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## Do we really need to hysteroscope all the women who have irregular bleeding on hormone replacement therapy?

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**Abstract** *Objective:* To find out the importance of hysteroscopy in patients with irregular bleeding on HRT. *Methods:* Retrospective case note analysis of women attending outpatient hysteroscopy clinic between 1 August 2000 and 31 July 2001. *Results:* A total of 352 patients were referred to hysteroscopy clinic at Castle Hill Hospital, UK. The mean age of the patients was 57 years (range 48–69 years). The mean duration of HRT usage was 3.5 years (range 2–10 years). Seventy-seven (22%) patients had irregular bleeding on HRT, where hysteroscopy showed normal endometrial appearance. All these patients underwent an endometrial biopsy. Eleven (14%) of the patients had an intrauterine polyp and a polypectomy was performed in each case. The histology results of the endometrial biopsy/polyp were as follows: 42 had atrophic or inactive endometrium; 11 had benign endometrial polyp; 10 had insufficient sample all in women with hysteroscopically normal endometrial cavities; 8 had HRT effect; and 6 had progestogenic effect. There were no cases of malignancy. *Conclusion:* The incidence of significant pathology in patients with irregular bleeding on HRT is very low; however, benign polyps are common. It is better to adopt “see and treat” policy, where facilities are available. If facilities are not available, consider ultrasound scan or saline infusion sonohysteroscopy and target appropriately.

**Keywords** Hysteroscope · Bleeding · Hormone replacement therapy

### Introduction

Abnormal uterine bleeding (AUB) is the most common reason for referral to outpatient gynaecology departments. Investigation of these women may reveal normal endometrium, endometrial hyperplasia, atypical hyperplasia, polyps, fibroids or carcinoma. A careful evaluation of this condition is very important because endometrial cancer is diagnosed in up to 10% of postmenopausal women with abnormal bleeding and is a plausible possibility in premenopausal women who present with this symptom [1].

Polyps or sub-mucous myoma are the common abnormalities in the uterine cavity of premenopausal women and have been reported in more than 40% of the patients referred for abnormal uterine bleeding [2] and even more frequently in patients with persistent bleeding and bleeding on hormone replacement therapy (HRT) [2, 3, 4, 5, 6]. Polyps in particular are common in peri- and postmenopausal women and occur even more frequently in patients with bleeding on HRT, and fibroids in premenopausal women.

Irregular bleeding associated with the use of a combination of oestrogens and progestogens is considered as an unacceptable side effect of HRT [7]. In continuous combined regimens, oestrogens and progestogens are administered together daily, and such treatment should produce an atrophic endometrium and amenorrhoea. Alternately, in sequential or cyclic regimens, progestogens are given after oestrogens in order to induce predictable withdrawal bleeding [8]. Persistent bleeding associated with combined regimens or occurring before the discontinuation of progestogens in the sequential regimens should be considered abnormal, and its cause should be investigated in order to exclude uterine pathology. Various diagnostic imaging modalities that can be used are transvaginal ultrasonography (TVS), saline infusion sonohysterography (SIS) and hysteroscopy (HYS) and biopsy [9]. The diagnostic strength and advantages and disadvantages of such techniques must be known, as must their observer dependence, to guarantee that the right

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technique is favoured over others and that it is applied in a cost-effective way.

The TVS is an easy, fast and inexpensive technique that has become widely used to evaluate any endometrial abnormalities. It is less invasive, well tolerated, generally painless, without complications and it can diagnose intrauterine, intramyometrial as well as other pelvic lesions. It produces a lot of equivocal findings and does not exclude polyps/sub-mucous myomas, as a result of which patients are subjected to further investigations [2].

The SIS is a fast, simple and first-line tool for investigation of the uterine cavity. It is an excellent tool in diagnosing polyps and sub-mucous myomas especially in units where there is no facility for an outpatient hysteroscopy. In those units, inpatient HYS can be only offered to patients with SIS suggestive of intrauterine lesions. The only problem is that once myoma and polyps are diagnosed on SIS, treatment cannot be offered to the patient there and then; instead, the patient has to undergo therapeutic hysteroscopy. The SIS has a higher failure rate. Both TVS and SIS not only assess the endometrial cavity but also diagnose other pelvic lesions such as simple ovarian cysts and sub-serous fibroids, which are unlikely to be related to the presenting problem and may not only cause unnecessary patient anxiety but also lead to unnecessary invasive treatment.

Hysteroscopy has generally been accepted as the gold standard for evaluation of the uterine cavity [10, 11, 12]. It can be performed in the office setting or as a day-case procedure. Hysteroscopy is an invasive procedure. The most important benefit of HYS over SIS and TVS is its "see and treat" potential, which not only obviates multiple hospital visits but also provides higher patient satisfaction. None of this procedure can exclude hyperplasia or carcinoma without endometrial sampling. To get the maximum benefits from an investigation it is important to select patients properly, and skilled personnel should perform these investigations to obtain optimal results so that patients are managed adequately and cost-effectively. A quarter of the patients referred to our outpatient hysteroscopy clinic are the ones with irregular bleeding on HRT. An important question is: Do we really need to hysteroscope all the women who have irregular bleeding on HRT?

