A study on correlation of hormone therapy and endometrial hyperplasia

Nutanbala N. Goswami[1], Alpeshpuri Goswami[2*], Umeshkumar Zinzala[3], Abhijit S Khandkar[4]

[1,2]Associate Professor, [3,4]Resident Doctor, [1]Dept. of Pharmacology, [2-4]Dept. of Pathology, Government Medical College, Bhavnagar, Gujarat, India

***Corresponding Author: Alpeshpuri Goswami**
Email: dralpeshgosai79@gmail.com

Abstract
Introduction: The most common reason for performing an endometrial biopsy is abnormal uterine bleeding, a term that refers to any nonphysiologic uterine bleeding. Endometrial hyperplasia occurs when the endometrium, become too thick. It can lead to cancer of uterus. Endometrial hyperplasia most often is caused by excess estrogen without progesterone.
Materials and Methods: A retrospective observational study on 198 D & C biopsy specimen was conducted in histopathology section, of pathology department government medical college, Bhavnagar, Gujarat. Cases with endometrial hyperplasia were categorised as simple, complex and complex with atypia. The cases were correlated with history of hormone therapy. Data recorded and analysed statistically.
Results: Out of total 198 D & C sample 43 cases having history of either taking oral contraceptive pills or combined hormone therapy. 26 cases were reported histopathologically as endometrial hyperplasia. Maximum cases having endometrial hyperplasia where from perimenopausal age group (13.79%). Statistically insignificant difference observed for endometrial hyperplasia in patient taking combine hormone replacement therapy or as oral contraceptive pills (13.95%) compare with 20 cases having no history of Hormone intake in any form(12.90%).
Conclusion: The present case-control study was conducted to examine the relationship between recent use of hormone intake and its association with development of endometrial hyperplasia. Combined Hormone replacement therapy is not associated with higher risk for the development of endometrial hyperplasia.

Keywords: D&C, Estrogen, Endometrial hyperplasia, OC pills.

Introduction
Endometrial biopsies and curetting are among the most common tissue specimens received in the pathology laboratory. The normal endometrium undergoes a variety of morphologic changes, especially during the reproductive years, when cyclical hormonal influences and pregnancy affect uterine growth. Interpreting the biopsy material demands a logical approach that takes into account many factors, including patient history; the specific requests of the clinician performing the biopsy; and an appreciation of the limitations, potential pitfalls, and complex array of patterns encountered in the microscopic sections. There are four main indications for endometrial biopsy or curettage. 1. Determination of the cause of abnormal uterine bleeding. 2. Evaluation of the status of the endometrium in infertile patients, including histologic dating. 3. Evacuation of products of conception, either spontaneous abortions or termination of pregnancy. 4. Assessment of the response of the endometrium to hormonal therapy, especially estrogen replacement in perimenopausal and postmenopausal women and Tamoxifen therapy for breast cancer. The most common reason for performing an endometrial biopsy is abnormal uterine bleeding, a term that refers to any nonphysiologic uterine bleeding. Age and menstrual menopausal status are especially important data, as causes of abnormal uterine bleeding vary significantly according to the age and menstrual status of the patient, Abnormal uterine bleeding is a common sign of a number of different uterine disorders ranging from dysfunctional (nonorganic) abnormalities or complications of pregnancy to organic lesions such as polyps, hyperplasia, or carcinoma. A practical approach to the possible diagnoses associated with abnormal bleeding takes age into account. Pregnancy-related and dysfunctional disorders are more common in younger patients whereas atrophy and organic lesions become more frequent in older individuals.[6] Polyps in perimenopausal and postmenopausal patients have been found in 2% to 24% of patients. Hyperplasia is found in up to 16% of postmenopausal patients undergoing biopsy, and endometrial carcinoma in fewer than 10% of patients. One consistent observation in studies of postmenopausal patients is the finding that atrophy is a common cause of abnormal bleeding, being found in 25% or more of cases.[1] Because the endometrium is responsive to hormones, the history of hormone use is important information. Clinical uses of steroid hormones (estrogens, progestins, or both) include oral contraceptive use; postmenopausal replacement therapy; and therapy for endometriosis, hyperplasia, DUB, infertility, and breast carcinoma. As with other facets of the clinical data, this information may be absent or if present, unreadable on the requisition. Women receive hormone preparations for a variety of reasons, including birth control and treatment for dysfunctional uterine bleeding, perimenopausal and postmenopausal symptoms, endometriosis, endometrial hyperplasia and carcinoma, breast carcinoma, and certain types of infertility. An endometrial biopsy or curettage may be performed when abnormal bleeding occurs or when hormone therapy does not correct abnormal bleeding that is thought to be dysfunctional. Sometimes, however, the biopsy is intended to evaluate the status of the endometrium following hormonal therapy, as in the case of hyperplasia managed with progestin therapy or routine follow-up of patients on hormone replacement therapy. Estrogen therapy is largely used in perimenopausal or postmenopausal

women to treat symptoms of the menopause, such as vasomotor instability, atrophic vaginitis, and osteoporosis. Estrogenic substances include conjugated estrogens and other synthetic estrogens, such as ethinyl estradiol or diethylstilbestrol (DES).[1]Focal adenomatous hyperplasia may develop after prolonged treatment with agents that contains predominantly estrogen, particularly after sequential oral contraceptive agents, or after metabolic conversion of gestagens into compounds with estrogenic action. Structurally, these foci are identical with those of complex hyperplasia. The early structural changes following sequential therapy are identical to those of the deficient secretory phase. [2,3]

