SOME OBSERVATIONS ON THE CHANGES IN CAPILLARY RESISTANCE IN ORAL CONTRACEPTIVE USERS

By

K. ZAKI (Ph. D.), M. N. YOUNIS (M. Ch.),

S. A. RAZEK (D. G. O., D. P. H.), T. E. MEKKAWI (D. M. Sc.)

and H. NOUR (B. Sc.)

INTRODUCTION

Progress in knowledg regarding the changes in the vascular factor in pill users has regrettably not kept pace with the recent great strides in the studies of blood coagulation changes and platelete function.

It is known that certain hormones have noticeable influence on capillary resistance. Glucocorticoids are especially active in increasing and maintaining capillary resistance at high levels (Kramar 1957 a). Oestriol has been found to have a protective action on the different organs of the body especially the vascular and perivascular connective tissue of capillaries, arteries, and venulae reducing their permeability and fragility (Poliwoda et al, 1963 and 1965, Pierer, 1964, Bergmann and Humber, 1965).

In a previous study by the first author with others (Zaki et al, 1972) it was found that oestriol as well as 17-ketosteroids decreased under the combined steroid contraceptive therapy for variable periods.

So the present work was carried out to investigate the vascular factor of haemostasis in pill users as a trial to establish a possible relationship between the possible role of the vascular factor in the occurrence of venous thrombosis in some cases and the hormonal status under such condition.

MATERIAL & METHODS

The present investigation was performed on 215 cases randomly selected from those attending the Family Planning Clinic, Cairo University Hospital. Of these : 165 were using the pills for a period of

6 to 30 months. The rest were attending for the first time to join the trial on oral contraceptives, they did not use any contraception before and were regared as controls. All were multipara, having 2—6 children and their ages ranging between 22 and 40 years.

They were divided into 5 groups :

Group I : 40 cases receiving cyclically a high dose combined pill (Megestrol Acetate 4 mg. + 0.5 mg. Ethinyl Oestradiol).

Group II : 36 cases receiving cyclically pills by the sequential regimen (16 pills containing 0.1 mg. Ethinyl Oestradiol followed by 5 pills combining the same dose of Ethinyl Oestradiol and 3 mg. of Megestrol Acetate.

Group III : 51 cases receiving cycically a low dose combined pill (Norgestrel 0.5 mg. + Ethinyl Oestradiol 0.05 mg.).

Group IV : 38 cases receiving continuously a small dose progestogen (Luteal supplementation pills ; 0.5 mg. Lynestrenol).

Group V : 50 cases (control) recieving no pills.

The capillary resistance was estimated using the Gothlin test as modified by Wright and Lilienfeld (1936) and Kramar (1962). It was done as follows :

A blood pressure cuff was applied to the upper arm of the participant. The pressure was maintained midway between the systolic and diastolic blood pressure for 5 minutes. Five minutes after the release of the inflated cuff, petechiae were counted in a fixed circular area 3 cm. in diameter below the elbow pit with the upper margin 4 cm. below the elbow crease. A count greater than 5 was regarded by Kramar (1962) as indicating decreased capillary resistance. In order to avoid the possible error resulting from the physiological variations in capillary resistance, the tests were always applied at 10 a. m. in the third postmenstrual day, and the estimations were all done during one month. Cases having a blood pressure over 140/90 were not included in the study. The test was done twice in each case, once on every forearm and the number of petechiae in both forearms divided by 2 was taken as the average of that case. The average number of petechaie for each group of cases was then calculated & the 't' test was applied to evaluate the statistical significance of the results obtained.

24 hour urinary collections were obtained from selected cases from groups I and III, as well as from 10 controls of almost the same age and parity, on day 13—16 of the cycle (time of expected oestrogen peak). The cases were using the pills for 6 months. The urine samples were analysed for the determination of oestriol by a method slightly modified from that of Eberlein et al (1958) and 17-ketosteroids by the method of Norymberski et al (1953) as modified by Diczfalusy et al (1955).

RESULTS

The number of petechiae in each group is shown in table I. It shows an increased fragility (i.e. decreased capillary resistance) in all groups except the control. The difference between the average number of petechiae in each group compared to the control was statistically significant at the 5 per cent level. The intergroup differences were however, statistically insignificant. The average number of petechiae calculated according to the number of treatment cycles of the different preparations is shown in table II. Oral contraceptives are shown to produce an increased capillary fragility in all cases, irrespective of the duration of use after the 6 months therapy. The differences (compared to the control) were again statistically significant at the 5 per cent level. The intergroup difference in the number of petechiae proved to be statistically insigificant.

