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Research Article

The Reproducibility of Treatment of Perimenopausal Abnormal Uterine Bleeding Due to Ovulatory Dysfunction with Hysteroscopic Endometrial Resection versus Mirena

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Abstract:

Objective: To compare the efficacy of local levonorgestrel intrauterine releasing system and transcervical resection of the endometrium (TCER) in the management of perimenopausal dysfunctional uterine bleeding.

Patients and Methods: This study was done at Ain Shams and Al-Azhar University Maternity Hospitals during a period started from January 2019 to January 2021. Patients were followed up at the outpatient gynaecology clinics at regular schedules (3, 6 and 12 months) for one year duration. Perimenopausal patients with DUB were assigned randomly to either the levonorgestrel intrauterine system (n = 35) or endometrial resection (n = 45). Blood loss assessment charts were used to measure menstrual blood loss.

Results: Total bleeding score/month decreased from a baseline median of 47.26 to 33.5 (P<0.01) for the levonorgestrel intrauterine system and from 47.13 to 33.9 (P<0.01) for transcervical resection of the endometrium. There was no statically difference in bleeding score before and during treatment between the two groups of women.

Conclusion: Both treatments levonorgestrel intrauterine system and transcervical resection of the endometrium efficiently reduced menstrual bleeding. levonorgestrel intrauterine system should be considered the first-line treatment for idiopathic menorrhagia because it is easy to insert, has a sustained effect, provides contraception, may reduce the need for surgery, and is cost-effective and well tolerated.

Key Words: levonorgestrel; menorrhagia; endometrium

Introduction:

Menorrhagia is the commonest cause of iron deficiency anemia in premenopausal women.[1] Anemia is one of the most widespread and neglected nutritional deficiencies in the world today, predisposing women to ill health and disease.[2] Menorrhagia is estimated to occur in 30% of women in their childbearing years. By definition, diagnosis of menorrhagia is made when the duration of bleeding is equal to or greater than six days or blood loss is at least 80 ml and other pathological conditions have been excluded. However, many women seek consultation for even milder bleeding episodes, due to the associated stress, discomfort, and quality of life impairment, thus making menorrhagia one of the most frequent reasons for gynaecological consultation [3-5].

Traditional medical treatment for menorrhagia has been only temporarily effective, if at all, and most patients refuse to be subjected to prolonged administration of medications. Surgical treatment, including hysterectomy and endometrial ablation, is not suitable for women wishing to preserve fertility. Though successful pregnancies have been reported after endometrial ablation, this procedure is generally not recommended for women wishing to retain the option of future pregnancy [3-5].

The levonorgestrel-releasing intrauterine system (LNG-IUS) has emerged in recent years as a valuable alternative to classical medical and surgical methods of menorrhagia treatment. The system consists of a 32-mm T-shaped polyethylene frame with a reservoir containing 52 mg of Levonorgestrel (LNG), covered by a silicone membrane.6 After insertion, the initial release of LNG into the uterine cavity is 20µg/d and a stable plasma concentration of 150-200 pg./ml is achieved after the first few weeks.6 The plasma concentration of LNG in patients using the LNG-IUS is less than 25% of that seen with 150 µg of oral LNG.6 By slowly releasing the progestin LNG into the uterine cavity, the LNG-IUS suppresses endometrial growth, causing atrophy of the endometrial glands, decidualisation of the stroma, thickening of the cervical mucous, and desensitisation of the endometrium to estrogen, which all lead to

excellent control of menorrhagia, providing in parallel a highly satisfactory contraceptive action.7 In the present study, the efficacy of the LNG-IUS LNG-IUS for menorrhagia control is compared to thermal endometrial ablation.

Patients and methods:

This study was carried out at Ain Shams and Al-Azhar University Maternity Hospitals during a period started from January 2019 to January 2021. It included 60 patients all had failed medical treatment (in the form of antiprostaglandins, hemostatics and progestins) for DUB for at least 6 months. All patients had at least one D&C which revealed no malignant changes but failed to improve the condition. So, the patients were good candidates for hysterectomy.

