ORAL CONTRACEPTIVES AND HYPERTENSION

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SUMMARY

1. The results of ambulatory blood pressure control in nineteen patients who were hypertensive on oral contraceptives are presented.
2. Withdrawal of the oral contraception in this group of patients reduced the average blood pressure significantly. Seven of the patients became normotensive after stopping the medication.
3. Hypertension was found among the relatives of the patients in twelve cases.

Key words: oral contraceptives, hypertension.

In previously normotensive women oral contraceptives (OC) have been found to increase the systolic blood pressure to a small but significant extent (Weir, Briggs, Mack, Taylor, Browning, Naismith & Wilson, 1971). The incidence of manifest hypertension during oral contraceptive treatment varies from 0 to 18% in prospective studies (Weir et al., 1971; Saruta, Saade & Kaplan, 1970).

The aim of the present study is to describe the influence of OC on the arterial blood pressure in a group of patients. The patients were admitted to our departments because of arterial hypertension during treatment with OC.

MATERIALS AND METHODS

Patients

Nineteen women were studied (mean age 34 years, range 21–47). Ordinary oral contraceptives had been used for 2 months to 7 years (mean 31 months) before this study began. In three cases the patients were known to be hypertensive before the oral contraceptive treatment began. In the remaining cases hypertension was discovered 2–6 months before the study.

In all the cases the complaints were few, mainly headache, dizziness or palpitation. None of the patients had any other medical problems.

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the patients had oedema. The optic fundi were without changes or grouped as stage I or II according to Keith and Wagener. Kidney diseases, adrenal hyperfunction and renal artery stenosis were ruled out by appropriate tests.

**Blood pressure control**

After the initial examination in the ward the patients were transferred to an out-patient clinic and reviewed at intervals of 2–4 weeks. The blood pressure was measured by an ordinary sphygmomanometer after 10–20 min of supine rest. Auscultation was used, and the diastolic pressure recorded at the disappearance of the sound. For analysis of the results the mean blood pressure (MBP) was calculated as the diastolic pressure plus one-third of the pulse amplitude.

The patients were seen during oral contraceptive therapy and after withdrawal of OC. During each period at least three controls were performed. For the calculation of the average MBP in each period three separate measurements were used: during OC treatment the last three measurements before stopping the medication were used. During the period of no treatment, three values obtained after a minimum of 3 months after withdrawal of OC were used.

Fourteen patients continued their OC treatment during the first part of the ambulatory control. Subsequently the oral contraceptives were withdrawn. In three of these patients a second trial was performed. Five patients had the oral contraceptive treatment withdrawn during the initial admission and were followed as outpatients without oral contraceptives for 4–5 months. Afterwards they were given oral contraceptives for at least 3 months.

None of the patients received diuretics or antihypertensive drugs while this study was performed.

**Measurement of renin substrate and renin concentration in plasma**

This was performed by the method described by Giese, Jørgensen, Nielsen, Lund & Munck (1970). In normal persons the renin substrate concentration in plasma varies from 1350 to 2000 ng of angiotensin I/ml. The plasma renin concentration varies from 6 to 60 μGU/ml.

**Statistics**

The tests used were performed as described by Therkelsen (1968).

**RESULTS**

In the patients continuing on OC the average MBP ranged from 97 to 150 mmHg (median 126 mmHg, n = 14). After stopping the medication the average MBP ranged from 93 to 154 mmHg (median = 108 mmHg, n = 19). During the second period on OC the average MBP ranged from 101 to 133 mmHg (median = 127 mmHg, n = 8). This difference is significant (Wilcoxon rank sum test of paired differences, P<0.01).

According to the tables of Master, Garfield & Walters (1952) the average MBP for each patient was classified as normal or abnormal. Three groups emerged from this analysis. 1. Normal MBP throughout the ambulatory period (four). 2. High MBP during OC and normal MBP after withdrawal of OC (seven). 3. Elevated MBP in both situations (eight). The number of patients is given in parentheses.

The variance of MBP in the single patient during each period was calculated. Bartlett's test did not reveal inhomogeneity of variances. Therefore, it was possible to calculate the
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The variance was 50 on oral contraceptives and 53 when oral contraceptives were withdrawn. SEM of the difference between two average MBP was 5.8 mmHg. Subsequently, if the difference between two average MBP was greater than 16 mmHg, this difference was significant (t test, P<0.01, d.f. = 76). The seven patients who became normotensive after stopping the medication fulfilled this criterion. None of the remaining patients did so.

The plasma renin substrate was influenced by OC. On treatment the mean value was 7800 ng of angiotensin I/ml (range 4700–9300, n = 15) and without treatment the mean value was 1800 ng of angiotensin I/ml (range 1000–2600, n = 12). This difference is significant (Wilcoxon rank sum test, P<0.01).

The plasma renin concentration ranged from 6 to 80 µGU/ml on OC and from 14 to 40 µGU/ml when OC was stopped. No correlation between changes in plasma renin concentration and blood pressure variations could be found.

In the total material twelve of nineteen patients had hypertensive relatives. Among the seven patients who responded to withdrawal of OC, four had hypertensive relatives.

DISCUSSION

Our results confirm earlier experience (Laragh, Sealey, Ledingham & Newton, 1967). The blood pressure is significantly reduced in a group of patients who have been found hypertensive during oral contraceptive treatment, when OC is withdrawn. In seven cases the fall was significant when the variation in blood pressure measurements was taken into account. These patients became normotensive during the ‘off-pill’ period.

The variation of plasma renin substrate was in accordance with the findings of Skinner, Lumbers & Symonds (1969). We have not been able to discern any relation between plasma renin concentration and the variation in blood pressure (Skinner et al., 1969; Saruta et al., 1970).

We have found a remarkably high proportion of hypertensive relatives of the patients. Weinberger, Collins, Dowdy, Nokes & Luetscher (1969), Laragh (1970) and Crane, Harris & Winsor (1971) mentioned the same experience. As in our material no final judgment of the possible significance of genetic factors can be drawn.

REFERENCES


