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ORIGINAL ARTICLE

The Outcome of Medical Treatment of Endometrial Hyperplasia

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ABSTRAK

Terdapat pelbagai cabaran dalam pengurusan klinikal hiperplasia endometrium (EH), terutamanya berkaitan dengan pemilihan kaedah perubatan dan keberkesanannya dalam mencapai penyelesaian simptom dan regresi perubahan hiperplastik. Untuk menangani masalah ini, kami telah menjalankan satu kajian retrospektif di Hospital Canselor Tuanku Muhriz (HCTM) untuk menyiasat hasil pelbagai rawatan perubatan untuk EH dengan/tanpa atipia selama tempoh 10 tahun dari 2007 hingga 2017. Maklumat latar belakang klinikal pesakit dan keputusan biopsi tisu endometrium mereka diperolehi daripada rekod perubatan dan makmal histopatologi. Kami menganalisis jenis dan tempoh rawatan perubatan, regresi simptom, dan hasil rawatan tersebut. Sebanyak 86 wanita telah menerima rawatan untuk EH dengan purata umur 48.2 ± 12.3 (median 46) tahun. Dari jumlah ini, 65 (75.6%) mengalami EH tanpa atipia, dan 21 (24.4%) mengalami EH atipia. Semua wanita mendapati simptom mereka pulih dalam tempoh kurang dari 6 bulan rawatan, dengan tempoh yang berbeza bergantung kepada regimen yang digunakan. Sistem levonorgestrel-intrauterine (LNG-IUS) memulihkan simptom dalam tempoh masa 3 hingga 6 bulan ($p<0.01$) manakala Medroxyprogesterone Acetate (MPA) intramuskular (2 daripada 86) mempunyai resolusi simptom dalam tempoh kurang dari 3 bulan. Analog Hormon Pelepasan Gonadotrofin (GnRH) dan progestogen oral mempunyai tempoh tindak balas yang berbeza antara 0-6 bulan. LNG-IUS gagal mencapai regresi endometrium dalam 12.5% dan 23.3% dengan progestogen oral. LNG-IUS, analog GnRH, dan MPA mempunyai kadar regresi EH yang boleh diterima. Progestogen oral mempunyai kadar kegagalan tertinggi dalam mencapai regresi EH. Ini mungkin disebabkan oleh isu pematuhan dengan rawatan oral.

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Kata Kunci: Gonadotropin; hiperplasia endometrium; medroxyprogesterone acetate; progestogen; sistem intrauterin

ABSTRACT

Endometrial hyperplasia (EH) poses significant challenges in clinical management, particularly concerning the choice of medical modalities and their efficacy in achieving symptom resolution and regression of hyperplastic changes. To address this, we conducted a retrospective study at Hospital Canselor Tuanku Muhriz (HCTM) to investigate the outcomes of various medical treatments for EH with/without atypia over a 10-year period from 2007 to 2017. Patient's clinical background and endometrial tissue biopsy results were obtained from medical records and histopathological laboratory respectively. We analysed the type and duration of medical treatments, as well as symptoms regression and outcome of the treatments. A total of 86 women received treatment for EH with average age of 48.2 $\pm$ 12.3 (median 46) years. Of these, 65 (75.6%) had EH without atypia, and 21 (24.4%) had atypical EH. All women had their symptoms resolved in less than 6 months of treatment, with varying duration depending on different regimes used. Levonogestrel-intrauterine system (LNG-IUS) had symptoms resolved by 3 to 6 months ($p<0.01$) while intramuscular Medroxyprogesterone Acetate (MPA) (2 in 86) had resolution of symptoms in less than 3 months. Gonadotropin-releasing Hormone (GnRH) analogue and oral progestogen had different duration of response rate between 0-6 months. LNG-IUS failed to achieve endometrial regression in 12.5% and 23.3% with oral progestogen. LNG-IUS, GnRH analogue and MPA had acceptable regression rate of EH. Oral progestogen had the highest failure rate in achieving EH regression. This is likely due to compliance issue with oral treatment.

