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Endometrium in Infertility

Neil S. Shastrabudhe, Sharmila Shinde, Mangal V. Jadhav
Department of Pathology, B.J. Medical College, Pune

Summary:

114 infertile endometrial specimens were evaluated in the light of menstrual history to find out the incidence of various endometrial changes in cases of infertility where possibilities of male infertility and female infertility due to obvious causes other than endometrial abnormalities were ruled out. Anovulatory infertility was present in 34.2% cases. Ovulatory endometrium was the most frequent endometrial change noted (62.3%). Amongst the cases of ovulatory infertility , 25.4% cases showed secretory inadequacy or corpus luteal deficiency. Intrinsic endometrial abnormalities were present in 3.5% cases with 3 cases of tuberculous endometritis and 1 case of endometrial polyp.

Introduction:

Female infertility may occur due to disturbances involving any part of the genital system or parts of the central nervous system that control the ovaries hormonally. Of these, intrinsic and functional abnormalities of the endometrium contribute significantly. To clarify the causes of infertility, the clinician has available an impressive array of diagnostic tests to choose from. However histological study of an endometrial biopsy remains one of the most reliable methods of diagnosing the etiology of female infertility (Annos et al, 1980).

Materials & Methods:

The clinical data of 120 infertile women attending the out-patient department of Gynaecology and Obstetrics department, Sassoon General Hospitals, Pune was collected by careful history with special reference to menstrual history regarding the duration of the cycle and last menstrual period and clinical examination to rule out the possibility of anatomical deformities of genital tract and obvious endocrinal abnormalities. Male infertility was ruled out by semen examination.

The endometrial specimens were obtained in the immediate premenstrual period by dilatation and curettage (94 cases) and endometrial biopsy (26 cases). The specimens thus obtained were fixed in 10% formation and processed routinely and the slides were strained by haematoxylin and eosin.

The slides were reviewed for evidence of ovulation, adequacy of glandular and stromal development of a particular menstrual phase and for the presence of intrinsic endometrial abnormalities, if any. The endometrial dating was done by the scheme suggested by Hendrickson and Kempson (1980). The findings were analysed to find out the incidence of various

changes in infertile endometria.

Observations:

Out of the 120 endometrial specimens, 6 were inadequate and were omitted from the study. The data was thus analysed on 114 cases. The incidence of changes in endometria are shown in Table I.

Table I showing the incidence of endometrial morphological changes in infertility

Endometrial change	No. of cases	Percentage
i Anovulatory (39 cases)		34.2
a) Deficient proliferation	18	
b) Intermediate Proliferation	16	
c) Irregular proliferation	5	
II) Ovulatory (71 cases)		62.3
a) Adequate secretory response	53	
b) Deficient secretory phase		
i) With co-ordinated apparent delay	10	
ii) With dissociated delay	8	
III) Intrinsic abnormalities (4 cases)		3.5
a Tuberculous endometritis	3	
b Endometrial polyp	1	
Total	114	100

Endometria classified as deficient proliferation showed retarded glandular and stromal development with the glands resembling those of early or mid-proliferative endometrium. Endometrium placed in the group of intermediate proliferation showed glands comparable those in late proliferative phase with occasional cystically dilated glands. Endometria classified as irregular proliferation showed glandular and stromal hyperplasia.

The secretory endometrium formed the most frequent morphological change noted in infertile endometrium. 53 of these showed adequate secretory response as they were in late secretary phase as expected in view of the immediate premenstrual sampling. 10 cases were in early or mid-secretory phase with co-ordinate glandular and stromal development. These cases were classified as deficient secretory phase with co-ordinated apparent delay. 8 cases showed poorly convoluted glands with a variation in development of glands and stroma from region to region and dissociation of development between glands and stroma. These were labeled as deficient secretory phase with dissociated delay. Theses 18 cases can be classified as corpus luteal deficiency or secretory inadequacy. Thus the incidence of adequate secretory response was 74.6% while that of corpus luteal deficiency was 25.4%.

Discussion

Presence of ovulation is the foremost pre-requisite of unassisted conception. But equally important is the adequacy of endometrial development. Hence there is more to female infertility evaluation than merely noting the presence of ovulation and intrinsic abnormalities of the genital tract. One needs to date the endometrium appropriately and evaluate adequacy of endometrial hormonal preparation which is facilitated by correlating endometrial biopsy serves as a bioassay measuring the hormone at tissue levels (Jones et al, 1974), on which can be based further treatment strategies.

Finding of deficient proliferation as seen in 18 of our cases, indicates deficient follicular maturation of stimulation and is characterized by raised FSH and LH levels and reduced estrogen levels. this needs to be treated with estrogen priming followed by clomiphene and progesterone.

Intermediate or irregular proliferation (which was seen in 16 & 05 cases respectively) occurs due to repeated anovolutary cycles or persistent follicle as in polycystic ovary syndrome. Deficient secretory phase with a co-ordinated apparent delay occurs due to a persistent follicle with delayed ovulation. Both these defects lead to a relative progesterone deficiency with a normal FSH levels and increased LH and estrogen levels in hormonal assays. These are the candidates which should be treated by clomiphene. Deficient luteal phase with dissociated delay occurs due to a central defect with insufficient FSH and LH formation or release (with or without hyperprolactinemia). These patients may be treated with FSH in the first half of the cycle followed by hCG and progesterone receptor defects respectively (pseudo-corpus luteum deficiency). These cases should be treated by estrogen or tamoxifen, both of which stimulate the production of progesterone receptors followed by hCG and progesterone receptor defects respectively (pseudo-corpus luteum deficiency). These cases should be treated by estrogen or tamoxifen, both of which stimulate the production of progesterone receptors (Dallenbach-Hellweg, 1980).

In the present study, evaluation of the adequacy of endometrial development was based on correlating menstrual history with glandular and stromal morphology. This allowed the diagnosis of deficient, intermediate and irregular proliferation. The diagnosis of corpus luteal deficiency is based on correlation between the time of ovulation, the levels of hormones and endometrial dating (Jones, 1976). Though the diagnosis of marginal corpus luteal deficiency could not be made, the cases showing a lag of more than 3 days in the secretory phase in the biopsies taken in the immediate premenstrual period could be considered as corpus luteal deficiency.

Table II showing the incidence of changes in infertile endometrium in different series (In percentage).

Endometrial change	Shetty (1959)	Gupta et al (1980)	Jadhav & Raichur (1987)	Krishnamohan et al (1993)	Present study
I) Anovulatory					
a) Proliferative (including deficient and intermediate proliferation)	14.1	16.9	25.0	7.5	29.8
b) Irregular proliferation and hyperplasia	11.1	5.9		2.5	4.4
II) Ovulatory					
a) Adequate secretory response	74.8	60.4	75.0	80.0	46.5
b) Deficient secretory phase		8.1		7.5	15.8
III) Intrinsic abnormalities					
a) Tuberculous endometritis		8.7			2.6
b) Endometrial polyp					0.9
c) Others (e.g. endometritis)				2.5	

The incidence of various morphological changes in infertile endometria in the present study and it's comparison with other series is summarized in Table II.

In all studies, functional abnormalities of the endometrium form the major change in comparison with intrinsic abnormalities. Diagnosis of these dysfunctions depends upon careful correlation between endometrial histology and clinical data. Hence simple courtesy of providing exact menstrual details of the patient to the pathologist will facilitate and markedly improve the endometrial evaluation regarding the adequacy of endometrial development.

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