risk of infection is very high in the 20 days following insertion and then decreases to baseline⁶. Hence these devices

should not be the first choice for the nulliparous woman because of the risk of infection affecting future child bearing.

Aside from the major side effects noticed after 2 years use of Cu-T, hemoglobin was lower in IUCD users when compared with controls. Cervical erosion was also significantly increased in IUCD users and cytological findings reveal predominantly inflammatory⁷.

In the present study four different types of hormonal contraceptives were compared with the non hormonal intrauterine contraceptive device for their hematologic variations.

MATERIALS AND METHODS

The study was carried out in family planning departments of different clinical setting. Young females maintained on any type of contraceptives for at least one year were randomly invited and reviewed for their complete medical and family history. Informal verbal consent had taken and blood samples of 54 women who responded and agreed to participate in the research were collected according to following eligibility criteria:

Eligibility criteria

Gender: females

Inclusion criteria

- Women of young age (20-50 yrs).
- Maintained on these methods for at least 1 year.
- Taking these drugs and methods for contraceptive purpose only.
- Subjects must be agreed to participate in this research.

Exclusion criteria

- Women less than 20 and more than 50 yrs of age.

- Maintained on these drugs and methods for less than 1 yr.
- Taking these drugs for indications other than contraception.
- Subjects not agreed to participate in this research.

Participants were assigned with one of the following 4 groups that contains one oral combined estrogen / progesterone form, two injectables containing progesterone only and subdermal implant containing progesterone only whereas non hormonal contraceptive is IUCD.

- a) Women on oral contraceptives.
- b) Women on injectables. (DMPA, NET-EN).
- c) Women on subdermal implants.
- d) Women on IUCDs.
- e) The chemical composition of the contraceptives used in this study is as follows.
 - OC: 0.3 mg norgestrol+0.03mg ethinyl estradiol+75 mg ferrous sulphate.
 - DMPA: Depo-medroxy progesterone acetate 150mg/ml.
 - NET-EN: Norethisterone enantate 200 mg/ml.
 - Implant: 36 mg of levonorgestrel.
 - Cu-T: non hormonal T-shaped contraceptive device containing copper.

Sample collection

Blood sample of about 7 ml were collected from these subjects by calling them in their fasting states to perform various hematological and biochemical analysis.

Hematological analysis

Blood (2 ml) was collected in EDTA.K3 tubes for hematological examination e.g. erythrocyte count (RBC), white blood cell count (WBC), Platelet count (PLT), hemoglobin (Hb) on automatic hematology analyzer, Humacount plus (Human Germany). The data was collected on a predesigned performa. All the values were

expressed as the means and standard error to the mean (S.E.M) and analyzed by calculating percentile differences among different contraceptive groups.

RESULTS

Evaluation of hematological parameters

Table 1 shows the hematological parameters of the subjects using contraceptives. All the values are expressed in terms of mean \pm S.E.M. There had been no variation in almost all the hematological parameters except for IUCD that showed decrease in hemoglobin concentration as compared to reference range. The mean platelet count, RBC count and TLC in subjects using contraceptives lie within the normal reference range.

Table 2 shows the comparison of hematological parameters of subjects in different contraceptive groups all values are expressed in terms of percentile difference of mean. Negative sign in the results depicts less value of tested contraceptive as compared to the compared contraceptive.

The IUCD group showed 14.75 % less hemoglobin, 1.26% more RBCs, 18.35 % high platelets and 3.49 % less total leukocyte count as compared to Implant group.

The IUCD group showed 15.13 % less hemoglobin, 5.388 % less RBCs, 1.126 % high platelets and 12.7 % less total leukocyte count as compared to NET-EN group.

The IUCD group showed 13.9 % less hemoglobin, 7.67 % less RBCs, 4.069 % low platelets and 11.6 % less total leukocyte count as compared to DMPA group.

The IUCD group showed 13.6 % less hemoglobin, 2.13 % less RBCs, 4.4 % low platelets and 5.43 % less total leukocyte count as compared to OC group.

Implant group showed 2.61 % less hemoglobin, 6.58 % less RBCs, 19.2 % low

platelets and 8.9 % less total leukocyte count as compared to NET-EN group.

Implant group showed 1.24 % less hemoglobin, 8.76 % less RBCs, 21.67 % less platelets and 7.8 % less total leukocyte count as compared to DMPA.

The Implant group showed 0.9% less hemoglobin, 3.3% high RBCs, 21.98% less platelets and 1.85 % less total leukocyte count as compared to OC groups.

The NET-EN group showed 1.39% high hemoglobin, 2.47 less RBCs, 3.067% less platelets and 0.97 % high total leukocyte count as compared to DMPA group.

DISCUSSION

When the hematological parameters of different contraceptive groups were reviewed in previous studies it showed different pattern among different hormonal and non hormonal contraceptives. Progestin-only hormonal preparations are associated with predisposition to higher risk of thromboembolism with reports of involvement of platelets. The menstrual irregularities were found to be more frequent in users of injectable hormonal contraceptives than in non-users, especially amenorrhea and irregularities of menstrual flow. In users of injectable hormonal contraceptives, hemoglobin and hematocrit were slightly better maintained as compared to non-users⁸. Norplant implants has relatively very low effect on blood coagulation–fibrinolytic system presumably due to the absence of estrogen and the low dose of progestogen delivered to the body⁹.

