HISTOPATHOLOGICAL AND HISTOCHEMICAL CHANGES IN ENDOMETRIUM IN CASES OF INTRAUTERINE CONTRACEPTIVE DEVICES

by

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Intrauterine contraceptive devices are playing an increasingly important role in modern contraceptive practice. They have come a long way from the camel driver who put a pebble in the womb of his beast to the present day when millions of women have it in place (Editorial, 1973). Until the past decade the use was limited because of general reluctance to insert any foreign material in uterine cavity, though numerous studies have shown that such prejudice is unwarranted. Opinions differ regarding its mode of action and possible biological response to this foreign body especially for prolonged periods. Thus, the present study was undertaken in an attempt to evaluate the recent and long term effects of Intrauterine Contraceptive Devices on the endometrium.

Material and Methods

One hundred women of proven fertility ranging from 1 to 11, attending Family Planning Centre, Medical College Hospital, Nagpur, were selected for the study. Some of them (72 cases) were already fitted with Lippes loop before the onset of the present study. The age group ranged from 20 to 45 years and had at least one period prior to insertion of the loop. The detailed obstetrical and menstrual history and complaints, if any, prior to insertion of loop, were recorded. The patients had general, systemic examination, vaginal and speculum examinations. Patients having vaginitis or cervical erosion were rejected for insertion of loop and called for review after appropriate treatment. Vaginal examination was done to note the size of the uterus and to exclude the diagnosis of uterine myomata and early pregnancy. Preinsertional control biopsy was possible only in 28 cases. The date of endometrial biopsy, the date of loop insertion and date of last menstrual period were noted. The patients were called for repeat biopsy every 3 months for a period of 1 year. Most of the patients did not turn up according to this schedule and hence follow up biopsy was possible whenever the patients attended the hospital. Endometrial biopsy was obtained for histo-

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pathology and histochemistry for study of alkaline phosphatase and glycogen. Follow up, pre- and post-insertional biopsies for a period of 1 year was possible in 28 cases. In the remaining 72 cases post-insertional biopsies were taken after 1 to 10 years of use of intrauterine contraceptive devices.

For histopathology the sections were fixed in 10 per cent formal saline, were processed and stained with H. & E. and were obtained from patients with normal regular menstrual cycles and were stained for glycogen and alkaline phosphatase.

Observations and Discussion

Majority of patients (45 per cent) belonged to the age group of 26 to 30 years. Most of the women who sought advice were second para.

Table I shows presenting complaints. Onethird of the women (33 per cent) did

TABLE I
Showing Presenting Complaints and Complications in Cases Studied

Complaints	No. of cases	Complaints	No. of cases
No complaints	33	Irregular bleeding	5
White discharge	25	Pelvic inflammation	1
Menorrhagia	22	Perforation	Nil
Backache	16	Pregnancy	Nil
Lower abdominal pain	8	Expelled	2
Cervical erosion	8	Displaced	8

examined for phase of the endometrium, haemorrhage, vascularity, stromal oedema and inflammation type of cells.

About 30 biopsies could be studied for histochemistry. For alkaline phosphatase the strips were fixed in 4 per cent calcium formol solution at O° C for 24 hours and then embedded in paraffin and sections were taken. The slides were stained with modified Gomori's calcium cobalt technique by incubating at 37° C for 24 hours (Pearse, 1968). The intensity of staining, the amount of alkaline phosphatase present was compared with endometrium of the same phase of cycle from control group and variation, if any, was determined. The endometrial strip for evidence of glycogen was fixed in formol alcohol at O° for 24 hours and paraffin sections were stained with PAS stain (Culling, 1963). The intensity of staining of study group was compared with that of control group. For control, biopsies not have any complaint. Patients presenting with white discharge, backache and lower abdominal pain were investigated to exclude pelvic inflammation, other local causes and erosion. Patients presenting with menorrhagia and irregular bleeding were treated symptomatically. Majority of the patients did not insist on removal of the loop.

Table II shows histopathological observations in 100 cases. No definite conclusions were drawn as number of preinsertional biopsies were less.

Early histological studies of Sujan-Tejuja *et al* (1965) disclosed no significant tissue alterations with the use of intrauterine device in human. In the present study histopathology of the endometrium showed thinning and ulceration of the endometrium adjacent to the device with increase in polymorphonuclear leucocytes in initial stage. (Fig. 1).

TABLE II

Showing Histopathological Observations in 100 Cases

Histopathological changes	No. of cases	
1. Proliferative phase	32	
2. Secretory phase	17	
3. Proliferative phase with chronic inflammation & lymphoid follicle formation	22	
4. Secretory phase with chronic inflammation	19	
5. Hormonal imbalance	2	
6. Metropathia haemorrhagica	4	(Seen in pre-insertional biopsy)
7. Secretory hyperplasia	1	
8. Decidual reaction	2	
9. Endocervical carcinoma	1	(Incidentally detected)

Relationship with the Cyclical Changes of Endometrium

The commonest histopathological finding was proliferative phase (32 per cent). In all these except two, the endometrial pattern corresponded to the phase of menstrual cycle. Sujan-Tejuja *et al* (1965) have concluded that intrauterine contraceptive devices do not affect ovulation and cyclic changes of endometrium.

