

SHORT AND LONG TERM EFFECTS OF VARIOUS CONTRACEPTIVES ON OVARIES

by

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Introduction

Oral tablets, I.U.C.D. and various conventional contraceptive devices often produce certain morphological and histological changes in the ovaries after varying period of their use.

Rock (1961), Satterthwaite and Gamble (1962), Garcia and David (1968) have reported the changes in the ovaries after short and long term use of different oral tablets. Eckstein (1970) reported that in most species tested so far the ovarian reaction to the I.U.D. is negative. There is little or no interference with the ovarian cycle or with the pituitary and ovarian hormones that regulate the cycles. Dass (1972) reported a high incidence of endometrial cystic glandular hyperplasia in cases using I.U.C.D. But no mention has been made in her article about the ovarian changes after use of I.U.C.D.

In this article direct assessment of the ovarian effects by different contraceptive

agents like oral tablets, I.U.C.D. (Lippes loop) and conventional contraceptive devices have been studied.

Material and Methods

Material has been collected from in-patients of N.R.S. Medical College Hospital, Calcutta from July 1972 to June 1974. Small wedge shaped ovarian tissue was collected during vaginal ligation of tubes for study. Total number of cases where biopsy was taken was 125. Out of these in 30 cases random sample of ovarian tissue was collected as a control. In 40 cases biopsy was taken during use of I.U.C.D. (Lippes loop), in 30 cases during treatment with oral tablets and in 25 cases during use of conventional contraceptive devices like male condom and spermicidal jelly or cream.

During operation both ovaries were examined macroscopically. The characteristic features which were noted were the size, shape, consistency and colour of the ovaries, presence of cysts or corpus luteum and adhesions with the tubes. The ovarian tissue was fixed in Bouin's fixative and haematoxylin-eosin stained paraffin sections were examined under microscope.

The histological changes in the ovarian tissue were scrutinized in details specially

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Accepted for publication on 27-10-75.

for the presence of recent corpus luteum, microcysts and the status of the ovarian stroma.

Out of 40 I.U.C.D. cases, in 16 where loop removal and vaginal ligation of tubes was done simultaneously, endometrial curettings were also collected and examined to note the effects of prolonged use of I.U.C.D. on the endometrium. These endometrial changes were scrutinized in relation to ovarian changes.

Analysis of cases and Discussion

Ovarian biopsies were collected during vaginal sterilization. The age of the patients including the control Group varied between 26 and 40 years. The minimum age was 26 and the maximum age was 38 years. Table 1 shows the age incidence in different groups of patients.

Since the multiparous patients usually attended for sterilization, more biopsies were studied in multiparous patients. Out of total 125 cases in only 39 cases the biopsy was taken in second and third

paras. The rest belonged to fourth para or more. Maximum parity was 9. Table II shows the parity distribution among the 4 above mentioned Groups.

Duration of use of contraceptives varied from 6 months to maximum period for 9 years. It was the I.U.C.D. which was retained for maximum periods. In one case it was retained for 9 years and in other 4 cases for more than 6 years. Oral tablets were used continuously for maximum period of 4 years and conventional contraceptives for 5 years.

Oral tablets which were used contained oestrogen 0.05 mg and progestogen 0.5 mg to 1 mg. Nature of I.U.C.D. was Lippes loop in all the cases and conventional contraceptive was either male condom alone or with spermicidal jelly or cream.

On reviewing the literature it has been found that various workers have reported the macroscopic appearance of the ovaries after long and short term use of oral tablets.

TABLE I
Age Incidence

	21-30 years	31-40 years	Total
Oral Group	21	9	30
I.U.C.D. Group	18	22	40
C.C. users Group	7	18	25
Control Group	21	9	30
Total	67	58	125

TABLE II
Parity Distribution

Parity	p2	p3	p4	p5	p6 or more	Total
Oral Group	2	10	9	5	4	30
I.U.C.D. Group	—	5	14	11	10	40
C.C. users Group	3	6	7	4	5	25
Control Group	—	13	7	6	4	30
Total	5	34	37	26	23	125

Garcia and David (1968) reported that ovaries in women treated with oral tablets appear relatively inactive at peritoneoscopy or laparoscopy. None of the ovaries examined at wedge resection performed at tubeligation showed evidence of recent ovulation or corpus luteum formation. Satterthwaite and Gamble (1962) reported that the ovary after use of Enovid 5 mg. is inactive and menopausal looking with rather thickened cortex suggestive of a Stein-Leventhal ovary. But Maqueo *et al* (1971) reported that there was no

group. Thus in the control group in 25% of patients the ovaries were enlarged and cystic, whereas among the contraceptive users, in half of the cases the ovaries were enlarged and cystic. Among the tablet users in 16 cases i.e. more than half of the cases the ovaries were enlarged and the rest were of normal size. In half of the cases of I.U.C.D. users the ovaries were enlarged and cystic and among the conventional contraceptive users in two third cases cysts were found in the ovaries (Table III).

TABLE III
Macroscopical Findings of the Ovaries During Operation

	Cystic	Firm	Adhe- sions	Corpus luteum	Friable
Oral Group	14	8	+	+	2
I.U.C.D. Group	12	—	26	19	—
C.C. users Group	14	—	5	—	—
Control Group	8	5	21	14	—

consistent ovarian changes in women using steroid contraceptives. Most of the ovaries were small, hard, of smooth surface and appeared inactive but several were moderately enlarged and had some microcysts. In two cases they resembled Stein-Leventhal ovaries. Eckstein (1970) reported that in most species tested so far the ovarian reaction to the I.U.C.D. is negative. There is little or no interference with the ovarian cycle and ovarian hormones that regulated the cycles. But on reviewing the literature so far no definite reports have been noted about the macroscopical and histological changes in the ovaries after long and short-term use of I.U.C.D. or conventional contraceptive devices.

