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Evaluation of Intrauterine Pathology: Efficacy of Diagnostic Hysteroscopy in Comparison to Histopathological Examination

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Abstract

The aim of this work is to evaluate the diagnostic accuracy of hysteroscopy compared to histopathological findings in cases with intrauterine pathology. This prospective clinical trial was carried out over a period of two years. 280 patients were recruited with an average of 45 years (range: 25-65 years). Two hundred and thirty patients (82.14%) with abnormal findings in ultrasound examinations, the remaining 50 (17.85%) had normal scan, referred mainly because of abnormal uterine bleeding (AUB) and infertility. Hysteroscopic findings divided into; uterine cavity lesions: endometrial or cervical polyps, myomas, cysts, placental derbis, adhesions, congenital malformations and IUCD retention, endometrial characterization including: functional, dysfunctional, atrophic endometrium, hyperplasia, polypoid and carcinoma. Biopsies or removal of pathology were performed and sent for histopathology examinations, results were compared with hysteroscopic findings. Sensitivity, Specificity and predictive value (PV) of hysteroscopy were calculated. Results: uterine cavity abnormalities were detected in (71.4%) patients, significantly more at ages of >30 years (58.3%) compared with ages of <30 years (34.6%) (P<0.05). In benign endometrial lesions, the sensitivity of hysteroscopy was (98.9%), specificity was (97.5%), positive predictive value was (98.8%), negative predictive value was (98.5%) with diagnostic accuracy of 98.3%, same parameters for endometrial characterization: (78.9%), (90.7%), (82.8%), (90.9%) with diagnostic accuracy of 87.8%. Conclusions: Hysteroscopy allows direct visualization of uterine cavity, it is a safe and reliable procedure for evaluating benign endometrial lesion, but in view of poor validity to exclude endometrial hyperplasia and cancer, it is recommended always to perform diagnostic hysteroscopy combined with biopsy procedures, giving it an irreplaceable value in diagnosis and treatment of intrauterine disease.

Keywords: Hysteroscopy; Abnormal uterine bleeding; Infertility; Endometrial pathology

Introduction

During the last decade hysteroscopy has become the tool of choice for the evaluation of the endometrial cavity including assessment of abnormal uterine bleeding (AUB), infertility, and recurrent pregnancy loss (RPL) [1-3]. The ever increasing value of diagnostic and operative hysteroscopy for patients with AUB serves as an appropriate tribute to Pantaleoni, who in 1869 described this procedure to look inside the uterus and could visualize an endometrial polyp [4]. AUB is the single most common reason for gynaecological referrals [5]. While there are various benign reasons for AUB, abnormal peri- and post-menopausal bleeding is associated with endometrial cancer in about 10% of cases [6]. Transvaginal sonography (TVS) is a valuable screening method to identify women with endometrial pathology, not only by measuring endometrial thickness but also by accessing focal abnormalities within the endometrial cavity, however, its value is limited in the endometrial characterization because the image of endometrium is given in a gray scale which makes interpretation difficult and less accurate, also because although in post-menopausal women the presence of thick endometrium (>5 mm) may predict some kind of pathology, the exact lesion cannot be discriminated until biopsy is performed [7,8]. Also, despite the diagnostic accuracy and mini-invasiveness of 3D sonohysterography (3D SHG), it was suggest that it cannot be a substitute of hysteroscopy in endometrial disease diagnosis, but it could be considered as a good method of screening to address patients to hysteroscopic confirmation [9]. Dilatation and curettage (D&C) has traditionally been considered as standard for investigation of AUB, however, it is a blind procedure that can miss a focal lesion like a polyp or a localized pathological lesions. In one study, 60% of patients had less than half the uterine cavity curetted and 16% had less a quarter. Negative endometrial biopsy in women with persistent AUB should be further investigated [10,11].