Relationship of Histopathological Findings With Menstrual Complaints

The histopathological changes did not have any specific correlation with menstrual complaints. In 4 cases diagnosed as metropathia haemorrhagica (Fig. 2) histopathology of endometrium in pre-insertional control biopsy revealed similar changes. Moyer and Mishell (1971) tried to correlate severity of clinical uterine bleeding with morphological changes in the endometrium. No significant correlation was detected. Erosion of superficial blood vessels or morphological abnormality, or thin walled dilated sinusoids described by Shahani and Kothari (1973) were not detected. The results of the present study agree with Moyer and Mishell (1971). Association of increased number of mononuclear cells with abnormal uterine bleeding has been noted by Moyer and Mishell (1971). No such correlation was noted by Shahani and Kothari (1973). In the present series mononuclear reaction was seen in asymptomatic patients as well.

Significance of Inflammatory Cell Reaction

The tissue trauma that results from the contact of intrauterine foreign body with the endometrium causes series of vascular and cellular events to set in motion. During early weeks following insertion of loop significant increase in number of neutrophils and mononuclears were noted by Moyer and Mishell (1971). They also noted presence of mononuclears for prolonged periods i.e. about 2 years after insertion. The plasma cells represent transient endometritis following insertion of device. Greenwald (1965) and Parr (1969) attribute the contraceptive activity to the presence of chronic endometritis resulting from insertion of loop. In our series presence of mononuclears (plasma cells and lymphocytes) were de-

tected in high percentage in 22 cases. In two cases they tended to form lymphoid follicles (Fig. No. 3) described by Moyer and Mishell (1971). Though the presence of mononuclears and neutrophils in the secretory phase is regarded as physiological (Noyes *et al*, 1950), their presence in significant number is recorded in 19 cases of our series. One case of endocervical carcinoma was accidentally detected during fractional curettage. As the preinsertional biopsy was not available no comment can be made.

Table V shows histopathological changes in relation to years of loop insertion. The severity of cellular reaction did not increase with the use of device. Similar findings are noted by Shahani and Kothari (1973).

TABLE V

Showing Endometrial Changes in Relation to Period of Loop Insertion

Yrs. of loop insertion	Proliferative phase	Secretory	P.P. with Chr. inflam.	P.P. with lymphoid foli.	Secretory hyperplasia	Hormonal imbalance	Secretory phase with Chr. inflammation	Decidual reaction
1 day to ½ Yr.	6	3	6	–	–	1	6	–
½ to 1 Yr.	5	6	5	–	–	–	6	–
1 to 2 Yrs.	–	–	1	–	–	1	1	–
2 to 3 Yrs.	5	3	1	–	–	–	5	–
3 to 4 Yrs.	4	2	3	1	–	–	1	–
4 to 5 Yrs.	7	1	2	1	1	–	–	2
5 to 6 Yrs.	3	–	1	–	–	–	–	–
6 to 7 Yrs.	1	1	1	–	–	–	–	–
7 to 8 Yrs.	–	1	–	–	–	–	–	–
8 to 10 Yrs.	1	–	–	1	–	–	–	–
Total:	32	17	20	3	1	2	19	2

Histochemistry

Thirty biopsies were studied for histochemistry. Sixteen were in proliferative phase and 14 were in secretory phase. Glycogen was found to be increased in the secretory phase than in the proliferative phase. The amount of glycogen present was same in each phase of study group fitted with intrauterine contraceptive device and in controls. Hall *et al* (1965) found normal glycogen distribution in intrauterine device users implying thereby no interference in ovarian activity. Alkaline phosphatase was estimated in 30 cases. In 16 cases the endometrium was in the proliferative phase and in 14 cases the endometrium was in the secretory phase. Alkaline phosphatase activity revealed no variation and was corresponding with the phase of the cycle as in the control group. In control group it was maximum in midcycle and dcelined thereafter. Findings are in agreement with Hall *et al*, (1965).

Summary and Conclusions:

Hundred women attending the Family Planning Centre, Medical College Hospital, Nagpur, fitted with intrauterine contraceptive device were studied to evaluate the recent and long term effects of intrauterine contraceptive device.

One-third patients did not have any complaints inspite of use of intrauterine contraceptive device for a long time.

No correlation was observed between clinical uterine bleeding and morphological changes in the endometrium.

Leucocytic infiltration and chronic endometritis noted in significant number of cases might be responsible for altering uterine milieu and prevention of implantation of ovum.

The severity of cellular reaction was not related to the duration of use of device. The amount of glycogen was same in controls and study groups.

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See Figs. on Art Paper VIII