CLINICOPATHOLOGICAL STUDY OF ENDOMETRIUM IN IUCD USERS

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ABSTRACT

Background and Aims: Use of intrauterine contraceptive device (IUCD) is now a common practice. The present study was taken up to study the clinicopathological changes in endometrium following use of IUCD. Methods: Endometrium obtained from 65 cases who had IUCD of varying duration, presenting with different symptoms were studied by Hematoxylin and Eosin stained slides. Results: Patients presented with various menstrual irregularities and pelvic inflammatory disease. Duration of IUCD use ranged from 4 months to 10 years. The spectrum of endometrial changes were interstitial edema 22(33.8%), hemorrhage 36(55.3%), focal hyperplasia 18(27.6%), diffuse hyperplasia 2(3%), cystoglandular hyperplasia 4(6.1%), predecidual changes 5(7.6%), inflammatory cell infiltrate 9(13.8%), lymphoid follicles 2(3%), vascular changes 2(3%), metaplasia 1(1.5%). Conclusion: The present study tries to focus on the spectrum of endometrial changes associated with IUCD use, their clinical symptomatology and possible pathogenetic mechanisms. The endometrial changes were possibly due to inflammation, hyperplasia and metaplasia induced by IUCD.

Keywords: Endometrium, Intrauterine contraceptive device, IUCD.

INTRODUCTION

Intrauterine contraceptive device (IUCD) is one of the very effective contraceptive methods, which has been used widely in family planning and population control programs for many years. It is thought to be safe with minimal side effects. However complications like abnormal uterine bleeding, infection and spontaneous expulsion are the main drawbacks.

The value and applicability of IUCD as a method of contraception on one hand and reports from varied quarters of medical profession about effects of these devices on uterine mucosa to which they are opposed are conflicting. It was Sujan-Tejuja et al. in 1964 who stated use of IUCD did not interfere with dating the endometrium. Wynn RM 1968 studied 168 biopsies at intervals from 6 weeks to 3 years with pre insertion control biopsy in 51 women. He showed that there are cyclic alterations characterized by early maturation and asynchronous development. The endometrial alterations per say did not vary with length of time the device was in use.
Despite increase in knowledge and investigative procedures, the etiopathogenesis underlying menstrual irregularity is still incompletely understood.
Several studies have focused attention on the menstrual irregularities after IUCD use such as menorrhagia, polymenorrhoea and pelvic inflammatory disease. An attempt to observe the spectrum of endometrial changes after IUCD with a possible correlation with the duration and a clinicopathological correlation of clinical symptomatology with histopathologic features was considered worthwhile. The present study is an effort to resolve the endometrial changes in relation to IUCD with clinicopathologic correlation and to explain pathologic mechanisms.

MATERIALS AND METHODS
The present study was undertaken to find out endometrial changes following the use of IUCD in the department of pathology, MR Medical College, Gulbarga.
A total of 65 cases, who had IUCD (copper T) of varying duration and reported for different symptomatology were subjected to clinical and histological examination. None of the cases showed clinical evidence of gross anaemia or pelvic pathology.
Dilatation and curettage was done immediately following removal of IUCD. The endometrial tissue was fixed in 10% formalin and paraffin blocks were processed. Sections were cut at 4 microns thickness and stained with H&E and studied. Endometrial findings were carefully analysed.
An attempt was also made to study age distribution, duration of IUCD use, clinical presentations after use of IUCD and to categorise clinical symptomatology and changes in each group of menstrual irregularities. The findings were correlated with the symptoms and possible mechanisms playing a role for various clinical and histopathological changes that are evident in this study.

