EXPERIENCE WITH A NEW LOW DOSE ORAL CONTRACEPTIVE

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An effective contraceptive pill has become a reality in the early fifties. Since then, various modifications, both in the chemical structure and in the dose, were introduced.

The present report presents our experience with ovral a new low dose antivulatory oral contraceptive. Each tablet of ovral combines two steroid components, 0.5 mg of Norgestrel which is described chemically as 1—13 B-ethy 1-17 a-ethyny 1-17 hydroxy-gon-4-en-3-one and 0.5 mg of ethinyl estradiol.

Norgestrel differes from other progestational agents in bearing an angular ethyl group at carbon 13 of the steroid nucleus, rather than the methyl group characteristic of all other progestational agents. It is totally synthetic and ows its high activity and low toxicity to its unique formula. According to the test employed, norgestral is 10 to 20 times more potent than progestrone. Detailed classical bioassays with Norgestrel in the doses employed for contraception demonstrated minimalo or undectable androgenic; estrogenic or mineralocorticoid activity.

MATERIAL METHOD

The Material of this study comprised 47 women. They were randomly selected from those attending the family planning clinic at Cairo University Hospital. All of them received no oral contraception for the last three months before joining the trial. All were multiparae with an average number of children of 4.8 and their age ranged between 18 and 40 years.

A thorough history and a careful general and pelvic examination together with a premedication vaginal and cervical smears were routine in all cases. Smears were sprayed by a spray-cite fixative and stained by a modified pap. technique.

Participants were instructed to use the pills cyclically for twenty one days starting from the fifth day of the menstrual flow. They were followed up monthly for a period of 7—24 months ; the total follow up cycles were 815 cycles.

At each follow up visit any complant was first noted than an inquiry was made about the menstrual pattern and any breakthrough bleeding, changes in the gastrointestinal, vasomotor, nervous and emotional functions together with any changes in the breast, in libido or any skin manifestations. At each visit the weight was recorded and compared to that of the previous visits.

At 6 months intervals, participants were re-examined both generally and gynecologically and the vaginal and cervical smears were repeated.

TESULTS

I.—Menstrual pattern

1. *Interval between end of tablets and onset of menstrual flow*

Table I shows the interval between the end of the tablets and the onset of flow. If mensturation did not start within seven days from the end of the tablets, another set of twenty one pills was started and the cycle was regarded as amenorrheic.

TABLE I

End of tablets-menstruation interval

Interval (days)	0	1	2	3	4	5	6	7
Number of cycles Percent	14.2	3 1	8.2	19.9	21.4	23.0	6.1	2.6

2. *Cycle length*

The average cycle length of the participants before therapy was 28.5 days. The length of the cycles during treatment is shown in table II.

TABLE II

Cycle Length

Cycle length (Days)	Number of Cycles Percent
—22	1.5
22+	2
24+	5
26+	15.3
28+	41.4
30+	28.1
Not determined	4.2
Average cycle length	2.6 days

3. *Amount of flow*

The amount of menstrual flow during therapy judged subjectively is presented in table III.

TABLE III

Amount of Menstrual flow.

	Slight	Moderate	Severe	Absect	Not Determined
Number of Cycles percent	12.7	77	6.1	1	8.2

The pretretment figures were ; severe flow in 14.3% of the cases, moderate flow in 70% and slight flow in 15.7%.

4. *Duration of flow*

The average duration of menstrual flow of the participants before joining the trial was 4.1 days. The duration of flow during the treatment cycles is shown in table IV.

TABLE IV

Duration of Menstrual flow

Duration of menstrual flow (Days)	2	3	4	5	6	7	8
Number of Cycles Percent	4.1	16.8	25.5	30.6	8.2	3.1	1
Average duration forall cycles	4.4 days						

5. *Breakthrough bleeding*

Spotting occurred in 2.6% of the cycles and bleeding in 3.1% of the cycles. Both occurred mainly in the first and second cycles and particularly during the third week of these cycles.

6. *Dysmenorrhea*

In 78% of the cycles no dysmenorrhea was reported. 18.4% of the cycles were accompanied by slight or moderate dysmenirrhea while in 3.6% of the cycles dysmenorrhea was described by the participants as severe. Before therapy the incidence was 11.4% and 8.6% respectively.

II.—Gastrointestinal Manifestations :

Loss of appetit was complained of in 15.3% of the cycles. It was more pronounced in cycle one and dropped from 29.8% at that cycle 11.8% to cycle three and remained nearly so for the rest of the treatment cycles.

