ORIGINAL ARTICLE

Levonorgestril Intrauterine System (LNG-IUS) Versus Medroxyprogesterone Acetate for the Treatment of Endometrial Hyperplasia: A Randomized Control Trial

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ABSTRACT

Aim: To compare the effectiveness of Levonorgestrel Intrauterine Device with Injectable Medroxyprogesterone in treating Endometrial Hyperplasia.
Study Design: Randomized Control Trial
Settings: Obstetrics & Gynecology Department, Lady Willingdon Hospital, Lahore.
Duration of the study: Six months, from 09-08-2016 to 08-02-2017.
Sample size: A total of 140 subjects taken by non-probability consecutive sampling technique, were divided into group A&B by lottery, with 70 patients in each group.
Selection Criteria: Women > 35 years, diagnosed with endometrial hyperplasia (endometrial. thickness>7mm on transvaginal ultrasound and were confirmed on histopathology of endometrial specimen obtained by D&N
Data analysis: Collected information was entered in SPSS Version 21and results obtained.
Results: Average age of patients was 55.91±11.16 years. The mean duration of diagnosis of EH was 2.94± 1.42 months. The effectiveness achieved in 121(86.43%) patients. After the statistical analysis, the groups under study showed significant difference i.e. p-value=0.026. **Conclusion:** It has been proved in our study that the LNG-IUD is significantly more effective and reliable as compared to Inj. Medroxyprogesterone in the management of EH.
Keywords: Endometrial Hyperplasia,LNG-IUD, Medroxyprogesterone

INTRODUCTION

An excessive proliferation of the endometrium is called Endometrial Hyperplasia (EH).Biologic and Morphologic changes in the endometrium due to the prolonged estrogen stimulation in the absence of progestin influence is Endometrial hyperplasia[1]. Endometrial hyperplasia is caused most often by use of unopposed estrogen for Estrogen Replacement Therapy and tamoxifen for the treatment of breast cancer[2]. EH is a precancerous lesion,[3] and a common diagnosis (5-10%) in women presenting with abnormal uterine bleeding[4]. 30% of patients can progress to cancer if left untreated[3,4]. The goals of treating women with EH include not only relieving the symptoms of abnormal uterine bleeding but also preventing progression to carcinoma[1,5]. Hysterectomy has been generally recommended for the treatment of EH except when the women have strong desire for fertility or have serious surgical risk factors.[1]Progestogens, can prevent cancer progression and induce endometrial regression[4,6]. The reason behind is that it antagonize the estrogen effect on the endometrium.The progestational agents used to treat EH are injectable and oral progestogens (medroxyprogesterone 17- acetate). More recently, the levonorgestrel-releasing intrauterine system (LNG-IUS; Mirena) developed primarily as a contraceptive device, has also been used successfully to treat EH[4]. It is reported that LNG-IUS has higher efficacy and lower side effects[6]. Moreover, it optimizes patient compliance and is significantly superior in treatment of EH[7].

With LNG-IUD, the effectiveness, in terms of complete regression of hyperplasia was achieved in 89.3% while 70.4% patients with medroxyprogesterone in a trial. The difference was reported to be insignificant (p>0.05)[8,9]. But in another trial, The difference was reported to be significant and LNG-IUD was more effective than medroxyprogesterone (p=0.001)[10]. Purpose of this study is to make a comparison between the effectiveness of Levonorgesterol intrauterine device vs injectable medroxyprogesterone in treating EH. In routine, both methods are adopted to manage EH, but the available evidence contains controversy. So, we want to conduct this study to find more appropriate methods to develop a proper protocol. Moreover, local evidence is missing. So, to attain the local evidence and to implement the more effective method, we want to conduct this study. The results obtained from this study will be helpful in our population in preventing progression of EH by having more safe and effective therapy.

MATERIAL & METHODS

Obstetrics & Gynecology outdoor, Lady Willington Hospital was chosen to carry out this controlled trial for 6 months i.e. from 09-08-2016 to 08-02-2017.A total of 140 patients satisfying the criteria's were recruited in study, after taking informed consent. Non-probability consecutive sampling technique was used. Women > 35 years, diagnosed with endometrial hyperplasia were included. The women taking progesterone by any other route (Oral, Pessaries), having hypertension (BP≥140/90mmHg), diabetes (BSR>186mg/dl), endometrial carcinoma or other intrauterine pathologies (on medical record) and having an allergy to progesterone agents were excluded from the study. Written consent was taken. Details of eligible women such as name, age, BMI, marital status, parity were also noted on proforma. Out of 140 two groups were made using lottery method. Group A, women were treated by