Oestriol excretion (table III) shows marked decrease from 27.4 to 6.1 mcg/24 hrs. in the cases selected from group I and to 7.3 mcg/24 hrs. in the cases of group III. 17-ketosteroids (table III) dereased also from a mean of 8.49 in the control group to 5.7 and 5.3 mg./24 hrs. in the cases selected from groups I and III respectively.

TABLE I

The average number of petechiae in the different groups compared to the control

	Average number of petechiae	Calculated «t»
Group I	15.0	3.166
Group II	13.7	3.511
Group III	16.4	4.995
Group IV	13.1	3.042
Group V (Control)	4.98	—

TABLE II
Average number of petechiae in pill users related to number of treatment cycles

No. of treatment cycles	Average number of petechiae	Calculated «t»
6	12.85	3.675
12	18.30	2.660
18	15.90	3.760
24	12.90	2.840
30	20.60	4.000

TABLE III
24 hour urinary excretion of oestriol and 17-ketosteroids in cases and controls

	No. of cases	Oestriol (mcg/24hrs.)	17-ketosteroids (mg/24hrs.)
Group I	5	6.1	5.7
S. D.		0.187	0.69
Group III	5	7.3	5.3
S. D.		1.03	0.866
Control	10	27.4	8.49
S. D.		3.75	2.54

COMMENT and CONCLUSION

Capillary resistance is subject to many physiological variations. It tends to decrease as the day advances (Kramar 1956). It is influenced by season, declining in late winter and early spring (Robert et al 1931). All the above changes suggest a systemic control.

It has also been shown that capillary resistance is subject to endocrine influence (Kramar 1957 a) as previously mentioned. Besides glucocorticoids a number of hormones have been reported to have short-lived effects on capillary resistance. Vasopressin (Kramar 1957 b) and the catecholamines (Parrot 1944) increase it while histamine (Sack 1938) and heparin (Cabor 1957) decrease it. These substances are

responsible for the so-called immediate type of stress response which sets in promptly and subsides in a matter of minutes or hours.

There are as well individual variations in capillary resistance, (Kramar 1956). Although healthy individuals may have high, medium or low resistance, yet each individual tends to maintain his or her individual level.

Evaluation of results of capillary resistance measurements is i. e. more significant when there is an opportunity to observe the patient for a longer period of time, to establish the individual resistance level and its physiological fluctuations.

In this study a significant increase in capillary fragility was demonstrated in the pill groups when compared to the controls. The cases using the pills for 6 months produced a number of petechiae which was not significantly different from those using it for 12, 18, 24 or 30 months. This means that the increased fragility once established does not increase in severity with the prolonged intake of the pill.

It is not easy to explain the increased capillary fragility observed in this study. A possible explanation is that the exogenous hormones administered play their part through the suprarenal cortex. The slight suppression of the adrenocortical activity found in the selected cases investigated in this study as evidenced by the decreased 17-ketosteroids may be an important factor in this respect. However, measurement of the free biologically active fraction of plasma cortisol is of great value especially in the series of cases having increased fragility under contraceptive therapy.

Another possibility which may explain this increased capillary fragility is the diminished production of endogenous oestrogens and in turn oestriol, which accompany the continued use of contraceptive steroids. Oestriol is known to be essential for the integrity of capillaries as mentioned before. Oestriol succinate have been successfully used in the treatment of hæmostatic disorders associated with increased capillary fragility (Kopera, 1970).

Estimations of urinary excretions of oestriol in the selected cases of groups I and III were significantly lower than the controls but it was not possible to correlate the amount of oestriol excreted to the number of petechiae produced.

A more detalied endocrinological study on a greater number of cases starting to use different types of steroid contraceptive pills and the effect of duration of therapy especially in the first 6 months is now under investigation.

SUMMARY

Capillary resistance to positive pressure was estimated in a group of 165 women. Cases were divided into 4 subgroups. Each subgroup received a different type and dose of the pills for a period of 5 to 30 months. Results were compared to a control group of 50 cases not receiving any pill. Urinary oestriol as well as 17-ketosteroids were estimated in selected cases of groups I and II, and 10 controls.

A significant increase in capillary fragility was demonstrated in the pill groups when compared to the controls.

The possible relation of this increased fragility to the changes in suprarenal cortical activity and to diminished oestriol is raised.

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