Keywords: Endometrial hyperplasia; gonadotrophin; intrauterine system; medroxyprogesterone acetate; progestogen

INTRODUCTION

Endometrial hyperplasia (EH) is defined as an abnormal proliferation of the endometrial glands with an increase in the gland to stroma ratio in endometrium (Petersdorf et al. 2022). Endometrial hyperplasia may manifest as heavy menstrual flow with intermenstrual bleeding and erratic bleeding in perimenopausal women. EH may also present as a breakthrough bleeding in women with hormone replacement therapy (HRT) or as postmenopausal bleeding (Thomas et al. 2000). The incidence is peak in the late forties and early fifties, and it is correlated with the risk of progression to endometrial malignancy. The WHO classification (revised 2014) divided EH into two categories based on the presence or absence of cytological

atypia: simple EH and atypical EH. The risk of developing endometrial malignancy is the most significantly associated with atypical EH. The cumulative risk of cancer in four years was 8.0% (95% CI 1.31-14.6), which increased to 12.4% (95% CI 3.0-20.8) and 27.5% (95% CI 8.6-42.5) after nine and nineteen years, respectively (Lacey et al. 2010). Atypical EH has also been linked to a 43.0% increase in endometrial carcinoma in women undergoing hysterectomy (Nees et al. 2022).

Treatment for EH aims to achieve a complete regression of the disease. However, there are no standard therapy for EH. Current literature proposed hormonal therapeutic options such as progestogens or gonadotrophin releasing hormone (GnRH) analogue, or combination as a treatment. The mechanism includes modifying the oestrogen effect on endometrium proliferation thus enhancing the secretory changes on the endometrium (Yu et al. 2022). The options of treatment differ depending on age, fertility status, premorbid status and presence of cytologic atypia. Besides, surgical options have been reported as the standard treatment of EH, specifically with atypia due to its higher risk progression to malignancy. Thermal balloon ablation, laser therapy or resectoscopic surgery may be offered as one of the interventions, provided malignancy has been excluded. EH among postmenopausal women or those with a higher risk for endometrial malignancy is subjected to hysterectomy as a definitive surgical treatment (Chelmow et al. 2022).

The trend of levonorgestrel-releasing intrauterine system (LNG-IUS) is gaining its popularity as the first-choice treatment of EH. The use of LNG-IUS has a higher rate of regression after a periods of three months (OR 2.30, 95% CI 1.39–3.82), 6 months (OR 3.16, 95% CI 1.84–5.45), 12 months (OR 5.73, 95% CI 2.67–12.33) and 24 months of treatment (OR 7.46, 95% CI 2.55–21.78) (Abu Hashim et al. 2015). It has negligible side effects, with amenorrhea or oligomenorrhoea as tolerable effects due to its impact on thinning endometrial lining (Mittermeier et al. 2020).

Oral progestogens such as medroxyprogesterone (10 mg/day), lynestrenol (LYN, 15 mg/day) and norethisterone (NET, 15 mg/day) for ten days per cycle are among of the available options and offered a disease regression up to 60.0% of cases (Ozdegirmenci et al. 2011). The use of progestogens may be limited due to significant side effects which are possible venous thromboembolism, decreased libido, acne and others (Stevenson et al. 2020). The use of progestogen may also be restricted in the morbidly obese patient. Therefore, long-term compliance with progestogen may be an issue, with an increased number of non-compliance (Gallos et al. 2010).

In addition, the traditional use of intramuscular medroxyprogesterone (MPA) and increasing experience in GnRH analogue use had been limited by the side effects (Chandra et al. 2016). Intramuscular MPA revealed a complete regression in 82.0% of atypical EH with recurrence rate of 47.0% between

7 and 36 months following 26 weeks of treatment (Ushijima et al. 2007). Meanwhile, GnRH analogue treatment for six months showed regression in 90.5% of cases (Agorastos et al. 1997). However, the hypoestrogen symptoms resulting from GnRH analogue need to be addressed, especially with risk of osteopenia on long term therapy.