Observations
A total of 65 cases of endometrial biopsies were carefully analysed. The mean age was 34.2 years. The youngest patient was 19 years old and the oldest 48 years old. Majority (69%) of the cases were in the age group of 20-30 years.
Analysis of presenting symptoms showed menorrhagia 35(53.8%), pelvic inflammatory disease 18(27.6%), vaginal discharge 15(23%), low backache 3(4.6%), polymenorrhoea 22(15.3%), and one case each of oligomenorrhoea and amenorrhoea.
The duration of IUCD ranged from few months to the other extreme of 10 years with an average of 2.9 years. The cases were grouped into less than one, 1-5 and 6-10 years depending on the duration of use. Majority 46(70.7%) cases were in range of 1-5 years of duration of use.
The cases were further categorised into groups depending upon the symptomatology into those with menorrhagia, pelvic inflammatory disease and polymenorrhoea.
It was observed that menorrhagia, polymenorrhoea and pelvic inflammatory disease occurred in all the duration groups. While single case of oligomenorrhoea was observed after 3yr and amenorrhoea after 7yr duration. It was apparent that with increasing duration of IUCD the incidence of menorrhagia decreased and incidence of pelvic inflammatory disease increased, while polymenorrhoea was consistent finding in all the duration groups.
Present study showed proliferative phase 42(64.6%), secretory phase 15(23%), necrotic 3(4.6%) and no endometrial tissue 5(7.6%) cases. Interstitial edema was seen in 22(33.8%), hemorrhage 36(55.3%), focal hyperplasia 18(27.6%), diffuse hyperplasia 2(3%), cystoglandular hyperplasia 4(6.1%), inflammatory infiltrates mainly lymphocytes, plasma cells and neutrophils 9(13.8%), lymphoid follicles 2(3%) cases. Predecidual changes seen as large pale cells of stroma with nuclei showing open chromatin and which were arranged in groups in edematous stroma were seen in
5(7.6%). Vascular changes in the form of capillary dilatation were seen in 2(3%) cases and squamous metaplasia in 1(1.5%) cases. However no bacterial or fungal colonies were demonstrated and the present series did not have any neoplastic changes.

On comparison of the microscopic findings in 3 symptomatic groups, finding of endometrial hyperplasia stand out prominently in menorrhagia and polymenorrhoea group. Diffuse hyperplasia was more obvious in polymenorrhoea group and vascular dilatation was seen only in menorrhagia group.

Menorrhagia group (35 cases) showed edema 12(34.8%), hemorrhage 23(66.7%), focal hyperplasia 14(40.6%), diffuse hyperplasia 1(2.9%), cystoglandular hyperplasia 2(5.8%), inflammatory cell infiltrates 3(8.7%), predecidual change 3(8.7%), lymphoid follicles 1(2.9%) and squamous metaplasia 1(2.9%) of the cases in present study. Proliferative endometrium was seen in 24(69.6%) cases as compared to 9(26.1%) cases of secretory endometrium. No endometrial tissue was seen in 2(5.8%) cases.

Pelvic inflammatory disease group (18 cases) showed interstitial edema 6(33.6%), hemorrhage in 9(50.4%), focal hyperplasia 1(5.6%), cystoglandular hyperplasia 1(5.6%), lymphocyte and plasma cell infiltrate in 4(22.4%), lymphoid follicles 1(5.6%) and predecidual change 1(5.6%) case. However no group showed fibrosis or neoplasia. Proliferative endometrium was seen in 9(50.4%) and secretory in 4(22.4%) of the cases. Necrotic tissue was seen in 3(16.8%) and no tissue in 2(11.2%) cases.

Polymenorrhoea group (10 cases) showed focal hyperplasia 3(30%), diffuse hyperplasia 1(10%), cystoglandular hyperplasia 1(10%), lymphomononuclear infiltrates 2(20%), edema 4(40%), hemorrhage 4(40%) and predecidual change 1(10%) case.
DISCUSSION

The introduction of a foreign body into the uterus as a contraceptive device is not new. The original device first used in 1909 was made of silkworm gut. Currently there are two types of devices, the medicated and the non-medicated. The medicated devices release either metal ions (copper) or hormones (progesterone) and are devised to reduce the incidence of side effects and to increase the contraceptive effectiveness.