Uterine abnormalities are estimated to play a causal role in a substantial number of couples seeking treatment for infertility and in women with recurrent miscarriages whether of the first or second trimester [12,13]. Their assumed pathophysiologycial mechanism is that they impair proper embryo implantation and growth due to poor vascularization with subsequent infertility or miscarriage [14]. The rate of uterine anomalies is reported to be as 2-5% in women with a good obstetric history or those at low risk for complications [15,16], whereas more than 30% of infertile patients are reported to suffer from abnormal intrauterine findings [17]. A wide discrepancy (from 6.3 to 67%) of the rate of anomalies has been described for patients with recurrent pregnancy losses [16,18]. These findings mirror differences in study designs and the variations of anomalies reported in the respective studies [18].

Hysteroscopy is an accurate and less invasive method for the evaluation of uterine cavity. It is a dynamic test and allows a direct visualization of the endometrium, revealing the nature, location, shape, size and vascular pattern of any uterine cavity abnormalities. The main advantage of hysteroscopy is that biopsies can be taken at

the same time with great safety, which improves the diagnostic accuracy. Also, its "see and treat" potential provides higher patient satisfaction. Hysteroscopy is increasingly replacing D&C for the evaluation of AUB [19,20]. The objective of this study is to evaluate the diagnostic accuracy of hysteroscopy in detection of uterine cavity lesions compared with histopathological results of excised biopsy.

Subjects and Materials

A prospective study was carried out from Jan. 2010 to Jan. 2013. Two hundred and eighty patients were referred with abnormal ultrasonographic scanning (USS), AUB, infertility or RPL were admitted into our gynecology departments at Misurata Central Hospital. Patients underwent a preliminary assessment by history, clinical examination and USS of the pelvis. Baseline laboratory investigations included a complete blood count were also done. All hysteroscopies were performed under general anaesthesia using video-assisted diagnostic hysteroscopy with outer sheath 5.2 mm (Storz GmbH, Germany). Pathology in the uterine cavity was treated at the same setting using an operative hysteroscopic 10 mm fibreoptic resectoscope (Storz GmbH, Germany). All procedure were video recorded. The uterine cavity was expanded using distension media (Glycine 1.5%) administrated via electronically controlled irrigation delivery system (Endomate) (Storz GmbH, Germany).

Hysteroscopy was performed with a standard sequence, inspecting ectocervix, endocervical canal, uterine cavity, endometrium and tubal ostia. Hysteroscopic findings were allocated either to "the uterine cavity lesions" or "the endometrial aspect characterization". The uterine cavity lesions that were found including: endometrial polyp, cervical polyp, myoma, endometrial adhesions, congenital malformation, placental rest, lost intrauterine device (IUD). In the endometrial aspect characterization, differentiation between functional, atrophic or thin endometrium, dysfunctional, endometritis, cystic atrophy, hyperplasia, polypoidal, and carcinoma was done. The hysteroscopic observation was documented, and an endometrial biopsy and/or the removal of the pathology was performed. The histopathological results were used as gold standard and compared with the hysteroscopic documented observation. The sensitivity, specificity, and predictive value of hysteroscopy were calculated. Statistical analysis was performed using SPSS software. The P value was calculated by applying student t test, and considered to be significant if (<0.05).

Results

In this study, 280 patients were recruited; the age ranges from 25-65 years with average of 45 years. Two hundred thirty patients (82.14%) with abnormal findings on USS such as endometrial thickness, endometrial irregularity, polyps, myomas, IUD, placental debris. The remaining 50 patients (17.85%) had normal scan but referred because of infertility (10 cases), (20 cases) of menorrhagia, (15 cases) of postmenopausal bleeding, and (5 cases) were of cervical polyp. Uterine cavity abnormalities were detected in 71.4% of patients, significantly more at age of >30 years (58.3%) compared with that of <30 years (34.6%) ($P<0.05$).