Inclusion criteria:

- Perimenopausal patients at the age of 40 -50 years
- The main complaint is dysfunctional uterine bleeding with no bleeding tendency.
- The patients completed their families & refusing hysterectomy
- Uterine enlargement ≤ 12 weeks size and the uterine cavity ≤ 12 cm, no uterine malformations
- No endometrial malignancy
- Normal adenexa

Exclusion Criteria:

- Patients not fulfilling the inclusion criteria
- Patients who were breast feeding or uncertain about a future wish for children.
- Congenital uterine anomalies, pelvic inflammatory disease and unstable general condition due to acute bleeding disorders.
- Serious illnesses including thrombophlebitis, thromboembolic disorders and blood diseases.

All patients were submitted to:

- Careful history taking, general, abdominal and pelvic examination
- Assessment of menstrual blood
- Routine laboratory studies as hemoglobin, hematocrit values, serum iron level, fasting blood level, liver and renal function tests and coagulation profile
- Chest X ray and ECG
- Premenstrual pelvic sonographic assessment for:
  - ❖ Uterine size and dimensions
  - ❖ Endometrial thickness
  - ❖ Presence of foci of adenomyosis or fibroids
  - ❖ Ovarian size, texture and the presence of follicles
- Assessment of menstrual blood loss

For proper evaluation of the patient complain and results of the treatment a numerical expression of subjective estimate of the menstrual blood loss was needed [7]

- Score 0: no bleeding
- Score 1: spotting- 1 pad/day
- Score 2: mild bleeding- 2 pads/day
- Score 3: moderate bleeding- 3-4 pads/day
- Score 4: severe bleeding- 5-6 pads/day

The total bleeding score per month was calculated for each patient before and after 3-, 6- and 12-months use of Mirena or endometrial resection.

Results

There was no statistically significant difference between the two groups as regards the demographic characteristics of the patients under the study as shown in table 1.

Tables of the study

Variable	Mirena group (n = 35)	TCER group (n = 45)	t- value	P- value
Age (years)	**42.1 ± 2.1**	**41.8 ± 1.2**	**0.8**	**0.43**
Body mass index	**28.3 ± 1.4**	**28.1 ± 1.23**	**0.68**	**0.5**
Parity	**4.8 ± 1.1**	**3.9 ± 4.2**	**1.23**	**0.22**
Values are expressed as means ± standard deviation or number and percentage. No significant difference between the two groups in all variables (P value > 0.05)				

Table (1): *shows the demographic characteristics of the patients under the study*

The clinical characteristics of the two groups were compared with no significant difference as regard duration of menses and symptoms, endometrial thickness by transvaginal ultrasound, bleedind score/month, hemoglobin and hematocrit value as shown in table 2.

Variable	Mirena group (n = 35)	TCER group (n = 45)	t- value	P- value
Menses (days)	8.1 ± 1.43	8.4 ± 1.12	1.05	0.3
Duration of symptoms (months)	10.1 ± 1.4	9.81 ± 1.23	0.98	0.33
Endometrial thickness (mm)	9.8 ± 3.1	10.1 ± 1.2	0.595	0.55
Bleeding score/month	47.26 ± 0.48	47.13 ± 0.21	1.6	0.11
Hemoglobin (g/dl)	8.13 ± 0.19	8.1 ± 0.14	0.8	0.42

Hematocrit (%)	32.66 ± 0.18	32.64 ± 0.13	0.58	0.56
Values are expressed as means ± standard deviation or number and percentage. No significant difference between the two groups in all variables (P value > 0.05)				

Table (2): *shows the clinical characteristics of the patients under the study.*

Table 3 & 4 compare the posttreatment data of the two groups. Both treatment modalities have a highly significant positive impact on patient's hematological profile (Hb, serum iron levels and HCT value) where hemoglobin level increased in LNG-IUS from mean baseline value of 8. 13 gm/dl to 11.1 gm/dl at the end of the study (p<.05) while in the resection group increased from baseline of 8.1 gm/dl to 11.3 gm/dl (p <0.05) at the end of the study, the same positive effects was observed in other hematological parameters.