Nausea was experienced by the participants in 14.8% of the cycles. Its incidence was lowered to 5.9% by cycle six compared to 17% at cycle one. Vomiting was experienced by three participants during the first cycle and it did not recur in next cycles.

Gastric discomfort and / or abdominal distension were complained of in 5% of the cycles. Gastric discomfort dropped from 8.5% in cycle one to zero percent by cycle 6 while abdominal distension increased from 2.1% at cycle one to 8.8% in cyle three to drop again to 5.9 % by cycle six. After cycle six the incidence remained almost the same.

III.—Headache and dizziness

The incidence of headache and dizziness is shown in Table V. Their incidence remained almost the same during the whole period of the tiral.

TABLE V

The incidence of Headache and Dizziness

	Number of cycles percent
Headache	50.5
Dizziness	30.1

IV.—Skin manifestations

Cloasma ocurred in two cases. In one of them the condition appear at cycle three, in the other it was noticed by cycle five.

Twenty eight percent of participants admitted having some fall of hair. It was described as slightly more than what they had before joining the trial.

V.—Breast changes

Changes in the breast size and the occurrence of breast tenderness is shown in table VI.

TABLE VI

Breast Changes

Breastsize	No change	Increased	Decreased	Not Determined
Percent of cases	84.6	3.1	10.2	3.1

Breast tenderness	Yes	No	Not Determined
Percent of cases	3.6	92.8	3.6

No breast swellings were reported or found in the participants during the period of a observation.

VI.—Changes in Libido

The frequency of intercourses per week did not show significant change.

Changes in libido are diffuclt to assess, yet on careful inquiry it was reported to increase in two cases while three cases noticed a decrease in their libido.

VII.—Weight changes

An increase in weight occurred in 26% of the cases during treatment and a decrease occurred in 18.9%. The increase in weight was mainly during the first three cycles so that the participants who continued to add weight after were only 11% of the cases. The average increase in weight was 1.8 kg. per women year

VIII.—Blood pressure and vascular changes

The blood pressure on admission ranged between 100 and 140 mm systolic 70 to 90 diastolic estimations at six twelve and twenty four months show no significant changes.

No thromboembolic manifestations occured during the treatment cycles.

IX.—Changes in the uterus and adnexa

The ovaries and tubes were normal in all cases before and during the trial and so also the average length of the uterus.

Cervical erosions pr eviously present in twelve cases were found in eighten cases after six months and twenty one cases after one year.

X.—Cytological findings

Three cases showed à'tpical cells (class II). No suspicious or malignant smears were found in any participant before or during the course of the trial.

XI.—Effectiveness

Not a single case of pregnancy occurred during the course of treatment. Even the two cases who missed one and two tablets repectively during the second week of cycle three and six did not conceive.

Comment :

Previous studies with the combined high dosage types of pills indicated their efficiency in preventing pregnancy. Various preparations containing one to ten mg of the different progestogens and .50 to 0.15 mg of ethnyl estradiol or its 3-methyl ether are now available.

An optimum ratio should be present between the progestogen and oestrogen part of any pill. Lowering too much the estrogen well lead to ovulation escapes. Lowering of the progestogen part is supposed to lower the side effects and leeds to a commercially cheap preparation.

Besides being effective a contraceptive pill should fulfil several crtieria it should be cheap and easily available for the average woman, the menstria pattern should not be greatly disturbed, and it should have minimal side effects.

The low dose pills used in this trial proved to be fully effective in preventing pregnancy. In 815 cycles not one unplanned pregnancy occurred. This was also the experience of Toland et al. (1967), of Makhlouf (1967) and of Kamal (1967).

The cycle length varied between 22 and 32 days with an average of 28.7 at cycle one, 28.4 at cycle three and 28 at cycle six. The average for all cycles was 28.6 days.

The amount of flow was moderate in 77% of the cycles. Cycle six showed the best results with no severe bleeding in any case, 94%, of moderate flow and 5.9% of slight flow.

The duration of flow varied between two to eight days with an average 4.6 in cycle one, 4.7 in cycle three, 4.4 in cycle six and it remained almost so during the rest of the treatment cycles.

Break through bleeding occurred in 3.1% of the cycles and spotting occurred in 2.6%. Roland et al. (1967) reported a 1.6% in cidence of bleeding in cycle six 1.3% in cycle twelve and non at all at cycle 18. Makhlouf had only 2 cases of break through bleeding in 52 cases followed for 3 to 6 months.

In the authers experience, the present preparation proved to have lesser side eFects than other preparations having larger doses except for the incidence of headache and dizziness which were much more pronounced in the users of this preparation. The cytological studies performed, proved no suspicious or malignant changes.

References

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