Regarding the uterine cavity lesions diagnosed by hysteroscopy-200 (71.4%) cases showed uterine abnormalities, out of them: 150 (53.6%) cases of endometrial polyps were diagnosed, one of them associated with endometrial carcinoma on histopathology result, some were associated with cervical polyps and myomas. There were 25 cases of Submucous myomas, 10 cases of cervical polyp, 3 of them were associated with endometrial polyp. Septate and subseptate uterus were found in 8 cases, one of them associated with endometrial polyp and the other with cervical polyp. Endometrial adhesions were found in 13 (4.6%) cases, one was associated with myoma, one associated with endometrial polyp and the other associated with cervical polyp. The other diagnosed lesions included 6 cases of IUD (2.1%), 5 (1.7%) cases of placental debris and 3 (1.07%) endometrial cysts. The remaining 80 (28.6%) cases did not have any uterine lesions on hysteroscopy. Compared with histopathology, 105 (37.5%) cases did not show any pathology, with false negative in 25 cases including, 10 cases of isolated intrauterine adhesion, 6 cases of isolated septate uterus, and 5 cases of isolated IUD, 1 case of destroyed cyst, and 3 cases of small myomas were not submitted to biopsy (Figure 1).

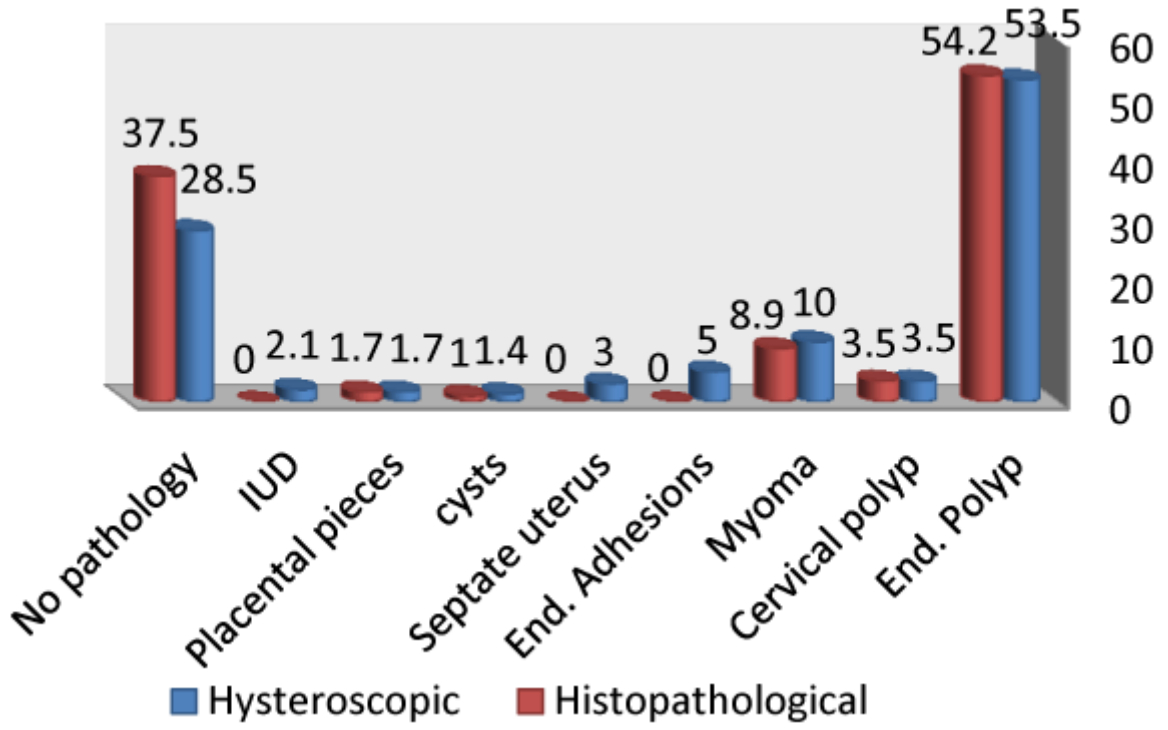

Figure 1: The uterine cavity lesions in hysteroscopy and histopathology.