variable	Bleeding score	Hemoglobin (g/dl)	Hematocrit value (%)	Endometrial thickness
Before treatment in LNG group	47.26 ± 0.48	8.13 ± 0.19	32.66 ± 0.18	9.8 ± 3.1
After 12 month in LNG group	33.5 ± 6.2	11.1 ± 1.5	35.9 ± 1.2	5.3 ± 1.4
t- value	13.1	11.6	15.8	5.8
p- value	There are highly significant differences between the two groups (P < 0.01)			
before treatment in TCER group	47.13 ± 0.21	8.1 ± 0.14	32.64 ± 0.13	10.1 ± 1.2
After 12 months in TCER group	33.9 ± 4.5	11.3 ± 1.2	36.6 ± 3.1	4.94 ± 1.5
t- value	19.7	17.8	8.6	18.01
p- value	There are highly significant differences between the two groups (P < 0.01)			

Table (3) : *shows the effect of treatment on bleeding score & hematological profile*

variable	Mirena group (n = 35)	TCER group (n = 45)	t- value	P- value
Bleeding score/month				
After 3 months	24.8 ± 3.1	23.9 ± 4.2	1.062	0.29
After 6 month	26.8 ± 4.5	27.2 ± 3.2	0.46	0.64
After 12 months	33.5 ± 6.2	33.9 ± 4.5	0.33	0.74
Hemoglobin (g/dl)				
After 3 months	9.9 ± 1.2	9.4 ± 1.3	1.76	0.08
After 6 months	10.9 ± 1.02	10.6 ± 2.2	0.75	0.455
After 12 months	11.1 ± 1.5	11.3 ± 1.2	0.66	0.511
Hematocrit (%)				
After 3 months	34.1 ± 2.2	33.9 ± 3.2	0.316	0.75
After 6 months	35.2 ± 3.1	36.1 ± 1.5	1.7	0.09
After 12 months	35.9 ± 1.2	36.6 ± 3.1	1.26	0.211
Endometrial thickness	5.3 ± 1.4	4.94 ± 1.5	1.1	0.27
Values are expressed as means ± standard deviation or number and percentage. No significant difference between the two groups in all variables (P value > 0.05)				

Table (4) : *shows the comparison between both lines of treatment on bleeding score & hematological profile*

Discussion

Oral medical treatments have been shown to provide partial relief of menorrhagia. Despite an average decrease in menstrual blood loss of up to 50%, many women remain menorrhagic when treated with tranexamic acid, mefenamic acid, flurbiprofen, norethisterone acetate, and ethamsy late [8]. The effectiveness of the levonorgestrel intrauterine system up to 1 year has been shown previously13 and, in a noncomparative study, up to 3 years9. Menstrual blood losses of less than 80 mL per cycle at one year were consistently achieved by 91.5% of women in these studies9.

Further, Rauramo et al., Clegg et al. and Gupta et al. [10,11,12] demonstrated that the levonorgestrel intrauterine system and transcervical resection of endometrium were comparable regard to efficacy, amenorrhea rate, and satisfaction in a 12-month comparative study. We showed that both the levonorgestrel intrauterine system and transcervical resection of endometrium substantially reduced menstrual blood loss during the first year of use where the total bleeding score dropped from mean baseline value of 47.26 to 33.5 and from 47.13 to 33.9 in the LNG-IUS and in the resection group respectively. This result is statistically

highly significant (P<0.01). There was no statically difference in bleeding score before and during treatment between the two groups of women. The effect of the levonorgestrel intrauterine system on menstrual bleeding is produced predominantly by local suppression of the endometrial epithelium. This endometrial effect has been shown to persist over the course of 5 years in women who were in their fertile years.8 Therefore; a long therapeutic effect of the levonorgestrel intrauterine system was expected.