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14µg/day LNG-IUD and in group B, women were treated by 150mg/ml Injectable Medroxyprogesterone. Then females were followed-up in OPD for 3 months (3 cycles). After 3 months, females underwent ultrasonography to check the response of treatment. Thickness of the endometrium was measured by transvaginal ultrasonography (TVU). If thickness <5mm and secretory, proliferative, inactive or atrophic pattern endometrium, then effectiveness of treatment was labeled. Collected information was entered in SPSS Version 21. Mean standard Deviation was calculated for quantitative variables like duration, age& BMI. Frequency and percentage was used to present qualitative variables i.e. parity, marital status and effectiveness. Chi-squared test was used for the comparison of effectiveness of both groups. P value less than or equal to 0.05 was assumed to be statistically substantial. Data was organized for parity, marital status, age, BMI & diagnosis duration of EH. After organizing the date the Chi-square test is applied for the comparison of effectiveness and samples having p value less than or equal to 0.05 are considered significant.

RESULTS

Total of 140 cases were included in this study. Mean age was 55.9±11.1 with maximum of 75 and minimum of 37 years. Results showed that mean value of age in Group A patients was 55.67±11.18 years and its mean value in group B was 56.14±11.21 years. In this study 29(20.71%) patients were with parity one, 24(17.14%) patients were with parity two, 30(21.43%) patients appeared with parity three, 28(20%) patients appeared with parity four and the 29(20.71%) patients appeared with parity five. In our study the mean value of BMI was 24.84±2.96 kg/m^2 with minimum and maximum BMI values of 20.20 & 29.97 kg/m^2 respectively. Results showed that mean value of BMI in patients of group A was 24.67±3.02 kg/m^2 and its mean value in group B patients was 25.01±2.91 kg/m^2. Results showed that mean value of diagnosis duration of EH was 2.94± 1.42 months with minimum and maximum values of 1 & 5 months respectively. In this study the mean value of duration of diagnosis in group A patients was 3.01±1.48 months and its mean value in group B patients was 2.86±1.36 months.

In this study the effectiveness achieved in 121(86.43%) patients and it was not achieved in 19(13.57%) patients.

The results of effectiveness from both groups showed that effectiveness is achieved in 121 cases from both groups combined and 65 and 56 from each group A and B respectively. Likewise, 19 cases were there in which effectiveness is not achieved 5 from A and 9 from B. With reference to effectiveness statistically significant difference is present between the groups i.e. p value=0.026 (Table 1).

Results showed that 47 patients from patients those who are equal or less than 50 achieved the effectiveness, 24 from A and 23 from B. Likewise for a group of above 50 effectiveness is achieved in 74 and 41 from A and 33 from B. Effectiveness statistically difference is more in group of above 50 i.e. p value = 0.024 (Table 2).

Study was carried out with single and multiple parity and results showed that in single parity group effectiveness is achieved in 21 cases, 15 from A and 6 from B. Likewise, in multiple parity group effectiveness is achieved in 100 cases 50, 50 from each group. Analyzing statistically it showed that there is insignificant difference between the groups i.e. p-value=0.197 & 0.058 respectively (Table 3).

Study was carried out for the Normal and Obese BMI. The results shows that the in Obese BMI group effectiveness achieved in 53 case with 31 from A and 22 from B. Likewise in normal BNI group effectiveness achieved in 68 case with 34 of each group. Analyzing the results statistically shows that there is significant difference between study groups with obese BMI i.e. p value=0.041 (Table 4).

Study was carried out for diagnosis duration less than 3 months and more than 3 months. The results showed that for less than 3 months group effectiveness is achieved in 75 cases with 39 from A and 36 from B. Likewise, for group with more than 3 months diagnosis duration, the effectiveness is achieved in 46 case with 26 from A and 20 from B. Analyzing the results statistically, there is insignificant difference between the study groups i.e. p value=0.120 & 0.234 respectively (Table 5).

Fig. Frequency distribution of effectiveness

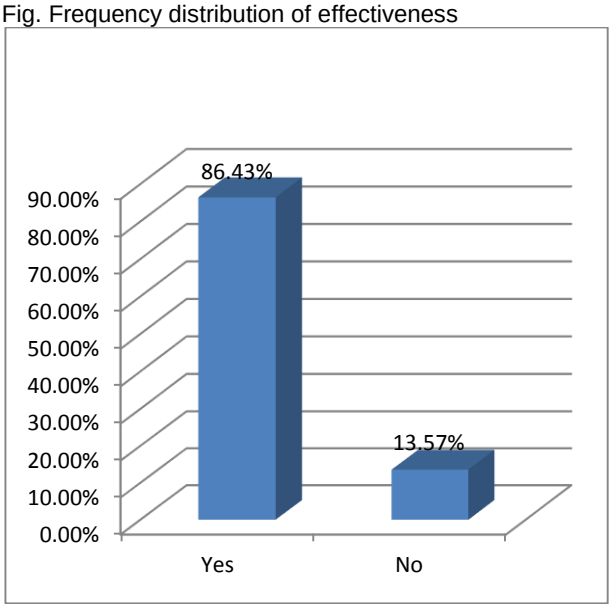

Table 1: Comparison of effectiveness with study groups

Effectiveness	Group A	Group B	Total
Yes	65	56	121
No	5	14	19
Total	70	70	140

Chi value=4.93 p-value=0.026 (Significant)