Regarding the endometrial aspect characterization- one case (0.36%) of endometrial carcinoma was detected, 27 (9.6%) cases of endometrial hyperplasia, 30 (10.7%) cases of dysfunctional endometrium, 15 (5.3%) cases of polypoidal endometrium, 3 (1%) cases of endometritis, 4 (1.4%) cases of cystic atrophic endometrium, and 34 (12.1%) cases of atrophic endometrium. Functional endometrium was found in 166 (59.2%) cases (Figure 2).

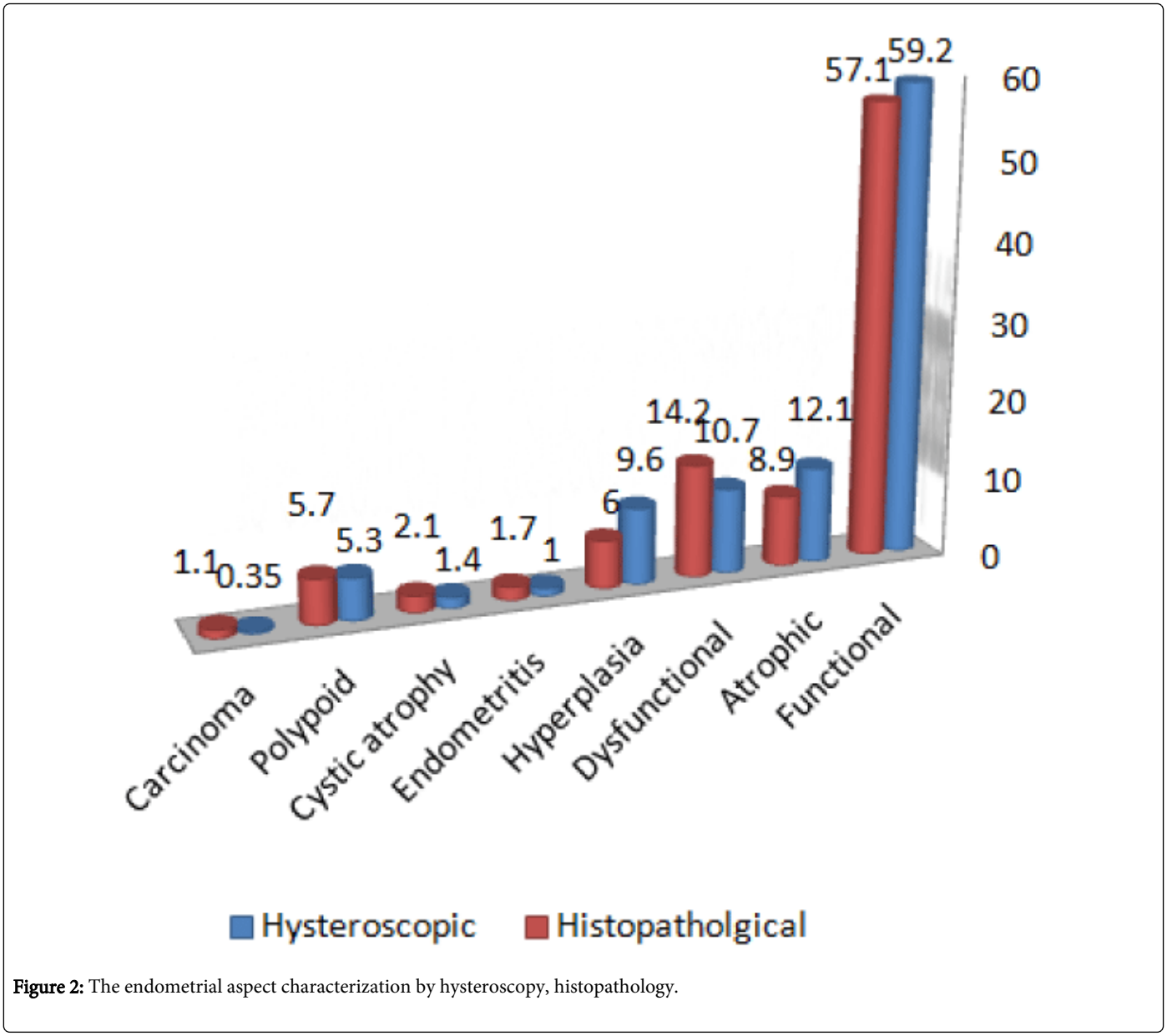

Figure 2: The endometrial aspect characterization by hysteroscopy, histopathology.

