Literature Review

The Role of Hysteroscopy in Endometrial Hyperplasia

Peran Histeroskopi pada Hiperplasia Endometrium

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Abstract

Objective: To review, presented the role of hysteroscopy in endometrial hyperplasia.

Method: Literatur review.

Conclusion: The high diagnostic accuracy, associated with a minimal trauma, renders hysteroscopy the ideal procedure for both diagnosis and follow up of conservative management of endometrial hyperplasia. Hysteroscopy has made the most significant progress, mainly because the ability to use fine diameter instruments makes it feasible to avoid both anaesthesia and cervical dilatation. The procedure may therefore be performed in an outpatient setting without the need for hospitalization. The hysteroscopic diagnosis should not replace histological diagnosis, mostly in hysteroscopies performed after progestagen therapy, because the changes induced by drugs make more difficult the interpretation of hysteroscopy. The hysteroscopic pattern of endometrial hyperplasia appears with an overdevelopment of the endometrial mucosa with increased glandular openings, increased vascularization, cystic dilatations, polypoid aspects. Innovations in the diagnostic aspect of serious endometrial diseases through hysteroscopy is still evolving.

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Keywords: hysteroscopy, endometrial hyperplasia

Abstrak

***Tujuan**: Untuk menelaah peran histeroskopi pada hiperplasia endometrium.*

***Metode**: Tinjauan pustaka.*

***Kesimpulan**: Akurasi diagnostik yang tinggi, serta trauma yang minimal, menjadikan histeroskopi prosedur ideal untuk diagnosis dan tindak lanjut dari manajemen konservatif hyperplasia endometrium. Histeroskopi telah membuat kemajuan yang paling signifikan, terutama karena penggunaan instrumen dengan diameter halus membuatnya dapat dilakukan tanpa penggunaan anestesi maupun dilatasi serviks. Prosedur dapat dilakukan pada pasien rawat jalan tanpa harus rawat inap. Diagnosis histeroskopi tidak dapat menggantikan diagnosis histologi, terutama pada histeroskopi yang dilakukan setelah terapi progestagen, karena adanya perubahan yang di induksi obat membuat sulit dalam interpretasi histeroskopi. Pola hyperplasia endometrium pada histeroskopi berupa pertumbuhan yang berlebihan dari mukosa endometrium dengan peningkatan pembukaan kelenjar, peningkatan vaskularisasi, dilatasi kistik, dan aspek polipoid. Inovasi dalam aspek diagnostik penyakit endometrial dengan histeroskopi terus berkembang.*

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***Kata kunci**: histeroskopi, hiperplasia endometrium*

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INTRODUCTION

Endometrial hyperplasia is an abnormal proliferation of the endometrium (i.e. greater than the normal proliferation that occurs during the menstrual cycle),[1] and it is the most common of Dysfunctional Uterine Bleeding (DUB) (90%). Endometrial hyperplasia is typical in perimenopausal age and more frequently symptomatic.[2,3] Endometrial hyperplasia may produce obvious space occupying lesions in which diagnosis is easy with hysteroscopy, but it may be not very obvious especially in early stages of the disease.[4]

Endometrial Hyperplasia

Four types of endometrial hyperplasia:[1]
Simple, complex, simple atypical, and complex atypical.

In one study progression to carcinoma occurred in:[1]
1% of patients with simple hyperplasia,
3% of patients with complex hyperplasia,
8% of patients with simple atypical hyperplasia, and
29% of patients with complex atypical hyperplasia.

Ninety percent of cases of simple and complex hyperplasia regress spontaneously.[1] Simple hyperplasia often regresses if the source of exogenous estrogen is removed. However, atypical hyperplasia often progresses to adenocarcinoma unless medical intervention occurs.[4]

Histological Appearance

The hysteroscopic diagnosis should not replace histological diagnosis, mostly in hysteroscopies performed after progestagen therapy, because the changes induced by drugs make more difficult the interpretation of hysteroscopy.[3] Endometrial hyperplasia is a non-physiological, non-invasive proliferation of the endometrium that results in a morphological pattern of glands with irregular shapes and varying sizes.[5]

Simple hyperplasia/cystic hyperplasia (Figure 1) glands are cystically dilated and with occasional outpouching surrounded by abundant densely cellular stroma and give a "Swiss Cheese" appearance. No cellular atypia is present.[6]

Complex hyperplasia (Figure 2) glands are complex with papillary intraluminal tufting and irregular

shapes accompanied by a crowded, back-to-back arrangement with very little intervening stroma. Cellular atypia is absent.[6]

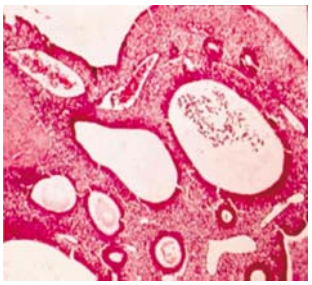

Figure 1

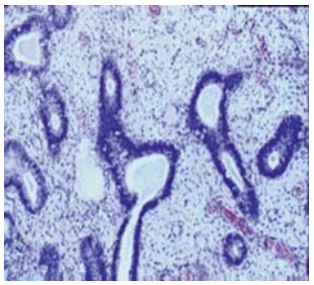

Figure 2

Simple atypical hyperplasia (Figure 3) glands are dispersed within abundant stroma and lined by enlarged cells with increased nuclear-cytoplasmic ratio and pleomorphism.[6]