During proliferative phase giant mitochondria are seen in epithelial cells of glands and after ovulation, stromal cells undergo predecidual changes. Predecidualization of stroma is mediated by prostaglandins F₂ and E₂. Histochemically endometrium revealed no significant change in enzyme reactions, contents of nucleic acid and glycogen, but acid mucin levels were increased. The premature secretory and decidual changes explain the contraceptive action. They also induce a local hormonal dysfunction secondary to inflammation, alterations in tubal transport, mechanical interference, local chemotactic effects on endometrium and focal release of cytotoxic products due to surface interactions with endometrium are also seen.

The copper incorporated into IUCD is absorbed by superficial layers of endometrium and present in secretory vacuoles of glandular epithelium, but electron microscopic studies failed to demonstrate binding of copper ions to cell organelles due to their rapid excretion. Biochemical estimations prove that copper and protein concentrations increase. Glycogen metabolism is also affected. The role of immunological mechanisms needs to be elucidated.

In the reported studies the average age was 33±2 years and age range was from 20-30 years. Present study had an age range from 19-48 years. The duration of use of IUCD was around 3 years in most studies, but we have presently studied endometrium of much longer duration i.e. up to 10 years.

Wynn RM reported alterations in cycle showing premature maturations and asynchronous development and changes not corresponding to the day of the cycle. Ober et al. divided his group into 2 categories, symptomatic 112 cases and asymptomatic 96 cases.

The present group had 35 cases of menorrhagia, 10 cases of polynenorrhoea, and 18 cases of pelvic inflammatory disease.

IUCD may lead to an enhanced decidual reaction in the endometrium. Inflammation, stromal bleeding, necrosis, cystic hyperplasia and vascular congestion have been reported by several authors. The present study showed edema in 33.8% cases and hemorrhage in 55.3% cases. Vascular changes notably dilatation seen in 3% of cases.

Histological dating of the endometrium was done. In presence of predecidual reactions, dating was performed based on pattern of endometrial glands. Lee YB et al. showed the IUCD insertion brings about inflammatory reaction and asynchronous endometrial maturation.

The possible pathogenesis of menorrhagia in relation to IUCD appears to be endometrial hyperplasia, along with other contributing factors like, increased fibrinolytic activity, plasminogen activators, permeability due to Prostaglandins I₂ and D₂ and local proteolysis, and vascular injury and endothelial defects.

Polynenorrhoea was another bleeding disorder seen in 10 cases in the present study. It is considered to be due to increased ovarian function. Diffuse hyperplasia was observed in this group and may be a contributory factor.

Oligomenorrhoea and amenorrhea cases in the present study were one each case. The possible explanation could be atrophy of functional endometrial layer and fibrosis.

On comparison of microscopic findings in 3 symptomatic groups findings of endometrial hyperplasia stand out prominently in menorrhagia and polymenorrhoea groups. Pelvic inflammatory disease was another major group. The present study showed pelvic inflammatory disease in 27.6% cases. Fiorino AS(1996)15 cited an incidence of 7 percent of Actinomyces species seen on cytology smears from women using IUDs compared with less than 1 percent in nonusers. In some cases, pelvic inflammatory disease may develop (Dunn et al. 2006) 16. The pathomechanisms could be introduction of microbes, mechanical trauma, chemotactic factors like degraded and degenerated endometrial cells, increased vascular response, and local or general immunological depression.

Squamous metaplasia was reported by Ober et al.11 (2cases) and Tamada et al.10 (3 cases). The presence of squamous metaplasia, atypical hyperplasia or adenocarcinoma suggests that a long term observation of women using IUCD is advisable. In the present study one case of squamous metaplasia was observed.

It is noted that curettage tissue does not reflect the entire spectrum of changes in the whole endometrium. The changes depend upon the site of biopsy. Not infrequently there are various and differing findings in endometrium itself in both pathological and physiological conditions. Since IUCDs constitute a mechanical and chemical stimulus, greater variations are expected. Hysterectomy specimens are preferred if feasible as multiple sections from different sites can be studied.

CONCLUSION

The present study highlights the microscopic endometrial changes in women using IUCD (Copper T) and their clinical presentation with IUCD use of varying duration and tries to suggest pathomechanisms to explain clinical features.

REFERENCE