In the present study, we were evaluating the treatment outcome of various hormonal treatment options for EH. Factors such as high body mass index (BMI), poor compliance to oral medication and sizeable uterine size may interfere with the treatment outcome (Pal et al. 2018). Failure of treatment may also be related to suboptimal placement of the hormonal device within the uterine cavity or low hormonal dosage in an enlarged uterus allowing development of resistance to EH (Pal et al. 2018). Otherwise, failure of medical treatment was defined as no regression of EH within six months (Mentrikoski et al. 2012).

MATERIALS AND METHODS

Study Design

This was a retrospective analysis in Hospital Canselor Tuanku Muhriz (HCTM) that included women who were diagnosed with EH with or without atypia and treated with medical treatment between 2007 and 2017. The Medical Research and Ethics Committee of Universiti Kebangsaan Malaysia Medical Centre approved this study (Project Code: FF-2018-391 and FRGS/1/2017/SKK02/UKM/02/1).

Patient Characteristics and Data Collection

This study enlisted 86 EH patients who fulfilled the criteria. They were subsequently separated into two groups: EH without atypia (n=65) and atypical EH (n=21). Patients' demographic data, medical diseases, family history, and symptoms were obtained from the archived medical records following research ethics approval. Endometrial biopsy results obtained from pipelle sampling or via dilatation and endometrial curettage were traced from the histopathology laboratory. Patients treated with Intrauterine system – levonorgestrel (LNG-IUS), oral progestogens, intramuscular medroxyprogesterone acetate (IM MPA) and endometrial ablation were selected. Duration, side effects and outcomes of the treatment regime were recorded. Patients who had successful treatment following with the respective management were defined as having histopathological regression within six months duration. Exclusion criteria were patients who opted hysterectomy as primary treatment and missing data.

Statistical Analysis

Statistical analysis was carried out using SPSS 23 (SPSS, Chicago, IL) and Minitab 16 (Minitab State College, PA). The Kolmogorov-Smirnov test was used to assess the normality of continuous data. Normally and non-normally distributed continuous data were analysed by using the Student t-test and Mann-Whitney U test, respectively.

Categorical variables were examined with Chi-squared testing. A *p*-value <0.05 was considered statistically significant. Differences between the two groups were expressed as Odds ratio (OR) or mean difference (β) with 95% confidence interval (CI).

RESULT

The Demographic and Baseline Characteristics of the Study Population

The mean age was 48.2 ± 12.3 (range 28-72) years. Majority were more than 50 years old (45.3%) women; while 26.7% were between 41-50 years old, and 23.2% were between 31-40 years old. Only a small portion (4.7%) of women were below 30 years old. A total of 61 (71.0%) women were pre-menopausal, while 25 (29.0%) were menopausal. The mean BMI was 31.73 ± 5.77 (median 32.40) kg/m^2. More than half of the women were categorised as obese; 29 (32.5%) obese class I, 18 (20.9%) were obese class II, and 8 (9.3%) were morbid obesity. In contrast only 11 (12.8%) of women had normal BMI, while 21 (24.4%) were overweight. The age (*p*=0.75) and BMI (*p*=0.98) of women with EH did not influence their outcome of regression rate in conservative management.

A total of 40 (46.5%) women were Malay, followed by 32 (36.0%) women were Chinese, while only 12 (14.0%) and 3 (3.5%) women were Indian and other ethnicity respectively. More than half of the women (59, 53.5%) had three or more children while 41 of them (46.5%) had parity of two or less. A total of 16 women (18.6%) with EH had a positive family history of malignancy in the form of gynaecological cancer, lung cancer, breast cancer and nasopharyngeal malignancy. A third of patients with EH had diabetes (n=29, 32.5%) or hypertension (n=30, 33.7%).