When compared with histopathological examination as gold standard, hysteroscopy failed to diagnose the following uterine lesions: one case of myoma that was really a polyp, two cases considered without endometrial lesions that had polyps on histopathological examination, the 2 polyps that were myomas. The hysteroscopy also failed in the endometrial characterization of the following cases: 2 cases of carcinoma were wrongly diagnosed as hyperplasia, 1 complex hyperplasia, 2 cases of dysfunctional endometrium, and 2 other polypoid endometrium were wrongly classified as atrophic endometrium.

The hysteroscopic evaluation was characterized as functional endometrium, dysfunctional endometrium in 12 cases, polypoid endometrium in 4 cases, simple hyperplasia in 1 case, and complex in another. Considering the 26 false-positive diagnosis, these include 3 cases of focal hyperplasia that were atrophic endometrium, 7 cases of polypoid endometrium, 6 cases of dysfunctional endometrium and 10 cases of hyperplasia that were all functional endometrium (Tables 1 and 2). Considering the diagnostic accuracy of hysteroscopy in the evaluation of intra-cavity lesions, the sensitivity, specificity, positive and negative predictive values were respectively 98.9%, 97.5%, 98.8%, and 98.5%. The values of the same parameters regarding the characterization of endometrium were as follow: 78.9%, 90.7%, 82.8%, 90.9%. The diagnostic accuracy was 98.3% for endometrial cavity lesions and 87.8% for endometrial characterization. The incidence of endometrial adenocarcinoma was 1.1%, the sensitivity and specificity of hysteroscopy were respectively 60% and 99% with a diagnostic accuracy of 99%. The incidence of endometrial hyperplasia was 9.6%, hysteroscopy has sensitivity of 88% and a specificity of 90% with diagnostic accuracy of 62%. The complication rate was 2%, including 2 cases of postoperative hemorrhage that were managed as in-patient for 24-h observation and then discharged, one perforation, 4 cases of false route were managed conservatively. Four cases of endometrial carcinoma (one in a polyp lesion) were submitted for hysterectomy (Figure 3).

Hysteroscopic exam	Histopathological exam	False negative
hyperplasia	Carcinoma	2
Functional	Polypoid	4
Functional	Hyperplasia	2
functional	Dysfunctional	12
Atrophic	Dysfunctional	2
Atrophic	Polypoid	3
Atrophic	Complex hyperplasia	1

Table 1: Failure of hysteroscopic diagnosis of endometrial characterization (False negative).

Hysteroscopic exam	Histopathological exam	False positive
Hyperplasia	Functional	10
Polypoid	Functional	7
Dysfunctional	Functional	6
Hyperplasia	Atrophic	3

Table 2: Failure of hysteroscopic diagnosis of endometrial characterization (False positive).

