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The outcome of levonorgestrel intrauterine device in the management of abnormal uterine bleeding -a Prospective observational study.

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1. INTRODUCTION

Abnormal uterine bleeding (AUB) affects up to 30% of women at any point in their life(1). It affects women's physical social andpsychological aspects of life. A wide variety of medications, hormonal and non-hormonal are available for the treatment of abnormal uterine bleeding. LNG IUS(Mirena) was approved for use in abnormal uterine bleeding by US food and drug administration since 2009(2). The device is a polyethylene T frame with a drug reservoir which releases levonorgestrel at 20 micrograms/ day for the intial 5 years. The local release of Progesterone causes suppression of the endometrial gland and decidualisation of the stroma thus bringing a significant reduction in the mean menstrual blood loss(3). There is a local foreign body reaction characterised by increase in neutrophils, lymphocytes plasma cells and macrophages. These histological changes are established by 3 months after insertion.(4)

Mirena being a safer and cost effective treatment option for heavy menstrual bleeding, is often opted by both patient and the gynaecologist. Desire for preserving fertility and the severe high risk comorbid conditions also make mirena the preferred treatment option among patients(5). Mirena can be inserted as an OP procedure, a less invasive procedure and is marketed for use for 5 years. All women opting for mirena must have a bimanual pelvic examination, papsmear and ultrasonography. Any contraindications for mirena insertion is screened. Endometrial sampling is done prior to insertion to screen for atypia.

Despite providing contraception, Mirena is also effective in alleviating dysmenorrhea associated with even endometriosis(6) . Mirena due to its local progestagenic action protects the endometrium from estrogen induced hyperplasia.(7)

Mirena is contraindicated in the following conditions

1. Pregnancy or suspicion of pregnancy.
2. Acute Pelvic inflammatory disease
3. Known or suspected uterine or cervical neoplasia or unresolved, abnormal Pap smear.
4. Genital bleeding of unknown etiology.
5. Postpartum endometritis or infected abortion in the past 3 months.
6. Known or suspected carcinomas of breast
7. Untreated acute cervicitis or vaginitis, including bacterial vaginosis or other lower genital tract infections until infection is controlled.
8. Acute liver disease / benign or malignant lesions in the liver
9. A previously inserted IUD that has not been removed.
10. Hypersensitivity to any of its components.

METHODS

This prospective observational study was undertaken at SAT Hospital, Trivandrum for a period of one year after obtaining Institutional Ethical Committee clearance.

Inclusion Criteria : All women with abnormal uterine bleeding attending SAT gynaec opd treated with LNG IUD who are willing to give consent and ready for follow up over a period of 1 year. Study subjects included

- Fibroids of size < 3 cm
- Adenomyosis
- Ovulatory dysfunction
- Endometrial sampling histopathology report as endometrial hyperplasia without atypia.

- Exclusion criteria
  - Patient not willing for follow up after mirena insertion

All women attending SAT OPD treated with LNG IUS were given structured questionnaire and details regarding average days of bleeding, total pad usage and the cycle length at the time of mirena insertion were collected. Their USS report and HPR report were noted and patients were assigned to each AUB Class as per FIGO PALM COEIN. These patients were followed up at 6 months and 1 year and their pattern of bleeding in terms of length of menstrual blood loss, average pad usage and cycle length assessed. Their Hb report was noted. USS at 1 year was taken and their endometrial thickness noted. Percentage decrease in mean duration of menstrual blood loss, average pad usage and rise in Hb at 6 months and 1 year was taken

Outcome variables

AT 6 MONTHS

1. Continuation, expulsion and removal rate of mirena
2. Reasons for mirena removal
3. Percentage reduction in the average days of bleeding from the date of insertion to 6 months post insertion
4. Percentage reduction in mean pad usage from the date of mirena insertion to 6 months post insertion
5. Percentage of patients amenorrheic at 6 months post insertion
6. Mean rise in hb from the date of insertion ot 6 months post insertion
7. Percentage of study population amenorrhoeic at the end of 6 months

AT 1 YEAR

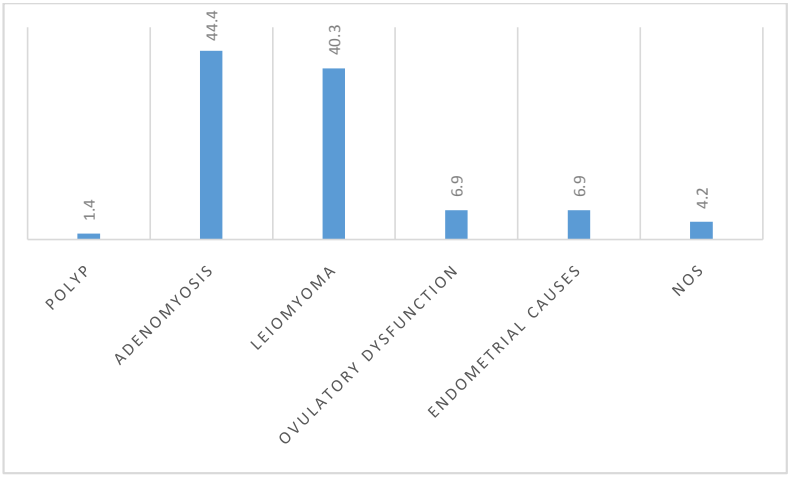
1. Continuation, removal and expulsion rate of mirena
2. Reasons for mirena removal
3. Percentage reduction in the average days of bleeding from the date of mirena insertion to 1 year post insertion
4. Percentage reduction in mean pad usage from the date of insertion to 1 year post mirena insertion
5. Mean rise in hb from the date of mirena insertion to 1 year postinsertion
6. Percentage of study population amenorrheic at the end of 1 year