Table 2: Comparison of effectiveness with study groups stratified by age

Effectiveness	Group A	Group B	Total
Age ≤50 years			
Yes	24	23	**47**
Age >50 years			
Yes	41	33	**74**
No	5	14	**19**

P value=0.024

Table 3: Comparison of effectiveness with study groups stratified by parity

Effectiveness	Group A	Group B	Total
Parity Single P value=0.197NS			
Yes	15	6	**21**
No	3	5	**8**
Multiple parity P value=0.058 NS			
Yes		50	**100**
No	2	9	**11**

Table 4: Comparison of effectiveness with study groups stratified by BMI

Effectiveness	Group A	Group B	Total
Normal BMI P value 0.615 NS			
Yes	34	34	**68**
No	1	3	**4**
Overweight & obese P value 0.041			
Yes	31	22	**53**
No	4	11	**15**

Table 5 Comparison of effectiveness with study groups stratified by duration of diagnosis

Effectiveness	Group A	Group B	Total
Duration of diagnosis ≤3 P value=0.120 NS			
Yes	39	36	75
No	3	9	12
Duration of diagnosis >3 P value=0.234 NS			
Yes	26	20	**46**
No	2	5	**7**

DISCUSSION

Endometrial Hyperplasia, the most common pathological condition of the female genital tract can progress to adenocarcinoma[11,12]. During reproductive years, the risk of EH is increased by conditions associated with intermittent or absent ovulation, in particular, polycystic ovary syndrome (PCOS)[13].

According to our study results the effectiveness achieved in 121(86.43%) patients in whom 65 cases were from LNG-IUD group and 56 were from Inj. Medroxyprogesterone group. In our study LNG-IUD group showed significantly more effective results as compared to Inj. Medroxyprogesterone group patients. i. e p-value=0.026. Some of the studies are discussed below showing the results in favor of our study as. Fariba Behnamfar et al reported that the response rate in patients in the LNG group was 89.3% (25 of 28 patients), versus 70.4% (19 of 27 patients) in patients in the medroxyprogesterone group. The use of LNG for treating EH for 3 months was associated with high-treatment response rate and the low proportion of patients with progression compared to the use of medroxyprogesterone[14]. Another trial showed that effectiveness was obtained for 96% women in the LNG-IUS group (n=50) and for 80% of women in medroxyprogesterone group (n = 50).The difference was reported to be significant and LNG-IUD was more effective than medroxyprogesterone (p=0.001)[10]. Seo Yeong Lee et al described in his study that the LNG-IUS appears to be as highly effective in treating Korean women with EH[15]. One more study by Hend S. Saleh et al concluded that in management of EH without atypia, LNG-IUS achieves higher regression rates and lower hysterectomy rates than oral Progesterone and could be the first-line therapy[16]. Several clinical studies have demonstrated during the last decades that in the treatment of EH the LNG-IUS have been a safe and effective therapy with complete response, and also it is shown to represent a sufficient alternative to hysterectomy[17,18].

In a study by Ismail et al. LNG-IUS and medroxyprogesterone (10 mg daily) were compared in 60 patients and authors reported that the rate of resolution in the LNG-IUS group was 66.67% and in the medroxyprogesterone group was 36.66%[18].

One study by David F. Archer et al [19] showed that after 6 months, women in the LNG-IUS arm had a 100% response rate, compared with 96% for the continuous medroxyprogesterone acetate group and 69% for cyclic medroxyprogesterone acetate.

On the other hand, one randomized trial showed that with LNG-IUD, the effectiveness (in terms of complete reduction in hyperplasia) was achieved in 89.3% females (n=28) while in 70.4% patients with medroxyprogesterone (n=27). The difference was reported to be insignificant but LNG-IUD was more effective than medroxyprogesterone (p=0.11)[3]. Another trial also showed that effectiveness was obtained for all women (100%) in the LNG-IUS group (n = 53) and for 96% of women in medroxyprogesterone group (n = 48).The difference was reported to be insignificant (p>0.05)[9].

CONCLUSION

It has been proved in our study that the LNG-IUD group showed significantly more effective and reliable results as compared to Inj. Medroxyprogesterone group in management of EH.

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