LEVENORGESTREL INTRA UTRINE SYSTEM (LNG IUS) IN MENORRHAGIA: A THREE YEARS FOLLOWUP STUDY

Naeema Utman[1], Fouzia Faheem[2]

ABSTRACT

Objective: *To find the role of Levenorgestrel Intra uterine system (LNG IUS) in menorrhagia in women over period of three years.*

Methodology: *This descriptive study was conducted in private setup and Gynaecology A unit, Lady Reading Hospital, Peshawar over a period of three years i.e., June 2004 to June 2007. The study population consisted of 60 women. All these women presented with heavy menstrual flow, having no contraindication for the device and consenting to Levonorgestrel Intra Uterine System after counseling. Those having organic cause for menorrhagia were excluded. Women were followed up at 6 week, 6 month and 12 month.*

Results: *The mean age of the sample was 35.98±7.66 years. In the sample, multipara were 86.66%(n=52) and nulliparous were 13.33%(n=8); married were 91.66%(n=55) and unmarried were 8.33%(n=5). The indication for the device were menorrhagia in 75%(n=45) cases; women having intrauterine contraceptive device previously and currently having menorrhagia in 16.6%(n=10) cases; and others 8.33%(n=5) cases (women who are unfit for general anesthesia or having other co-morbidity i.e., asthma, uncontrolled diabetes). The acceptance rate was 80% (n=48) and discontinuation rate was 20%(n=12). In these 12 cases, expulsion of device, pelvic inflammatory disease and no improvement in the condition was seen in 10%(n=6), 3.3%(n=2) and 6.6%(n=4) respectively. At follow up 3.3%(n=8) women had irregular period while 73.3%(n=44) were amenrroheic and13.33%(n=8) women had regular period at the end of one year.*

Conclusion: *Levonorgestrel IUS is one of the effective treatment modality which can be used for menorrhagia with reasonable efficacy.*

Key words: *Levonorgestrel IUS, Abnormal Uterine Bleeding, Menorrhagia.*

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INTRODUCTION

Levonorgestrel releasing-intrauterine systems (LNG-IUS) were originally developed as a method of contraception in the mid 1970s. The only LNG-IUS approved for general public use is the LNG-IUS (mirena IUS), which releases 20mcg of levonorgestrel per day directly in to the uterine cavity. However, new lower dose (10 and 14mcg per day) and smaller sized LNG-IUS (MLS, Fibro Plant-LNG) are currently under clinical development and investigation. Research into the non-contraceptive uses of LNG-IUS is rapidly expanding. In UK, LNG-IUS is licensed for use in menorrhgia and to provide endometrial protection to perimenopausal and postmenopausal women on estrogen replacement therapy. There is limited evidence to suggest that LNG-IUS may also be beneficial in women with endometriosis, adenomyosis, fibroids, endometrial hyperplasia and early stage endometrial cancer (where the patient is deemed unfit for primary surgical therapy) [1, 2].

Menorrhagia is defined as regular heavy uterine blood loss (> 80ml) or excessive uterine bleeding with normal cycle length. Abnormal uterine bleeding is the most common reason for gynecological visit for both pre-menopause and post-menopausal bleeding. Up to 33% of women refer to gynaecology OPD having abnormal uterine bleeding and this proportion rises to 69% in peri or post menopausal age group. Conservative treatment for heavy menstrual flow has been disappointing and surgical alternative like endometrial ablation and endometrial resection

[1-2]Department of Obstetrics and Gynecology, Lady Reading Hospital, Peshawar - Pakistan

Address for Correspondence:
Dr. Naeema Utman
Associate Professor,
Department of Obstetrics and Gynecology,
Lady Reading Hospital, Peshawar - Pakistan
E-mail: naeemautman@yahoo.com

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have been developed now. However, the role of these surgical alternatives in the treatment of menorrhagia is currently unclear. One minimally invasive procedure for control of menorrhagia is the insertion of progestogen releasing intra uterine device[3, 4].

The data for use of the LNG IUS is especially compelling for management of menorrhagia. Multiple national and international studies substantiate the equivalence of an LNG IUS for achieving quality of life outcomes and improvements in hematological parameters as ablation. In Finland, out of those women waiting for hysterectomy indicated for menorrhagia, a significant proportion that received a Levonorgestrel intra uterine system cancelled their surgery[1, 2].

Women of all ages can use Levonorgestrel Intra Uterine System which is also safe in breast feeding mothers. There is no evidence that the efficacy is reduced when used with other medicine. It is indicated in women where estrogen is contraindicated. Before insertion screening for Chlamydia trachomatis and other sexually transmitted infection should be carried out[5-7].