7. Mean decrease in endometrial thickness in uss at the time of mirena insertion to 1 year post insertion

RESULT

The mean age of study participants was 40 years. Majority of patients, 47. 2% of the cases were between 35 to 40 years while only 8.3 percent of the study population was more than 45 years of age. From the total study population,44.4 % of the patients treated with mirena had adenomyosis, 40.3 % had leiomyoma and endometrial and ovulatory causes were seen in 6.9 % .

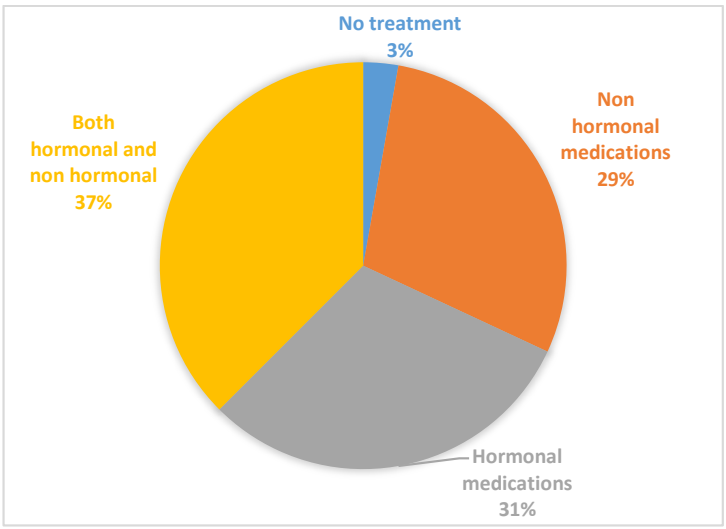
DIAGRAM 1: AUB CLASS OF THE STUDY POPULATION



Only 2 of the 72 patients opted for mirena as their first line treatment option. Rest 97.2 % of patients had some form of treatment taken prior to mirena insertion. Non hormonal pills (tranexamic acid and NSAIDS) were taken by 29.2% while hormonal medications (OCP, MPA, Leuprolide injection) alone was taken by 30.6% and both hormonal and non-hormonal pills were taken by 37.5 % of population.

Comment [A1]:

DIAGRAM 2: TREATMENT MODALITIES ADOPTED BY PATIENTS PRIOR TO MIRENA INSERTION



At the time of Mirena insertion average duration of menstrual flow in the study population was 11.3 days and average pad usage per month was 32.71 pads. 67 percentage of the study population had Hb less than 7 g % and 10 % had Hb between 7 and 10 g%.

At 6 months

Of the total 72 cases, 5 women removed IUCD while 2 mirena was expelled, Expulsion rate at 6 months- 2.8% and removal/discontinuation rate was 6.9 % and the continuation rate was 90.3% at 6 months.

TABLE 1: Reason for mirena removal within 6 months of insertion

REASON FOR MIRENA REMOVAL	Number of cases
Post insertion pain	3
Persistent heavy bleeding	2

TABLE 2: menstrual cycle characteristics at 6 months follow up

	At insertion	At 6 months	Percentage difference in mean	P value
Mean duration of menstrual blood	11.3	5.12	54.8 %	<0.001

flow				
Mean pad usage per month	32.7	13.01	60.2 %	<0.001

Of the rest 65 individuals followed up to 6 months, around 50 percent of them had a decrease in mean duration of blood flow by 50 to 75 %, while 17.9 % of the cases had a decrease by more than 75 %.2 of the patients had amenorrhoea (2.8 %) and none experienced an increase in mean blood flow duration at 6 months.

There is an average decrease in days of menstrual flow by 54. 8% and total pad usage was decreased by 60.2 % at 6 months post insertion. Mean rise in Hb after 6 months of mirena insertion 1.7 g/dl (21.53% rise from its intial Hb value noted in the study population)

At 1 year

Continuation rate of mirena at 1 year- 86.1%. 7 patients removed mirena(9.7%). Expulsion was seen in 3 patients(4.3%). In the 62 patients who were continuing on mirena 84.6 % of the population experienced a decrease in menstrual blood loss duration by more than 75 %. 10.8 % of the patients had a decrease in mean menstrual blood loss duration by 50 to 75 %.

TABLE 3: comparison of menstrual flow days and pad usage before mirena insertion with 1 year post mirena insertion

parameter	Before insertion	At 1 year	Percentage decrease	P value
Mean duration of menstrual flow	11.3 days	1.45 days	86.63%	<0.001
Mean pad usage	32.71 pads	1.03 pads	96%	<0.001

Total flow duration decreased by 86.63% after 1 year of mirena insertion and Total pad usage per month decreased by 96% by the end of 1 year.

