BLOOD COAGULATION AND FIBRINOLYSIS WITH AN INJECTABLE LONG-ACTING PROGESTOGEN—OESTROGEN CONTRACEPTIVE

by

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The problem of a possible association between Deladroxate (*), a long-acting injectable Progestogen-oestrogen contraceptive and thrombosis may be examined from two aspects ; firstly ; Has the incidence of thrombophlebitis increased as a result of Deladroxate usage?. From the careful analysis of the available figures in our country, the frequency of thrombophlebitis amongst women using Deladroxate appears to be no higher than in non pregnant women of the same age group who have not taken Deladroxate. Secondly ; are there any changes in the blood coagulation and fibrinolysis in women given Deladroxate ? This is the subject of this report.

MATERIAL AND METHOD

This study presents our experience with the changes in blood coagulation and fibrinolysis in a group of 67 women receiving Deladroxate for 12—14 cycles. All were multiparae having 2—8

(*) 150 mg. 16 a-17 a-dihydroxyprogesterone acetophenide and 10 mg. oestradiol enanthate in one ml. oily solution supplied by : The Squibb Institute for Medical Research.

children (average 4.2) their age ranged between 18 and 40 years (average 30.2) having no history of previous thrombosis of any form. They were followed up monthly for a period of one year.

The following tests were made use of to determine the coagulability and fibrinolysis of their blood :

1. Prothrombin consumption index (Quick's method)
2. Prothrombin percentage (Quick's method).
3. Whole blood clotting time (Lee & White method).
4. Plasma fibrinogen (Stirland method).
5. Clot retraction (Hepler's method).
6. Bleeding time (Dukes method).
7. Fibrinolytic activity (Stefanini and Dameschek method).

These tests were performed before giving the medication to provide base line data and were repeated after the 6th and 12th injection.

RESULTS

I.—Tests of Blood Coagulation :

1. *The Prothrombin Consumption index :*

Table I shows the Prothrombin consumption index of participants before and during the trial.

TABLE I

Prothrombin Consumption Iindex Percent

	Admission	6 m.	12 m.
Mean	18.27	16.58	18.12
Variations	5-35	10-25	11-28

Normal Range 0—40%.

2. *Prothrombin Activity :*

The Prothrombin activity percent of participants is shown in Table II.

TABLE II

Prothrombin Activity Percent

	Admission	6 m.	12 m.
Mean	83.8	83.95	82.9
Variations	65-100	67-100	60-100

3. *Whole Blood Clotting Time :* (w.b.c.t.)

The W.B.C.T. in minutes shown in Table III.

TABLE III

Whole Blood Clotting Time (minutes)

	Admission	6 m.	12 m.
Mean	5.06	6.21	5.79
Variations	4-8	5-8	4.5-8

Normal range 5—10 minutes.

4. *Plasma Fibrinogen :*

Estimations of the Plasma fibrinogen are presented in Table IV.

TABLE IV

Fibrinogen (mg./100 cc. plasma)

	Admission	6 m.	12 m.
Mean	366.86	480.00	347.9
Variations	200-500	290-517	250-500

II.—Tests of the Platelet and Vascular Factors :

1. *Clot Retraction Test :*

Table V shows the changes in Clot retraction test of Participants during the course of the treatment.

TABLE V

Clot Retraction

	Admission	6 m.	12 m.
Mean	53.3	53.91	53
Variations	49-60	50-58	43-57

2. *Bleeding Time :*

The bleeding time in minutes is shown in Table VI.

TABLE VI

Bleeding Time (minutes)

	Admission	6 m.	12 m.
Mean	1.94	1.90	1.90
Variations	1.15-3.30	1.34-3	1.15-3

Normal Range 1—3 minutes.

III.—Fibrinolytic activity of the blood of Participants was shown to be within the normal range before and during the treatment cycles.

DISCUSSION

Ecberg and Owrens reported an increase in the Prothrombin, Proconvertin, Fibrinogen, and stuart factors in 5 women taking oral contraceptives.

Kirchhoff and Poliwoda and Haller found a tendency to slight activation of the coagulation system during the first 8 to 10 days of treatment with combined Progestogen/Oestrogen products but they concluded that the findings were not significant.

Brehm reported that during administration of Lyndiol the coagulation and fibrinolytic system in the same test subjects showed more marked differences than those of the fluctuation in the course of a normal cycle. The general coagulation time was shortened, the Quick Prothrombin time and the Proconvertin showed a marked increase. Whereas antithrombin III was reduced there was an increase in Plasminogen. The significance of these findings however is not known as some of these factors increase in normal pregnancy though there is no increase in the thromboembolic phenomena. It is in the puerperium that the incidence of thromboembolic phenomena is at its highest and this is normally taken to be due to the trauma at the time of confinement.

Payling Wright considers that the increase in venous thrombosis occurring post-partum and after trauma is due to an increase in the number and stickiness of the platelets. Occasionally this response may be excessive and if associated with other factors such as local retardation of circulation, intravenous thrombosis may occur. These changes in platelets have not been found in normal pregnancy. Thus though the information available suggest that a slight increase in coagulation factors occurs in some women taking oral contraceptives the importance of these changes is uncertain even the effect of oestrogen Per se on the clotting mechanism is not understood so that such changes as are found could be physiological that is, normal oestrogen induced changes.

Indeed it is commonly agreed that there is at present no valid test for measuring the coagulability of the blood and the raising of this whole problem has underlined the absence of available knowledge of thrombophlebitis in normal women of the child-bearing age and the gaps in our understanding of blood clotting in physiological as well as pathological conditions.

Throughout the trial done on deladroxate for one year the above mentioned observations were not recorded. Investigations done in this study before, during and after medication showed that values of the clotting function tests fell within the normal limits of these tests. The menorrhagia observed in some cases during the trial could not be related to the presence of any clotting defect.

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