The aim of this study was to find out the importance of performing hysteroscopy in patients with irregular bleeding on HRT.

## Patients and methods

A total of 352 patients with various indications were referred to our outpatient hysteroscopy clinic between 1 August 2000 and 31 July 2001. Seventy-seven (22%) patients had irregular bleeding on HRT. A retrospective case note analysis of these women was performed.

The endometrial cavity of all these patients was evaluated by means of a hysteroscopy (Olympus, Keymed, UK) followed by an endometrial biopsy. Hysteroscopy was performed using a 3.1-mm flexible hysteroscope with Normal saline as the distension medium.

In the event of finding an intrauterine pathology, a Versa scope (Gynaecare, Scotland) was used with intracervical injection of Citanest 3% with Octapressin and the polyps were treated using either polypectomy forceps or Versa point (Gynaecare).

After hysteroscopy and treatment was completed, a suction curette was used to aspirate the uterine cavity and the polyp and endometrial biopsy was sent for a histological examination. Cervical dilatation was only performed if required. All the patients who had no intrauterine pathology were managed conservatively. Outpatient hysteroscopy was successfully performed in all the 77 cases.

## Results

A total of 352 patients were referred to hysteroscopy clinic at Castle Hill Hospital, Cottingham, UK. Seventy-seven (22%) patients had irregular bleeding on HRT. The mean age of the patients was 57 years (range 48–69 years). The mean duration of HRT usage was 3.5 years (range 2–10 years). Eleven (14%) of them had an intrauterine polyp and a polypectomy was performed using either polypectomy forceps or the 2-mm Versa point system (Gynaecare) in each case.

An endometrial biopsy was obtained in all the cases and sent for a histological examination. Hysteroscopy revealed normal or atrophic endometrium in 52 cases which was confirmed on the histological examination of the endometrial biopsy. Similarly hysteroscopy showed thickened or normal endometrium in 14 patients and intrauterine polyps in 11 patients and the histology suggested either HRT or progestogenic and benign polyps, respectively.

The results of the hysteroscopy and histological examination of the endometrial biopsy/polyp are shown in Table 1.

## Discussion and conclusion

This study shows that the incidence of significant pathology in patients with irregular bleeding on HRT is very low; however, benign polyps are common. In our study group 14% (11 patients) had intrauterine polyps. Hysteroscopy has generally been accepted as the gold standard

**Table 1** Results of histological and hysteroscopy examinations

Histology ( <i>n</i> =77)	Hysteroscopy
Atrophic/inactive endometrium ( <i>n</i> =42)	Normal/atrophic endometrium
Insufficient ( <i>n</i> =10)	Normal/thickened endometrium
HRT effect ( <i>n</i> =8)	
Progestogenic effect ( <i>n</i> =6)	Intrauterine polyps
Benign endometrial polyp ( <i>n</i> =11)	
No malignancy	
All polyps treated in outpatient department	
No further hysteroscopy or biopsy required	
All patients discharged after their initial visit	

for evaluation of the uterine cavity. It can be performed in the office setting or as a day-case procedure. The intrauterine polyps and sub-mucous myomas are commonly seen in patients with abnormal uterine bleeding and their frequency was probably underestimated in some previous studies where hysteroscopy was altogether omitted in these patients [13]. "See and treat" intrauterine lesions are one of the most important benefits of HYS over SIS. All our patients had successful outpatient diagnostic hysteroscopy as well therapeutic procedures in patients with intrauterine lesions.

The HYS is a very sensitive tool for diagnosis of endometrial polyps: 92% sensitivity and 82% specificity [14, 15]. Cacciatore found sensitivity, specificity and positive predictive value of diagnosing lesions in postmenopausal women with AUB to be 87, 91 and 90%, respectively [16]. Even 10% of postmenopausal women with no symptoms and a normal endometrial stripe by TVS have endometrial pathology detected by office HYS [17]. The same group found that 28% of asymptomatic postmenopausal women with an endometrium >4 mm had intrauterine pathology detected by office HYS, and that 76% of symptomatic postmenopausal women had endometrial pathology detected by office HYS. Lozzi et al. suggested that the positive predictive value of office HYS in postmenopausal women with a thickened endometrium to be 97% and the negative predictive value to be 100% [18]. A quantitative review by Clarke et al. provides an estimate of accuracy of hysteroscopy in the diagnosis of endometrial hyperplasia and cancer. Their results indicate that HYS is highly accurate and clinically useful in diagnosing endometrial cancer in women with AUB, and it is moderately useful in diagnosing endometrial disease [19].

The overall performance of hysteroscopy is intermediate to high. Polyps and sub-mucous myomas were most identified, although discrimination between abnormalities is at times difficult. But overall patient satisfaction is much higher with HYS and it also avoids multiple hospital visits, a reduction in waiting time for the patients and less wasting of resources [20].

It is better to adopt "see and treat" policy, where facilities are available. If facilities are not available, ultrasound scan or saline infusion sonohysterography should be considered and applied when appropriate.

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