In the present study, majority of women; 65 (75.6%) were diagnosed with EH without atypia, and 21 (24.4%) women had atypical EH. Majority of women experience abnormal uterine bleeding in the form of irregular or prolonged bleeding (n=33, 38.4%), followed by heavy menstrual bleeding (n=28, 32.6%) and postmenopausal bleeding (n=25, 29.0%). The mean pre-treatment endometrial thickness was 12.12 ± 5.87 (median 11.06) mm and the outcome of conservative modalities was not affected by the initial thickness of the endometrial lining, as indicated by a non-significant *p*-value of 0.39. Following treatment, there was a reduction in endometrial thickness, with a mean of 7.39 ± 3.54 (median 6.9). This decrease in thickness after conservative treatments was statistically significant, with a *p*-value of 0.04, suggesting a notable decline in thickness post-treatment. Table 1 showed the study population's demographic and baseline characteristics.

Duration Taken to Control Symptoms Following Therapy

Table 2 showed the duration taken to control symptoms following conservative management. All women with LNG – IUS, 4 (50.0%) women with gonadotrophin-releasing

TABLE 1: Demographic data

Demographic data	n	%	p-value
Age (years): 48.2 ± 12.3 (range 28 – 72)**			0.75
Less than 30 years	4	4.7	
31-40 years	20	23.2	
41-50 years	23	26.7	
More than 50 years	39	45.3	
Mean body mass index: 31.1 ± 5.8 (med, 32.40) kg/m^2**			0.98
Normal	11	12.8	
Overweight	21	24.4	
Obesity Class 1	28	32.5	
Obesity Class 2	18	20.9	
Morbid Obesity	8	9.3	
Race			
Malay	40	46.5	
Chinese	31	36.0	
Indian	12	14.0	
Others	3	3.5	
Parity			
Less than 3	40	46.5	
More than 2	46	53.5	
Diabetes mellitus	28	32.5	
Hypertension	29	33.7	
Family history	16	18.6	
Type of endometrial hyperplasia			
Without atypia	65	75.6	
Atypical	21	24.4	
Clinical presentation			
Abnormal uterine bleeding	33	38.4	
HMB	28	32.6	
Post-menopausal bleeding	25	29.0	
ET thickness (mm)			
Pre-treatment: 12.12 ± 5.87 (med: 11.06)**			0.39
Post treatment: 7.39 ± 3.54 (med: 6.9)**			0.04

HMB; heavy menstrual bleeding, ET; endometrial thickness
*data presented as n (%), analysed using Fisher exact test
**data presented as mean ± standard deviation (median), analysed using Student t-test

hormone and 35 (58.3%) women with oral progestogens needed 3-6 months to control the symptoms. On the other hand, 4 (50.0%) women with the gonadotrophin-releasing hormone, 2 (100.0%) women with intramuscular depo-medroxyprogesterone acetate and 25 (41.7%) women with oral progesterone required shorter duration less than 3 months to control symptoms of EH. All women using LNG-IUS achieved symptom control by 3-6 months (p<0.01), while the women using other modalities such as GnRH analogue (p=0.45), intramuscular MPA (p=0.13) and oral progestogens (p=0.14) did not have a significant timeline to achieve control of symptoms.

TABLE 2: Duration taken to control symptoms following conservative management

	Duration taken to control symptoms		OR/ß (95% CI) p-value
	Less than 3 months n (%)	3 – 6 months n (%)	
LNG-IUS (n=16)	0 (0)	16(100.0)	1.80 (1.46-2.21) <0.01
GnRH analogue (n=8)	4(50.0)	4(50.0)	1.89 (0.44-8.2) 0.45
IM MPA (n=2)	2(100.0)	0(0)	2.90 (2.16-3.89) 0.13
Oral Progestogens (n=60)	25(41.7)	35(58.3)	2.38 (0.84-8.79) 0.14