Materials and Methods

This is a retrospective observational study conducted in histopathology section, of pathology department government medical college, Bhavnagar, Gujarat. Data was collected from laboratory information system between January to October 2019, recorded and analysed to study. In this study total 198 samples of D&C specimen received in histopathology department were included. Endometrial biopsy were processed, stained by H & E stain and studied. Inadequate information in request form and cases have inadequate obtained material were excluded from study. Endometrial hyperplasia was diagnosed and categorised as simple, complex and complex with atypia according to WHO terminology which is based on architectural complexity and degree of nuclear atypia. All the cases reported as endometrial hyperplasia were correlated with history of hormone intake. Data recorded and analysed statistically.

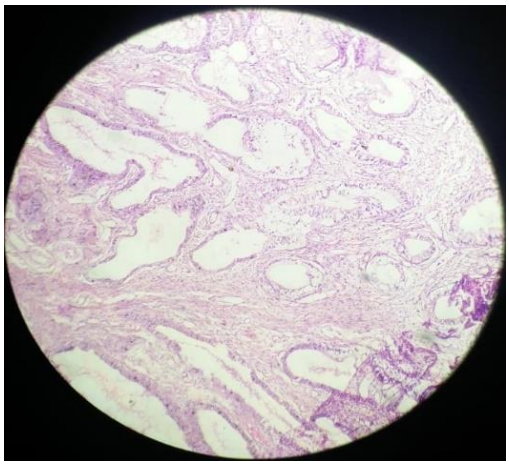

Fig. 1: Simple endometrial hyperplasia

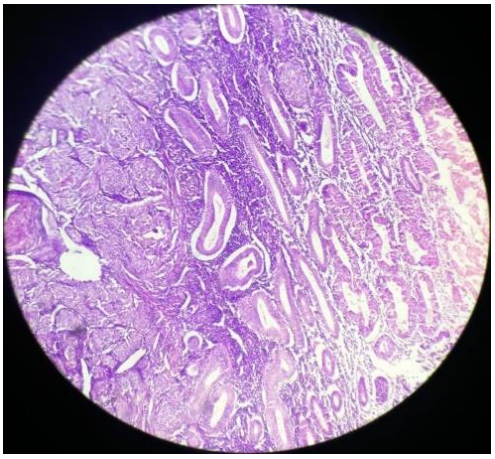

Fig. 2: Complex endometrial hyperplasia

Result

Table 1: Correlation between patient age group with endometrial hyperplasia

Age group of patient	D&C material received	Diagnosed cases of endometrial hyperplasia
Reproductive age <40	38	3 (7.89%)
Perimenopausal age 41-50	116	16(13.79%)
Post menopausal age >50	52	7(13.46%)
Total	198	26

Table 1 showing maximum number of D & C material received during perimenopausal age group. Out of 198 cases 26 case were reported histomorphologically as endometrial hyperplasia. Maximum cases having endometrial hyperplasia where from perimenopausal age group (13.79%).

Table 2: Correlation between Combined Hormone intakes with endometrial hyperplasia

History of hormone intake-	No of patient	Endometrial hyperplasia	Types of endometrial hyperplasia		
			Simple hyperplasia	Complex hyperplasia Without atypia	Complex hyperplasia with atypia
Yes	43	6 (13.95%)	04 (66.66%)	01(16.66%)	01(16.66%)
No	155	20 (12.90%)	16 (50%)	03(15%)	01(5%)

Table 2 showing endometrial hyperplasia observed in 6 cases (13.95%) in patient taking combine hormone replacement therapy or as oral contraceptive pills compare with 20 cases (12.90%) having no history of Hormone intake in any form. The difference is statistically insignificant (p>0.05)

Discussion

Endometrial hyperplasia (EH) is a precancerous, non-invasive proliferation of the lining of the uterus Known risk factors for the occurrence of EH are related to an imbalance of excess estrogen as compared to progesterone, resulting in the stimulation of endometrial cell growth[4,5] In our study we observed 26 cases for their association between endometrial hyperplasia and combined hormonal therapy was statistically insignificant. K M Feeley et al[6] in his study reported approximately 20% of women given unopposed oestrogen for one year develop endometrial hyperplasia. D W Sturdee et al[7] observed that D Cyclical unopposed oral oestrogen treatment (98 cases) was associated with a 12% incidence of endometrial hyperplasia, but among those given an additional five-day course of progestogen in each cycle (37 cases) the incidence was only 8%. No case of hyperplasia occurred among 102 women taking regimens including 10 or 13 days of progestogen. A strong positive association of estrogen-only post-menopausal hormone therapy with EH has been demonstrated in numerous studies.[8,9] The two case-control studies that did analyze the relationship between oral contraceptives and incidence of EH did not find an association, but were limited by self-report of medication use and did not examine recent use specifically.[10,11] K M Feeley[12] in his study observed Continuous combined HRT is not associated with the development of endometrial hyperplasia or malignancy.

Conclusion

The present case-control study was conducted to observe the correlation between recent use of hormone therapy and its association with development of endometrial hyperplasia. Combined Hormone replacement therapy has statistically insignificant association with risk for the development of endometrial hyperplasia.

Source of funding

None.

Conflict of interest

None.

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