The use of Cu-T380A IUD produced a statistically significant drop in the hemoglobin content and percent iron saturation levels after 12 months of use, as compared to the use of OC for the same period. The drop was greater with longer IUD use, initial high Hb levels, and among urban and semi urban residents. It is recommended

that iron supplementation be part of the IUD services provided in family planning units¹⁰. Present study confirms the results of these previous studies as IUCDs showed 14.86%, 18%, 16.45% and 15.92 % low hemoglobin levels when compared with implant, NET-EN, DMPA and OCs respectively.

Packed cell volume, platelet count, erythrocyte deformability, plasma fibrinogen concentration, and plasma and whole-blood viscosity varied cyclically throughout the menstrual cycle in the non-users of hormonal contraceptives. This variation was abolished by the use of oral contraceptives, and the values of these indices were raised by an amount likely to predispose to thrombosis¹¹.

The present study evaluated hemoglobin, RBC, platelets and total leukocyte count of different contraceptive users. The hemoglobin levels are highest among OC and injectable users while IUCD showed decreased hemoglobin levels. Implant showed the levels in between these two extremes. All the contraceptive groups showed the hemoglobin levels within normal range except for IUCD that was below normal range. The possible reason for these decreased hemoglobin levels in non hormonal intrauterine contraceptive device is the increased vaginal blood loss which is often experienced by the subjects using IUCDs. Hormonal contraceptives showed the favorable pattern of hemoglobin levels due to decrease in menstrual blood loss in OC users and decreased menstrual loss with episodes of amenorrhea in most of the Injectables contraceptive users. So it can be concluded that these hormonal contraceptives are the better choice for anemic females commonly found in the population of low socio-economic status, while IUCDs should not be prescribed to anemic females without added support in the form of iron supplements etc. Study groups showed no drastic variations in RBC count.

Platelets and total leukocyte count are the determinants of coagulation and inflammation respectively. Both of these parameters are the markers for atherosclerotic cardiovascular disease. Inflammation is supposed to play a major role in the pathophysiological mechanism of atherosclerosis and cardiovascular disease. Various markers of inflammation, such as C-reactive protein, IL-6, soluble intercellular adhesion molecule type 1, and white blood cell count, are found to be significant predictors of the risk of coronary heart disease and future cardiovascular events. Specifically, an elevated WBC count is a risk factor for atherosclerotic vascular disease. Inflammation may also be associated with a raised WBC count. Therefore the association of leukocyte count with cardiovascular risk factors may represent a chance of subclinical disease, or alternatively leukocyte count could be part of a chain leading to atherosclerosis¹². When the relation between platelet count, total leukocyte count and platelet aggregation was reviewed it is found that age, white blood cell count, platelet count, mean platelet volume, and serum arachidonic acid raise platelet aggregation¹³.

In the light of present study it can be noticed that new low dose hormonal preparations posed low risk of hypercoagulation and inflammation. However it is less important but it is worth mentioning that though within normal reference ranges but still OCs showed highest platelet count followed by DMPA, NET-EN and Implant among different groups. Total leukocyte count is high in injectable contraceptive groups followed by OCs and Implant and lastly in IUCD group. Though platelet count and TLC are two important markers of atherosclerosis but more specific parameters that measure the aggregation properties, C-reactive protein and other coagulation and inflammation markers in the Pakistani population maintained on hormonal

contraceptives should be studied in order to analyze the risk of thromboembolism and inflammation.

CONCLUSION

The use of intrauterine non hormonal contraceptives poses the risk of well defined anemia due to irregular intravaginal bleeding. Whereas hormonal contraceptives are associated with good hemoglobin profiles due to the low blood loss episodes. It is therefore suggested to use non hormonal intrauterine contraceptives with special monitoring of anemia in the population of low socio economic status.

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Table 1. Effects of different contraceptives on hematological parameters

Parameters	Reference ranges	Type of contraception / no. Of subjects in each group				
		IUCD	IMPLANT	NET-EN	DMPA	OC
		6	4	18	14	12
Hemoglobin g/dl	11.5-15.0	10.36±0.51 1	11.90±0.793	12.225±0.287	12.055±0.336	12.010±0.296
RBC count (/cmm)	3.90-5.60×10 ³	4.583±0.13 0	4.525±0.193	4.843±0.111	4.963±0.1243	4.680±0.129
Platelet count (/cmm)	150000-450000	300667±21 732	245500±4665 9	304125±21533	313455±12454	314700±2286 1
Total leukocyte count (/cmm)	4000-11000	7733±448.3 4	8000±956.5	8712±655.82	8627±440.79	8150±427.25

Table 2. Percentile differences of haematologic parameters of different contraceptive groups

Contraceptives Compared	Hemoglobin	RBC count	Platelets count	Total leukocyte count
IUCD – IMPLANT	-14.86	1.26	18.35	-3.49
IUCD –NET-EN	-15.13	-5.388	1.126	-12.7
IUCD-DMPA	-13.9	-7.67	-4.069	-11.6
IUCD-OC	-13.6	-2.13	-4.4	-5.43
IMPLANT -NET-EN	-2.61	-6.58	-19.2	-8.9
IMPLANT – DMPA	-1.24	-8.76	-21.67	-7.8
IMPLANT-OC	-0.9	3.3	-21.98	-1.85
NET-EN – DMPA	1.39	-2.47	-3.067	0.97
NET-EN –OC	1.74	3.41	-3.36	6.45
DMPA-OC	0.33	5.98	-0.39	5.52