In the present series, cystic enlargement of the ovaries was more common among those who used some forms of contraceptives than among the control

group. During treatment with oral tablets in 8 cases the ovaries were found very firm, whereas in 5 cases in the control group they were firm. Thus, it is difficult to conclude whether the firmness was due to prolonged use of oral tablets without studying more cases. Among the tablet users in 7 cases corpus luteum was noted even on naked eye examination, and in one case only the ovaries had the appearance of Stein-Leventhal ovary.

Adhesion of the ovaries with the tubes was a common feature when I.U.C.D. was retained for a long time. In 20 cases where loop removal and ligation of tubes was done simultaneously flimsy adhesions of the ovaries with the tubes were noted. Tubes were found congested, thickened and there were peritubal adhesions, but the fimbrial ends were found patent in most of them. In another 5 cases where biopsies were taken 2 to 4 years after re-

removal of loop, no adhesions were noted proving that the above mentioned changes during use of I.U.C.D. are reversible. Table No. IV shows the macroscopical findings of the ovaries during operation.

Histological examination of ovarian tissue during use of oral tablets has been reported by several workers.

Garcia (1972) reported that Enovid users show a greater follicular activity. Maqueo *et al* (1972) also reported that the ovarian changes showed the morphologic alterations mainly in follicular development. In the present study histological examination of ovarian tissue among various contraceptive users showed the evidence of increased follicular activity by formation of follicular cysts (Fig. 1). follicular cysts were found only in 16% cases among the control group, whereas with oral tablets in 40%, after I.U.C.D. in 30% and among the conventional Group in 56% of cases. Follicular cysts were formed even after 5 to 7 months' use of conventional contraceptives. In 2 cases where conventional contraceptives were used for 6 and 7 years, bilateral polycystic ovaries were felt with multiple follicular cysts. Increased follicular activity in these cases, particularly after use of oral tablets does not seem to be due to increased pituitary activity since these follicular cysts are lined by flattened and atrophic epithelium and not by active granulosa cells.

About the suppressive action of ovulation by the oral tablets, there is a diversity of opinion even at the present day. Garcia (1968) claimed that none of the ovarian biopsies performed at tubal ligation showed evidence of recent corpus luteum formation (Fig. 2). But there are others who are of the opinion that in not all contraceptive steroids action involves suppression of ovulation, and

have reported that there are certain enzymes that produce energy in the endometrium. These enzymes are decreased in amount after giving contraceptive steroid.

In 4 cases in the present series recent corpus luteum was found. Two cases were using oral tablets for 4 and 6 years continuously. In 4 cases biopsy was taken 2 to 7 months after withdrawal of oral tablets. Out of these in 2 the biopsy showed presence of maturing graffian follicle and corpus luteum. This shows normal taking up of ovarian function within 3 months of stopping tablets.

Maqueo *et al* (1972) claim increased ovarian connective tissue in about half the women using combined preparations. In the present study stroma cells were found dense at places and plump in appearance (Fig. 3). But this stromal activity was not related to any androgenic activity clinically.

Among I.U.C.D. users where biopsy was taken in luteal phase ovulation was evidenced by presence of corpus luteum even in presence of multiple small cysts and extensive adhesions with tubes. The bilateral polycystic ovaries which have been found in some cases of I.U.C.D. resembled the bilateral polycystic ovaries of metropathia haemorrhagica, but clinically there was no history of amenorrhoea. In some cases menorrhagia was complained of which might be due to excessive adhesions and congestion.

Dass (1972) reported a study of endometrial biopsies in women wearing loop which indicated that ovulation was not interfered with.

In the present study, in 16 cases endometrial curettage was studied in loop cases. Endometrium was secretory in nature in all the cases where it was taken in the luteal phase, showing that ovulation was not interfered with.

Summary and Conclusion

1. Ovarian morphology and histology of 125 patients has been studied by taking a wedge shaped ovarian tissue during non-puerperal vaginal ligation of tubes.

2. Biopsy was taken in 30 cases from the oral tablet users, in 40 cases where I.U.C.D. was used, in 25 cases where conventional contraceptive was used and in another 30 control cases where no contraceptive was used.

3. Minimum age where biopsy was taken was 24 years and maximum was 38 years.

4. Parity varied from 3rd para to 9th para.

5. Duration of use of contraceptives was from 6 months to 9 years.

6. Macroscopical examination of the ovaries revealed increased incidence of enlarged and cystic ovaries among the contraceptive users as compared to the control group. Extensive flimsy adhesions of the ovaries with the tubes were noted where I.U.C.D. was retained for few years. The functional activity of the ovaries was maintained which was proved by presence of mature graffian follicle and recent corpus luteum in the ovary and secretory endometrium. In one case among the tablet users the ovary had the appearance of Stein-Leventhal ovary.

7. Histological examination has shown presence of recent corpus luteum where oral tablets has been used for few years. Follicular activity has been observed more frequently among the contraceptive users than among the control group. The cysts were found lined with flattened epithelium and not by granulosa cells which shows that gonadotrophic hormone activity is not in excess. Stroma cells were dense in some places and plump in appearance among oral tablet users.

Acknowledgement

We express our gratitude to Dr. G. C. Mukherjee, Superintendent, N.R.S. Medical College Hospital, Calcutta for giving us permission to use the hospital records.

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See Figs. on Art Paper III-IV