Complex atypical hyperplasia (Figure 4) characterized by crowded glands showing cellular stratification, piling of epithelium into tufts, and atypia in the form of enlarged, pleomorphic and hyperchromatic nuclei and prominent nucleoli.[6]

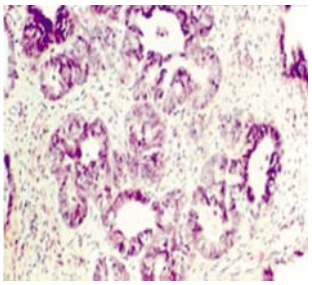

Figure 3

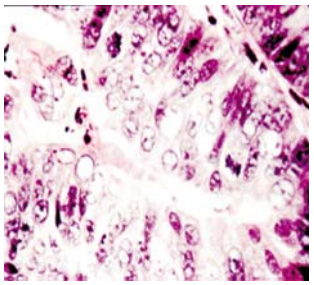

Figure 4

Endometrial Hyperplasia Classification and Risk of Progression to Cancer[4]

Endometrial hyperplasia may be a precursor to the most common female genital malignancy, endometrial carcinoma. Unopposed estrogens from anovulatory cycles and exogenous use in postmenopausal women have been shown to increase the likelihood of endometrial hyperplasia and endometrial carcinoma. Less than 2% of hyperplasias without atypia progress to carcinoma, and the mean duration of progression to carcinoma take almost 10 years. Atypical hyperplasia progresses to carcinoma in 23% of cases over a mean duration of four years.

Atypical hyperplasia can be triggered by increased demand for that tissue or organ; chronic inflammatory response; hormonal dysfunction; or neoplasia. Or it may be triggered by no obvious cause at all. Even if the atypical hyperplasia is not cancerous, it will increase the chances for getting cancer later. Most atypical hyperplasia are triggered by a normal hyperplasia. For instance, amenorrhea or oligomenorrhea may result in thickening of the uterine endometrium, a hyperplasia. The increased production of cells makes it more likely that some will mutate into a cancer. In the endometrium, this indicates endometrial cancer. The longer endometriosis is left untreated, the more likely it will develop into cancer.

Postmenopausal patients with endometrial hyperplasia invariably present with vaginal bleeding. Although carcinoma must be considered in this age group, endometrial atrophy represents the most common cause of postmenopausal bleeding. In a study of 226 women with postmenopausal bleeding, 7% were found to have carcinoma, 56% were noted to have atrophy, and 15% were diagnosed with some form of hyperplasia.

Hysteroscopy

Endoscopy began in 1805 with Bozzini but it was Pantaleoni who, in 1869, performed the first hysteroscopy.[3] Among diagnostic techniques, hysteroscopy presents several advantages: it is an out-patient procedure, minimally invasive, repeatable, of rapid execution and with low cost.[2] Hysteroscopy has a high diagnostic accuracy for endometrial cancer but only moderate for hyperplasia.[7]

The accuracy of hysteroscopic evaluation of the uterine cavity is extremely encouraging. Office hysteroscopy, which has a high diagnostic reliability and minimal discomfort, appears to be an ideal method of diagnosis and follow-up of patients with endometrial hyperplasia.[8] Hysteroscopic diagnostic accuracy for hyperplasia was 72%. So, sensitivity, specificity, positive predictive value and negative predictive value of hysteroscopy for hyperplasia were 75, 92.5, 71.4 and 93.67%, respectively. Loverro (1996), stated the sensitivity, specificity, positive predictive value and negative predictive value as 98, 95, 63 and 99%, respectively, for endometrial hyperplasia. Arslan (2005), did hysteroscopy in 216 premenopausal and 114 postmenopausal women for diagnosing hyperplasia. The positive predictive value was 71.4% and negative predictive value was 95.4% in diagnosis.[9] Positive predictive value was higher in postmenopausal patients compared to women in the fertile age (72 vs. 58%).[10] The errors of hysteroscopy were observed in other study was 8%.[2]

The correlations between hysteroscopic findings with histopathologic report of hyperplasia by different studies is shows in Table 1. Report in 100 women between 20 and 65 years of age who presented with complaints of abnormal uterine bleeding pattern had undergone two modalities of investigations to reach a conclusion - diagnostic hysteroscopy and endometrial histopathology report.[9]

Table 1. Correlation between hysteroscopic findings with histopathologic report of hyperplasia.[9]

Autor	Year	Incident of Hyperplasia (%)
Silander[8]	1963	6.66
Dexus[15]	1981	21
Sheth[9]	1989	26
Anuradha Panda[5]	1999	28.3
Jyotsana[11]	2004	22.6
Present Study	2008	20

