Alteration in Routine Coagulation Profile of the patients taking Injectable Contraceptives

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The proposed study is aimed to record the coagulation parameters like fibrinogen degradation products (FDPs), fibrinogen levels, thrombin time (TT), Prothrombin time (PT) and activated partial thromboplastin time (APTT). In this study, coagulation parameters were compared in injectable contraceptives and control group. Forty subjects of injectable group with 20 normal females without hormonal contraceptives were included in the present study with a contraceptive duration from 3-18 months. Blood samples were collected for special coagulation parameters. FDPs and TT levels were significantly elevated in subjects using injectable contraceptives as compared to normal control. PT and APTT were not significantly altered by injectable groups, where fibrinogen levels were significantly reduced in injectable group as compared to normal controls.
Key words: Coagulation profile, injectable contraceptives

In some cultural settings, injectable or subdermal routes of administration are preferred. Now-a-days, long-acting injectable contraceptives containing just a synthetic progestogen e.g. depot medroxyprogesterone acetate (DMPA), norethisterone enantate (NETEN) have been in clinical practice for more than 20 years[1]. World health organization has identified contraception as one of the most important issues facing the world today. The aims of contraception is to prevent fertilization of ovum or its implantation[2]. Kelleher[3] reported a 50% increase of factor VIIc in women taking oestrogens and a fall in the relatively protective antithrombin III.

Bonnar[4] studied that coagulation effects depend on the dosage of oestrogen and type of progestogen used in combination. Bulent-Tiras[5] and his associates studied the effects of once-monthly injectable contraceptives (mesigyna) on coagulation parameters that PT and APTT measures did not change at the end of 6 months. Spona et al[6] reported that there is significant increase in FDPs and factor VII by using injectable contraceptives. Norris and Bonnar[7] studied that there is balanced effect on the hemostatic system stimulating both procoagulatory and fibrinolytic activity.

Subjects and methods: Forty females of child bearing age on injectable contraceptives for at least three preceding months were included in this study. Twenty, age matched females, not taking any contraceptives were included as controls. Subjects were selected from Sir Ganga Ram Hospital, Services Hospital and Lady Willington Hospital.

Exclusion Criteria: Following women were not included in the study.

- Women with history of patichae or easy bruising before the start of contraceptives.
- Women with history of drug intake that is known to change the coagulation parameters.
- Women having past history of jaundice, diabetes mellitus, hypertension and nephrotic syndrome.

Grouping of the Subjects:

Group I: Twenty age-matched healthy females, not taking contraceptives were kept in this group. It is control group.

Group II: Forty patients using injectable contraceptives for at least three preceding months were included in this group. The injectable contraceptive used was "DEPOPROVERA" which contains 1.5mg/ml depotmedroxy progesterone acetate (progestogen). 3.6 ml of blood was mixed with 0.4ml of 32mg/l trisodium citrate for the estimation of prothrombin time, activated partial thromboplastin time, thrombin time, fibrinogen assay and fibrinogen degradation products.

Results

In group II (injectable group), 17.5% were related to the age group of 15-20 years, 60% were in the group of 21-30 and 22.5% were in 31-40 years. In group I, 40% were in age group of 15-20 years, 55% of 21-30 years and 5% of 31-40 years (Table 1).

The mean prothrombin time in group I was 13.7±2.05 with a range of 10-17 seconds. The mean PT in group II was 14.0±0.55 with a range of 8-15 seconds. There was no significant difference between group I and group II.

The mean APTT in group I was 33.7±1.52 with a range of 30-37 seconds and the mean APTT observed in group II was 33.4±2.54 with a range of 26-35 seconds. However, there was no significant difference on comparison with group I. The results of group II did not show a significant difference from the control (Table 2).

The mean TT in group I was 12.6±1.27 with a range of 10-15 seconds. The mean TT in group II was 13.8±0.74 with a range of 12-15 seconds. On statistical evaluation, TT was highly significantly prolonged in group I as compared with the controls (Table 2).

The mean value of fibrinogen in group I was 305.9±45.99 with a range of 248-330 mg/dl. The mean value of fibrinogen in group II was 273.8±19.04 with a range of 245-330 mg/dl. On statistical evaluation the fibrinogen levels were highly significantly shortened in

group I as compared with controls (Table 2).

In the present study, all control group subjects (100%) had FDPs levels in the range of <5 µg/ml. In group II (injectable group), 15 out of 40 subjects (37.5%) had FDPs levels of >5 ≤20 µg/ml and 21 out of 40 subjects (52.5%) had FDPs levels >20 µg/ml but 4 out of 40 subjects (10%) in this group had levels in the range of <5 µg/ml which were normal. The FDPs level was found to be increased in subjects taking injectable contraceptives as compared with control group and difference was statistically significant (Table 3).

Table 1. Age-wise distribution in subjects of control group (I) and injectable contraceptive group (II)

Age in years	Group I (Control subjects)		Group II (Injectable contraceptives)	
	n=	%age	n=	%age
15-20	8	40.0	7	17.5
21-30	11	55.0	24	60.0
31-40	1	5.0	9	22.5
Total	20	100.0	40	100.0

Table 2. Distribution of PT, APTT, TT and Fibrinogen in Groups I and II

Parameters Control	Group I (control)	Group II (Injectable)	Statistatical Analysis
PT	13.7±2.05	14.0±0.55	I vs II*
APTT	33.7±1.52	33.4±2.54	I vs II*
TT	12.6±1.27	13.8±0.74	I vs II**
Fibrinogen	305.9±45.99	273.8±19.04	I vs II**

*Non-significant, **Significant

Table 3. Distribution of Fibrinogen Degradation Products in cases of injectable contraceptives and control subjects

FDPs (µg/ml)	Control Group I	Injectable contraceptives II
< 5	20	04
> 5 ≤ 20	00	15
> 20	00	21
Total	20	40

Statistical analysis (Chi-square test) II vs I (p<0.001)

Discussion

Prothrombin Time: In the present study, PT of subjects on injectable group was found to be comparable with that of control group. This study was in favour of Bulent[5] who observed no change in PT during the use of injectable contraceptives.

Activated Partial Thromboplastin Time: In the present study, APTT of subjects on injectable contraceptives was reduced as compared to control subjects but the difference was statistically non-significant. These results were consistent with the findings of Bulent[5] who observed no significant change in APTT during the use of injectable contraceptives.

Thrombin Time: In this study, TT was found to be increased significantly (p<0.001) in injectable group. However our findings are not consistent with that of Bulent[5] who observed no change in TT of women taking injectable contraceptives.

Fibrinogen Level: In the present study, fibrinogen level was found to be significantly reduced (p>0.001) in subjects on injectable medication when comparing with control. These reduced levels may be due to enhanced fibrinolysis in subjects on injectable contraceptives. However, our findings do not confirm with the results of Bulent[5] who observed no change in fibrinogen level while using injectable contraceptives.

Fibrinogen Degradation Products: In the present study, FDPs were found to be significantly increased (p<0.001) in the subjects on injectable groups when compared with the controls. These increased levels of FDPs may be due to enhanced fibrinolysis. These findings were consistent with the results of many investigators who observed increased levels of FDPs in women taking injectable contraceptives as compared to control group[7,8,9,10].

Conclusion

The study confirms that by the use of injectable contraceptives, PT and APTT are not significantly altered while TT and FDPs are prolonged, on the other hand fibrinogen levels are decreased as compared to control group. So comparison of injectable with control group reveals that changes in coagulation parameters are less marked in injectable group showing the beneficial effects of injectable contraceptives.

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