LNG-IUS: intrauterine levonegestrel; GnRH analogue: gonadotrophin releasing hormone analogue; IM MPA: intramuscular medoxyprogestogrogen acetate
*data presented as n (%), analysed using Fisher exact test, difference between two groups expressed as odds ratio (OR) (95% Confidence interval (CI))

Endometrial Regression Outcome Following Conservative Management

Table 3 below showed regression outcome following conservative management. At least 14 (87.5%) women used LNG – IUS, 8 (100.0%) women with GnRH analogue, 2 (100.0%) women with IM MPA and 46 (76.7%) women with oral progesterone achieved endometrial regression by 6 months. A total of 2 (12.5%) women with LNG-IUS and 14 (23.3%) women with oral progestogens failed to achieve endometrial regression by 6 months and needed further management. It is observed none of the conservative modalities had a significant influence in achieving endometrial regression as

TABLE 3: Endometrial regression following conservative management

	Outcome of conservative treatment		OR/ß (95% CI) p-value
	Regression n (%)	Failed regression n (%)	
LNG-IUS (n=16)	14(87.5)	2(12.5)	1.75 (0.36-8.61) 0.73
GnRH analogue (n=8)	8(100.0)	0(0)	1.26 (1.12-1.41) 0.34
IM MPA (n=2)	2(100.0)	0(0)	1.24 (1.11-1.37) 1.00
Oral Progestogens (n=60)	46(76.7)	14(23.3)	0.27 (0.06-1.31) 0.13

LNG-IUS: intrauterine levonegestrel; GnRH analogue: gonadotrophin releasing hormone analogue; IM MPA: intramuscular medoxyprogestogrogen acetate
*data presented as n (%), analysed using Fisher exact test, difference between two groups expressed as odds ratio (OR) (95% Confidence interval (CI))

TABLE 4: Hysterectomy rate following conservative management

	Hysterectomy outcome of conservative treatment		OR/ß (95% CI) p-value
	Yes	No	
LNG-IUS (n=16)	2(12.5)	14(87.5)	0.69 (0.14-3.44) 1.00
GnRH analogue (n=8)	0(0)	8(100.0)	1.22 (1.10-1.35) 0.34
IM MPA (n=2)	0(0)	2(100.0)	1.20 (1.09-1.32) 1.00
Oral Progestogens (n=60)	12(20.0)	48(80.0)	3.00 (0.62-14.94) 0.21

LNG-IUS: intrauterine levonegestrel; GnRH analogue: gonadotrophin releasing hormone analogue; IM MPA: intramuscular medoxyprogestogrogen acetate
*data presented as n (%), analysed using Fisher exact test, difference between two groups expressed as odds ratio (OR) (95% Confidence interval (CI))

p value >0.05. Table 4 below showed the hysterectomy rate in patients with EH following conservative approach. While 12 (20.0%) women with oral progestogens required hysterectomy, only two (12.5%) women using LNG – IUS ended up with hysterectomy. There was also no significant difference in the type of conservative modalities influencing the hysterectomy rate.

DISCUSSION

In the present study, we have evaluated the efficacy of various option of medical treatment in treating EH. There is still no standard treatment in treating EH. Considerably the choice would depend on age, desire of fertility, co-morbidities histopathological pattern and patients' preference. Göl et al. (2001) revealed that incidence of EH in asymptomatic premenopausal is less than 5.0% compared symptomatic women the risk increased to 10.0%. In the present study, most affected group for developing EH was perimenopausal aged more than 50 years (45.3%) with our mean 48.2 ± 12.3 (median 46) years. Our least affected age group was less than 30 years (4.7%). All participants in this study were symptomatic, and there were no asymptomatic cases included in the analysis. 38.4% of the participants experienced abnormal uterine bleeding, 32.6% had heavy menstrual bleeding and 29.0% presented with postmenopausal bleeding.