The hysteroscopic appearance of low risk endometrial hyperplasia includes an increase in the thickness of the endometrium, its dyshomogeneous regeneration, increased vascularization and the presence of ciliated images, cystic dilatation, increased bleeding, polypoid formation, necrotic zones and the concentration and irregular arrangement of the glandular openings. If one or more of these elements are found, hyperplasia must be suspected. Guided endometrial biopsy can then be performed.[3,4]

The hysteroscopic appearance of high risk endometrial hyperplasia or endometrial intraepithelial neoplasia (EIN) clearly defines these pre-neoplastic and neoplastic lesions: Polyps are often present and abnormal vascularization produces an arborescent appearance which surrounds groups of glandular orifices. The architecture and organization of the uterine cavity is altered. The endoscopist can easily confirm the hysteroscopic suspicion with endometrial sampling of specific areas.[3,4]

Investigations for Endometrial Hyperplasia

Meta analyses restricted to postmenopausal women with abnormal bleeding show that a positive test result following hysteroscopy is more useful for predicting endometrial cancer or hyperplasia disease than TVS. In contrast, a negative test result following Trans Vaginal Ultrasound (TVS) in postmenopausal women (4 or 5 mm cut-off to define abnormality) is highly accurate in excluding serious endometrial disease and more useful than hysteroscopy. Applying the accuracy estimates from three TVS reviews, assuming a 5% pretest probability of cancer and endometrial thickness cut-offs of 4 or 5mm, the positive probability of cancer following a negative TVS is between 0.4 and 0.8%. Endometrial thickness measurement using ultrasound is of minimal use in premenopausal women because specific cut-off levels or morphological features do not accurately define the presence or absence of endometrial hyperplasia or cancer.[1]

Outpatient endometrial biopsy has high accuracy in diagnosing endometrial cancer and hyperplasia and should be employed when serious endometrial disease is suspected in both pre and postmenopausal women. At the beginning of the 1990s, transvaginal sonography greatly improved the accuracy of evaluations of endometrial morphology, whereas in the last 10 years hysteroscopy has become, in some hospitals, the gold standard procedure for evaluating the uterine cavity, particularly if performed in an office setting and if associated with eye-guided biopsies. Hysteroscopy without endometrial biopsy is unreliable in differentiating between pre-malignant and malignant disease in the uterine cavity, although if the cavity is clearly atrophic it may be possible to omit endometrial sampling. Endometrial cancer may be found in symptomatic and asymptomatic women with an essentially atrophic or focally hyperplastic endometrium, which cannot be detected by ultrasound.[4] MRI-scan can also demonstrate endometrial hyperplasia and, though not often used, may be helpful in cases where TVUS is not possible, or when superimposed invasive endometrial carcinoma is suspected.[1]

Treatment for Endometrial Hyperplasia[11]

Medical therapy is generally recommended for patients with non-atypical hyperplasia. Treatment for Endometrial Hyperplasia without atypia are progestin therapy continuous or cyclical and repeat biopsy in 3 - 4 months. Women of childbearing age are generally treated with progestin dominant combination OCPs. Alternatively Depo-Provera at the usual contraceptive dose (150mg IM q3) or oral Provera at 10mg/month may be used. Some patients may be diagnosed via biopsy obtained during an infertility work-up. May follow with ovulation induction after normal biopsy if pregnancy desired. Treatment for peri or postmenapausal women is similar except slightly higher doses of progestins are used (Provera 20mg po 10 days/ month or Depo-Provera 200mg IM q2 months.

Treatment for atypical endometrial hyperplasia when childbearing is complete is total hysterectomy (abdominal or vaginal) as a standard treatment, but the specimen should be examined at the time of surgery to rule out a coexistent endometrial carcinoma, which may occur as much as 20% of the time. Conservative medical therapy can be attempted in younger patients who request preservation of fertility. D&C (possibly with hysteroscopy) should be performed prior to initiation of medical therapy to rule out carcinoma. Conservative therapy may also be attempted in young patients with early, well differentiated endometrial carcinomas.

CONCLUSIONS

Endometrial hyperplasia may produce obvious space occupying lesions in which diagnosis is easy with hysteroscopy, but it may be not very obvious especially in early stages of the disease. Endometrial hyperplasia is a non-physiological, non-invasive proliferation of the endometrium that result in a morphological pattern of glands with irregular shapes and varying sizes.

Among diagnostic techniques, hysteroscopy presents several advantages: it is an out-patient, procedure, minimally invasive repeatable, of rapid execution and with low cost. The accuracy of hysteroscopic evaluation of the uterine cavity is extremely encouraging. Office hysteroscopy, which has a high diagnostic reliability and minimal discomfort, appears to be an ideal method of diagnosis and follow up of patients with endometrial hyperplasia.

Hysteroscopy has made the most significant progress, mainly because the ability to use fine diameter instruments makes it feasible to avoid both anesthesia and cervical dilatation. Innovation diseases through hysteroscopy is still evolving.

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