Pattern of menstrual cycle length at 1 year

Cycle length	Number of patients at insertion	Number of patients at 1 year
Less than 21 days	31 (43.1 %)	0

21 to 45 days	27 (37.5%)	5 (6.9%)
More than 45 days	14 (19.4%)	28 (38.9%)
amenorrhoea	0	32 (49.2 %)

6.9 percent of patients had regular cycles, occurring once in a period of 21 to 35 days. 38.9 percentage of the patients had cycle length of more than 35 days, 49.2 percent of the patients had amenorrhoea. The average rise in Hb seen at 1 year is 2.3 g%.

DISCUSSION

Abnormal uterine bleeding interferes significantly with women's physical, social and psychological aspect of life. There are numerous studies showing the effectiveness of mirena in heavy menstrual bleeding compared to various hormonal and non-hormonal medications(8–10). NICE recommends Mirena as the first choice for heavy menstrual bleeding(11). Mean age of the study population was 40. 3 years. Majority of patients, 47. 2% of the cases were between 35 to 40 years while only 8.3 percent of the study population was more than 45 years of age. Singh et al. in the study on the role of levonorgestrel intrauterine device in management of heavy menstrual bleeding, majority of patients (76.9 %) were aged between 30 and 50 years of age(12).

At6 months follow up, in this prospective study there is a **continuation rate of 90.3 %**, **expulsion rate of 2.8 %** and **removal rate of 6.9 % with mirena insertion** . In the study of levonorgestrel intrauterine device in management of heavy menstrual bleeding by Van Schoubroeck et al, the discontinuation rate was 5.55%, and expulsion rate was 0 percentage(13)

There was **a significant** reduction in duration of bleeding by 54.8 % (p value < 0.001). Mean days of bleeding was reduced from 11.33 to 5.12 days by 6 months and **a significant** reduction in total pad usage per month by 55.4%(p value < 0.001) . Mean pad usage dropped from 32.7 to 13.01 after 6 months of mirena usage. 2.9 % of patients became amenorrheic at the end of 6 months.In the study by Garg et al on non-surgical lifeline for abnormal uterine bleeding- LNG IUS, Amenorrhoea was seen in 10 % of the population, 20 percent had regular scanty bleeding at 6 months post Mirena insertion.

At 1 year follow up, continuation rate of Mirena is 86.1%, removal rate of 9.7 % and expulsion rate of 4.2%. There is **asignificant** reduction in flow duration by 86.63 % (p value less than 0.001). There is **a significant** reduction in the total pad usage by 96% (P value less

than 0.001). pallavi et al on the study levonorgestrel intrauterine device as an emerging tool in management of abnormal uterine bleeding, 95 % decrease in mean menstrual blood loss was seen by 1 year(15).

49.2 percent were amenorrhoiec at 1 year. Rethnamalia et al in his study LNG IUS amenorrhea was seen in 22.2 % of the population at the end of 1 year(16)

A rise in haemoglobin was used to assess the effectiveness of mirena in the management of abnormal uterine bleeding. Of the total 72 individuals, 19 cases failed to follow up with Hb reports. In the remaing population a **significant** rise in Hb was noted by a mean of 1.6 g/dl at 6 months (p value less than 0.001). Patients on attending opd were prescribed iron medications , but their compliance cannot be ensured. Patients who were on oral iron had different iron preparations which had different bioavailability. 5 of the patients after mirena insertion had iron sucrose iv medication from local hospital. There were 10 individuals who had a fall in Hb. These patients though had a significant fall in the number of bleeding days and pad usage, they were non complaint with iron medications. Other causes like worm infestation/ occult stool loss were not assessed in these individuals.

Only 53 patients reported with uss after 1 year of mirena insertion. Endometrial thickness decreased by 50.24 % in the studied population. Mean fall 6.06 mm was noted in the studied group.

LIMITATIONS OF THE STUDY

The study had 2 limitations. The severity of heavy menstrual bleeding was assessed using questionnaire, with a recall method. Majority of patients didn't maintain a menstrual calendar or diary and hence Total days of bleeding and pad usage was assessed as a subjective perception resulting in inadverent recall bias.

Second, the study was conducted during the period of COVID pandemic, and SAT being made a COVID tertiary care hospital, OP were restricted to only high risk gynec and antenatal patients. Data regarding the pattern of bleeding and pad usage in patients after mirena insertion was elicited by telephonic interview using structured questionnaire at 6 months and 1 year. Follow up of patients with review USS report and haemoglobin values were hence difficult

CONCLUSION

After mirena insertion there is a significant reduction in the mean menstrual blood loss at 6 months and 1 year. Its useful in wide pathologies such as adenomyosis, small fibroids, ovulatory dysfunction and endometrial hyperplasia. A significant rise in haemoglobin is seen after mirena insertion. Hence mirena is emerging as a highly effective medical management option for abnormal uterine bleeding

Conflict of interest None

Funding of the study NIL

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