The risk factors for EH such as obesity and medical diseases were observed in this study, and study has shown that these are also important risk factors for developing endometrial cancer (Shafiee et al. 2020). Theoretically, most of these diseases are linked to elevated circulating oestrogen relative to progesterone, and unopposed oestrogen predisposes to EH. In a case-control study by Epplein et al. (2008), obese women (BMI 30 kg/m^2) had a nearly 4-fold increase in the incidence of EH with atypia, while women with a BMI 40 kg/m^2

had a 13-fold increased risk of EH with atypia and a 23-fold increased risk of EH without atypia (Epplein et al. 2008). From Pasquali (2006), obesity cause increased conversion of androstenedione to estrone within adipose stores, decreased circulating sex hormone – binding globulins and increased rates of chronic anovulation which lead to increased level of circulating estrogen.

In study by Farquhar et al. (1999), nulliparity and infertility also link with chronic anovulation and obesity and carry risks for EH with odds ratios of 2.8 (95% confidence interval [CI], 1.1-7.2) for nulliparity and 3.6 for infertility (95% CI, 1.3-9.9) (Farquhar et al. 1999). According to Shrestha (2018), EH is more likely in primipara (25.0%) because endometrial tissue becomes dormant or inactive during pregnancy, resulting in a decreased frequency of EH and malignancy. However, in our study parity more than 2 were most common to have EH. This is possible due to small sample size and may not reflect overall Malaysian population.

On the other hand, study by Zhang et al. (2021), concluded that hypertension and diabetes mellitus also risk factors for EH. De Barros Machado et al. (2016) suggested increased insulin level affiliated with cell survival and proliferation. It may play an important role in regulation of cancer. This was also shown in our study as 32.5% women were diabetic and 33.7% were known hypertensive.

The present study revealed a significant association between post-treatment endometrial thickness and the regression rate following conservative treatment (p=0.04). In contrast, pre-treatment endometrial thickness showed no significant association (p=0.39). Additionally, a study by Louie et al. (2016) found that an endometrial thickness of 14 mm or more was strongly associated with atypical hyperplasia, an endometrial subtype known to increase the risk of cancer (OR 4.29; 95% confidence interval 1.30-14.20; p=0.02). Importantly, Louie et al. (2016) reported a negative predictive value (NPV) of 98.3% for endometrial thickness below this threshold. In other words, if the endometrial thickness is below 14 mm, there is a high likelihood of not having atypical hyperplasia. However, Louie et al. (2016) did not specify whether the endometrial thickness threshold of 14 mm, associated with atypical hyperplasia, pertains to pre-treatment or post-treatment measurements.

Analysis showed a significant different between duration taken to control the symptoms with conservative treatment with p value <0.01 in LNG-IUS group of women compared to other modalities which was failed to show association with GnRH analogue p=0.45, IM MPA p=0.13 and oral progestogens p=0.14. Most of patients needed between three to six months duration to control the symptoms regardless type of conservative modalities. In a multicentre randomised study by Kaunitz et al. (2012), compared the effects of the LNG-IUS with cyclic oral progestogens in women with confirmed HMB over six cycles of treatment and results showed improved bleeding pattern and increased in haemoglobin

level is more seen in LNG – IUS group compare to oral progestogens. According to Sriprasert et al. (2017), GnRH analogues are known to cause endometrial atrophy within 3 to 4 weeks of therapy initiation, with amenorrhoea rates of up to 90.0%, as found in our study.

We also found no significant difference in regression rate between various medical treatment. Majority of patients achieved regression rate with higher number seen in GnRH analogue group 100.0% and LNG – IUS group with 87.5%. However, Abu Hashim et al. (2015) and Orbo et al. (2014) found that after 3 months (OR 2.30, 95% CI 1.39-3.82), 6 months (OR 3.16, 95% CI 1.84-5.45), 12 months (OR 5.73, 95% CI 2.67-12.33), and 24 months of treatment (OR 7.46, 95% CI 2.55-21.78), the LNG-IUS demonstrated a higher regression rate than oral progestogens (Abu Hashim et al., 2015; Orbo et al. 2014). Abu Hashim et al. (2015) similarly found that the regression time with LNG-IUS ranged from 3 to 12 months (median, 3 months), with a substantial percentage of patients (67.8%) achieving regression within 3 months.