Routine prophylactic antibiotic administration is not necessary in all cases. The present study was undertaken to assess the efficacy of Levonorgestrel Intra Uterine System in idiopathic menorrhagia.

METHODOLOGY

This descriptive study was conducted in gynaecology A unit Lady Reading Hospital, Peshawar and private clinic over a period of 3years (June 2004 - June 2007) including 60 women presented with heavy regular menstrual flow (menorrhagia). The device was inserted in patients under light sedation /analgesia. General anesthesia was used during fitting in unmarried women. Out of these five unmarried females, 3 were presented with Heavy menstrual flow with normal endometrial thickness on Ultrasound and 2 patients were presented with Heavy menstrual flow with normal endometrial histopathology.

he women were excluded from the study if they had fibroid assessed on ultrasound or clinically, a history of malignancy (diagnose by EUA or biopsy) clinical suspicious of malignancy, active liver disease, and adenexal tumor or cyst and pelvic inflammatory disease. Follow up was carried for a period of six weeks, six months and twelve months in woman having the device for manorrhgia while for other complication they were followed over a period of three years. Prophylactic antibiotic (single dose of Azethromycine/Metranidazole) were given to all patient except un-married.

RESULTS

During this study 60 women had the insertion of Levonorgestrel Intra Uterine System for heavy menstrual flow over a period of 3 years (June 2004 - June 2007). The mean age of the study sample was 35.98 $\pm$ 7.66 years. Majority of women [45 cases (75%)] were above 30 years of age while there were 15 cases (25%) below 30 year. Fifty five women (91.66%) were married while 5 (8.3%) women were single. Regarding parity 52 (86.66%) women were multipara. The women having the device primarily for menorrhagia were followed up at six weeks, 6 months and 12 months (Table 1). At 6 week 40 women (66.66%) had irregular period and at 12 month only 8 women (13.33%) had the complaint of irregular period, at 12 month 44 women (73.33%) were amenorrheic while 8 women (13.33%) had regular periods (Table 2). Complications were seen in 8(13.33%) women with expulsion of the device in 6(10%) patients (these women had severe intractable bleeding and

Table 1: Demographic Characteristics (n=60)

Age		
<30 years	15 cases	25%
>30 years	45	75%
Marital status		
Married	55	91.6%
Un married	05	8.3%
Parity		
Nulipara	8	13%
Multipara	52	86.6%

Table 2: Effect on menstrual flow total cases (n=60)

Time Period	6 weeks	6 months	12 months
Irregular period	40(66.6%)	20(33.33%)	8(16.6%)
Normal	15(25%)	15(24.5%)	8(15.09%)
Amenorrhea	05(8.3%)	25(41.66%)	44(73.33%)

Table 3: Acceptability total cases (n=60)

Acceptance of device	48	80%
Discontinuation	12	20%
Satisfaction	48	80%
Alternate end hysterectomy	18	30%

passage of clot with which they expel the device and they are ended up on hysterectomy). Infections were seen in 2(3.33%) cases. Satisfaction rate were 48(80%) women (at follow-up they have improved symptom of heavy menstrual flow; anemia and health related quality of life). The discontinuation of device in the three years was in 12(20%) women and the main reason was irregular period, pain, infection and expulsion of device. Eighteen (30%) women were ended up on hysterectomy (Table 3).

DISCUSSION

Our study provides further evidence of the effectiveness of the LNG-IUS in patients having menorrhagia. Levonorgestrel Intra Uterine System is available in more than fifty countries for over ten years. Approximately two million women have used Levonorgestrel Intra Uterine System for contraceptive purposes[8]. the endometrium undergoes structural and histological changes in response to Levonorgestrel Intra Uterine System. These changes are uniform through out the endometrial mucosa as for as the basal layer irrespective of the proximity of the device. Histopathological study shown a thinning of the endometrium, atrophy at glandular layer, decidualization of the endometrial stroma, capillary thrombosis and inflammatory cell infiltration with levonorgestel intrauterine system .These changes lead to low blood loss[9].

In December 2000 US food and drug administration approved Levonorgestrel Intra Uterine System manufactured and marketed by the name of Mirena IUS. With a few exceptions the mechanism of action, indication, precaution, side effect, complication and time of insertion are same as copper containing intra uterine contraceptive device (CU-T).

The expulsion rate with Levonorgestrel Intra Uterine System are little higher than CU-T. In our study 10% of women expelled the device. The main reason for expulsion was heavy menstrual flow. The ovarian cyst are three time more common with Levonorgestrel Intra Uterine System i.e. 1.2% compare to 0.4% of non user[10, 11].