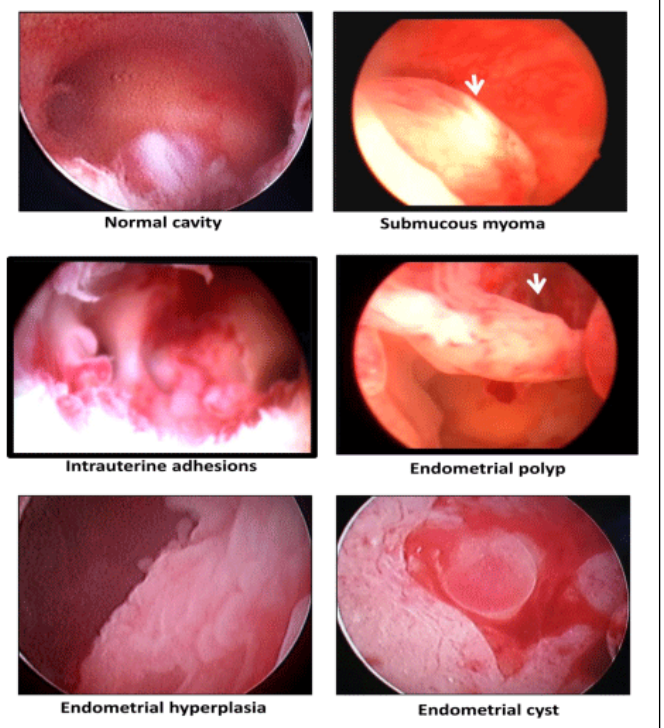

Figure 3: Different pathologies of endometrial cavity on hysteroscopy.

Discussion

Hysteroscopic inspection of uterine cavity is a simple and well accepted method for investigation of intrauterine pathology. The direct visualization, real-time, real-color, hydrated, well-illuminated, and augmented vision of the uterine cavity make this diagnostic tool very accurate to detect minute focal endometrial pathology and small lesions otherwise not possible, complemented to the ability of performing guided direct biopsies and treatment on the same diagnostic setting. Hysteroscopic examination may predict endometrial lesions with a good accuracy as well as endometrial aspect characterization, adopting a nomenclature similar to that used by the pathologist. This approach makes correlation between hysteroscopic findings and histopathological results easier.

In our study, hysteroscopic abnormalities in the uterine cavity were seen in about 71.4% of cases. The accuracy of hysteroscopy to diagnose uterine cavity lesions is better than that of endometrial characterization (98.3% versus 87.8%). The false diagnosis was lower and include: one case of hysteroscopic diagnosis of myoma that was a polyp, two cases of polyps that were myomas on histopathological examination. The false negative include two focal thicker lesions interpreted as dysfunctional endometrium that were polyps on histopathological examination. The false diagnosis on endometrium characterization is a concern, particularly the false negative; 12 cases of dysfunctional endometrium were misdiagnosed as functional endometrium.

Dysfunctional endometrium means a discordant maturation between endometrium and hormonal cycle, or a focal discordance with focal areas in various phases of endometrial cycle at the same time [21]. The two false negative for carcinoma occurred in postmenopausal women. Both were diagnosed as hyperplasia but their histopathological examination revealed atypical hyperplasia with focus of adenocarcinoma. After hysterectomy, adenocarcinoma was confirmed on histopathological examination. Hysteroscopic guided biopsy permitted the correct histopathological diagnosis. Our study showed that for endometrial cancer, hysteroscopy has sensitivity and specificity of 60% and 99%% with a diagnostic accuracy of 99%. There is continuing debate about the value and accuracy of hysteroscopy in diagnosis of endometrial diseases that is endometrial cancer and its precursor, endometrial hyperplasia. Previous studies showed that hysteroscopy was more accurate in identifying intrauterine pathologies like endometrial polyp, Submucous myoma and misplaced IUD than endometrial biopsy or D&C alone, whereas diagnosis of hyperplasia, its types and carcinoma was only possible after histopathological examination [22-24]. In comparison with our study, some studies showed an overall sensitivity and specificity of hysteroscopy for endometrial cancer was 86.4% and 99.2% respectively [21]. The conclusion of many studies was that hysteroscopy has high accuracy in diagnosing endometrial cancer rather than excluding it, with high accuracy in postmenopausal women rather than in premenopausal [25-27]. Add to that it also demonstrates any possible involvement of the lower uterine segment and cervix. Therefore, since the incidence of focal lesions in patients with AUB is 47-74% [28] (71.4% in our study), and the main purpose is to detect endometrial cancer, combined hysteroscopy and biopsy [29-31] is considered to be the new gold standard which showed an accuracy of almost 100% in diagnosis of carcinoma and its precursors.

Conclusion

Hysteroscopy is a safe and reliable procedure for evaluating benign endometrial lesion, allows direct visualization of uterine cavity and this particularly confer it a high diagnostic accuracy, that associated to the possibility of simultaneous treatment or biopsy procedures gives it an irreplaceable value in diagnosis and treatment of intrauterine disease.

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