Although GnRH analogue also showed promising result, it was not considered as first line of treatment to treat EH. Study by Agorastos et al. (1997), GnRH analogue proven effective in treating EH by direct anti-proliferative effect to the endometrium. It caused thinning of endometrium by induced anti-oestrogenic effect (Agorastos et al. 1997). Nevertheless, due to profound side effects, GnRH analogue usage only limited within short period of time. Add-back therapy with tibolone can be an option however prior study showed 19.0% recurrence within 2 years after cessation of therapy as mentioned by Agorastos et al. (1997).

Progestogens generally well tolerated by patients including in our study. Although rate of regression in oral progestogens group is slightly lower in our study but it still accountable as one of popular treatment of EH especially in reproductive age group. Comparison between intramuscular medoxyprogestrone acetate and oral progestogens, intramuscular medoxyprogestrone acetate cause significant side effects such as weight gain and amenorrhoea. We observed side effects in our patient used intramuscular medoxyprogestrone acetate (n=2) and revealed excessive weight gain within short period. Fortunately, repeat endometrial assessment showed regression of EH in both patients. A multicenter trial by Ushijima et al. (2007) revealed 82.0% complete and 18.0% partial response rates in EH patients receiving a medoxyprogestrone acetate regimen with a 25-73 month follow-up. Another study by El Behery et al. (2015), showed almost similar response with complete regression in 80.0% of women. The present study concluded 76.7% (n=46) women with oral progestogens achieved regression within 6 months of therapy and minimal tolerable side effects. Only one patient was non–compliance to oral progestogens and developed progression from EH without atypia to atypical EH.

Kim and Seong (2014) consider hysterectomy as definitive treatment

of atypical EH due to higher risk of malignancy. This option should be limited to pre and postmenopausal women instead of childbearing age. Conservative measures can be promising option however in failed our medical treatment cases, hysterectomy was seen in 14 women with higher rate seen in oral progestogens group (12; 20.0%) rather than LNG-IUS group (2; 12.5%) as seen in our study. One of our patients failed to achieve regression within six months due to spontaneous expulsion of device after 6 months and another patient failed to achieve regression subsequently opted for hysterectomy. Other consensus by Chandra et al. (2016) stated that extremely high dosage of progestogens is not vital to treat EH. However, optimal dosage of progestogens to achieve complete regression with minimal adverse reaction for treatment EH is yet to be definite.

The present study has limitations. Most notably, our study was not a randomised trial, and we only provided a limited sample size. This study was conducted in teaching hospital and our sample population may not reflect the actual population. Majority our endometrial samples were from pipelle sampling and although 97.9% of sample obtained from pipelle is adequate of histopathological assessment however there was still possibility of actual disease was not picked up from first sampling especially after finding endometrial carcinoma in subsequent follow up. Women with atypical EH have higher risk of concurrent endometrial carcinoma at the time of first biopsy (Doherty et al. 2020).

Other limitations include the dosage of therapy administered, and we did not completely analyse the potential impact of progestogen duration, dose, and type on the likelihood of persistence or progression to each kind of medication. Finally, because our data was collected solely from the patient's file, we were unable to measure compliance or discover the reasons why women did not continue treatment. As a result, it may not accurately reflect the actual data. Nonetheless, our findings may help gynaecologists and women with EH to make decisions about different types of medical treatment.

CONCLUSION

To date, there is still inconclusive optimal choice of conservative therapy in treating EH. Following this study, we able to conclude that LNG-IUS is most acceptable choice among women as treatment of EH. It has good outcome, widely available, easy to administer, less side effects and less likely to have poor compliance. Therefore, LNG-IUS can be recommended as first line treatment. Nevertheless, a proper case selection with comprehensive counselling with long term follow up is paramount to ensure a complete resolution of EH can be achieved with minimal side effects.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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