A study conducted by WHO on 22000 women showed that the risk of Pelvic Inflammatory Disease was higher during the first twenty days. Thereafter, the risk of developing infections was not significantly higher than that among women using no contraceptive (<1.5 per 1000 women year). This risk can be reduced by proper screening of women and take measure for prevention at the time of insertion[12]. In our study the infection rate was 3.17%, diagnosed at first follow up visit.

Only two randomized trial have directly compared Levonorgestrel Intra Uterine System to other form of medical treatment. A study by Irvin et al, in which the efficacy and acceptability of the Levonorgestrel Intra Uterine System compared to the high dose of norethisterone 5mg three time daily from day 5th to 26th of the cycle for three cycle were observed[13]. Reduction of the blood loses by Levonorgestrel Intra Uterine System was 94% and with oral norethisterone 87% after three cycles. While 76% of the women wish to continue with Levonorgestrel Intra Uterine System compared to 22% in norethisterone group[13]. in our study the result are comparable to the above study though there was no control group.

Another study was conducted to compare the cost-effectiveness of most effective treatment modalities in menorrhagia, LNG-IUS and hysterectomy[14]. Overall, 236 women aged 35 to 49 years who were menstruating, had completed their family and were eligible for both treatments were

randomized to either receive a LNG-IUS or undergo hysterectomy. The follow-up visits took place six months and 12 months after the treatment, and again five and ten years after the randomization. The one-year follow-up data was published in Lancet and five-year data in JAMA. After 5 years of follow-up the groups did not differ substantially in terms of health related quality of life or psychosocial well-being (anxiety, depression and sexual function). Although 42% of women assigned to the LNG-IUS group subsequently underwent hysterectomy, the overall direct and indirect costs after 5 years were still approximately 40% lower in the LNG-IUS group. After 10 years of follow-up, 221 women (94%) were analyzed for the primary outcomes. The preliminary results analyzed by intention to treat.

The preliminary 10-year results of Vuokko study show that LNG-IUS is a good alternative option to hysterectomy in the treatment of menorrhagia. Although half of the women assigned to the LNG-IUS group eventually underwent hysterectomy, the costs remain significantly lower than in hysterectomy group[13, 14].

The absolute risk of ectopic pregnancy is extremely low with Levonorgestrel Intra Uterine System, being the lowest of any intrauterine methods for contraception. A study by Andersson et al, the rate of ectopic pregnancy was 0.02 per 100 women year compared to other methods i.e., 0.25 per 100 women year and in sexually active women not using any contraceptive which was 1.2-1.6 per 100 women years[15,16]. In the study, no ectopic pregnancy over a three year period of follow up was seen.

Most hysterectomies are performed for benign condition usually for intractable menorrhagia and pain where medical therapy failed. For a while there was optimization that the hysterectomy rate could be dramatically reduced by resection or ablation of endometrium but enthusiasm waned when it was realized that the procedure was not without its complications[17]. Now the trend is more towards the Levonorgestrel Intra Uterine System because it definitely reduces bleeding and also number of hysterectomies[18, 19]. In the study the hysterectomy rate was 33.96% and these were the women who had heavy flow even after insertion of the device. The effect of Levonorgestrel Intra Uterine System on ovarian function is minimal in suppression of ovarian function. As Levonorgestrel Intra Uterine System release only 20 mcg per 24 hours so the serum level of progestin is very low and the suppression rate for ovarian function (50 mcg/24 hours) is not achieved. The patient satisfaction with hysterectomy remains high as the definitive cure for menorrhagia but. Considerable morbidity and occasion mortality may occur. Substantial costs are increased due to convalescence in both hospital and at home. Hurskainen et al conducted a trial on quality of life and cost effectiveness of levonorgestrel intrauterine system versus hysterectomy for treatment of menorrhagia in 236 women. After 12 month, 20% of women in the LNGIUS group underwent hysterectomy and 68 % continued to use the system while 69% experience amenorrhea or minimal bleeding[19]. In our study the results are comparable but the number of patient were small .The main reason was the cost of device and ambiguity about its role in the treatment of menorrhagia which was cover to some extent by counseling of women.

CONCLUSION

LNG-IUS is an effective treatment for menorrhagia due to benign cause and could be an alternative to hysterectomy. LNG-IUS is a reasonably good and safe treatment. Further randomized control trail are needed to confirm the reliability, efficiency and cost effectiveness. It provide a wide spectrum of benefit beyond their contraceptive capabilities Side effect can be reduced by careful pre insertion counseling and insertion difficulty can be minimized by a skill person who are trained in fitting the device.

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None Declared

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CONTRIBUTORS

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