In contrast, other investigators reported that endometrial resection is superior to LNG-IUS in reduction the amount of menstrual blood loss, Irvine et al. [13] reported that the mean reduction in MBL was not significantly different from that achieved with high dose norethisterone at 3 months (P 0.56). While Crosignani et al. [14] reported that the mean MBL of 79% with LNG IUS at 6 months was less than that achieved with endometrial resection 89% (P=0.015). Furtherly, Kittelsen and Istre15 reported a mean MBL reduction of 90% with LNG TUS at one year, compared with 98% MBL reduction for endometrial resection.

As regard to suppression of endometrial growth, it was found that the endometrial thickness measured by transvaginal ultrasonic examination decreased significantly 12 months after insertion of the device (P<0.01). This is in accordance with several studies which found that LNG IUS can cause endometrial atrophy by suppressing endometrial growth and this takes about three cycles after insertion of the system [16,17]. Sturdee [18] reported a possible application for the LNG IUS in cases of endometrial hyperplasia, hormonal replacement therapy to protect the endometrium and in combination with tamoxifen for treatment of breast cancer.

Also, in this study found that both treatment modalities have a highly significant positive impact on patient's hematological profile (Hb, serum iron levels and HCT value) where hemoglobin level increased in LNG-IUS from mean baseline value of 8. 13 gm/dl to 11.1 gm/dl at the end of the study (p<.05) while in the resection group increased from baseline of 8.1 gm/dl to 11.3 gm/dl (p <0.05) at the end of the study, the same positive effects was observed in other hematological parameters. The increase in hematological profile corresponds to the decrease in the bleeding patterns (TBS/M). The increase in hemoglobin concentration and other hematological profile was reported by many authors [12,19,20].

The need for further surgical treatment was higher in the TCER group than LGN-IUS group; however, it was of non-significant importance as five of the LNG-IUS users (14.2%) subsequently underwent surgery following 12 months of their treatment, three of these patients (8.6%) underwent hysterectomy and two patients (5.7%) had endometrial resection. Three patients (8.6%) refused further treatment. In TCER group ten patients (22.2%) required further treatment, four patients (8.9%) underwent hysterectomy within the study-reporting period and other six patients (13.3%) underwent surgery following 12 months of their treatment, two of these patients (4.4%) underwent hysterectomy and four patients (8.9%) had endometrial resection, while five patients (1.1%) refused further treatment. Our results are in accordance with that observed by **Fedele et al. [21]** who reported that three of the LNG-IUS users (2%) subsequently underwent surgery within the study-reporting period, following discontinuation of their treatment. Two of these patients underwent hysterectomy and it is not clear whether the third patient had hysterectomy or endometrial resection**. Molnár [22]** ***reported*** that in TCER group 35.7% of women had repeated surgery for failed endometrial resection, 20.4% of women required dilatation and curettage, while 15.3% underwent hysterectomy, he reported that the chance of avoiding hysterectomy reached plateau after 72 months. **Litta** [23] reported failure of TCER in 24.6% of women, half of this group underwent hysterectomy.

Conclusions

In the present study, Mirena and endometrial resection were both highly effective in reducing menstrual blood loss at one year of follow up. There was no significant difference between the two groups in frequencies of different menstrual patterns and degree of patient satisfaction. Mirena requires minimal skill and can be applied everywhere with reproducible results, this is of particular importance for developing countries, where other treatment modalities are more costly, less effective, more invasive or inaccessible and for women who would prefer to preserve their reproductive potential. Furthermore, the need for hysterectomy after insertion of the Levonorgestrel-releasing intra-uterine device should diminish with time, whereas the contrary is true after endometrial resection. The side effects were significantly higher in the endometrial resection group. Most side effects encountered with wearing Levonorgestrel-releasing device can be managed conservatively with proper counseling, so that the problems can be tolerated and levonorgestrel-releasing intrauterine device represents a good alternative to transcervical endometrial resection.

Recommendation

On the basis of our data and the literature, strong evidence exists to suggest that the levonorgestrel intrauterine system should be considered the first-line treatment for idiopathic menorrhagia because it is easy to insert, has a sustained effect, provides contraception, may reduce the need for surgery, and is cost-effective and well tolerated.

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