Levonorgestrel Releasing IUS (Metraplant E) in the Management of Copper IUD Related Heavy Painful Menstrual Loss

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ABSTRACT

Background: the LNG-IUD was first introduced in Finland in 1990 and is currently marketed in most European countries and in the US since 2000. The Levonorgestrel IUD is approved for 5 years, but lasts up to 10 years and reduces the menstrual blood loss and pelvic infection rates.

Aim of the Work: this study aimed to evaluate safety and efficacy of levonorgestrel releasing IUS (Metraplant-E) in the management of copper IUD related heavy painful menstrual loss. Among women of low socioeconomic status attended to family planning clinic at Abo-Elnomros Hospital (Abo-Elnomros is small village –Giza Government, Egypt. Patients and Methods: this was a prospective cohort study and it was performed in Abo-Elnomros hospital. Women who attended to the hospital (Family planning clinic) for IUD follow up and had complications (bleeding and dysmenorrhrea) for which copper IUD is removed. Results: all women in the present study reported a marked reduction in MBL, which started from the first menstrual period following insertion of Metraplant –E. Bleeding was reduced further over the next months until the 6th month except two cases. Amenorrhrea occurred in 38 cases. The difference in menstrual bleeding was highly significant (P <0.0001). Hemoglobin level increased from a mean baseline value of 10.0 ± 1.3 at baseline controls to a mean level of 10.5 ± 1.2 after 6 months of Metraplant-E use. Differences in hemoglobin levels were highly significant P <0.0001.

Conclusion and Recommendations: the copper IUD is the most commonly used method of reversible contraception worldwide and is used by an average of 23 percent of female contraceptive users. The copper IUD is associated with increased menstrual flow both in length of menses and in amount of blood loss. The most common reasons for the discontinuation of this method are menstrual bleeding and dysmenorrhea. Metraplant-E is effective in significantly reducing the amount of menstrual blood loss in women with heavy painful menstrual loss related to copper IUD. Strong endometrial suppression is the principal mechanism, explaining both the effect on menstrual blood loss and the contraceptive performance of the IUS. Proper treatment of the chronic endometritis prior to Metraplant-E insertion is recommended. Actively informing women about benefits, risks and common side effects of IUS appears to improve consideration and acceptance of the method. Keywords: levonorgestrel releasing IUS, metraplant E, IUD, LARC.

INTRODUCTION

Intrauterine methods of contraception (IUC) include the copper intrauterine device Cu-IUD and the Levonorgestrel releasing intrauterine systems LNG-IUS. IUC is considered to be a long acting reversible method of contraception (LARC) (1,2). The IUD is the most commonly used method of reversible contraception worldwide and it is used by an average of 23 percent of female contraceptive users, with a range of <2 to >40 percent depending on the country (3).

In 2014, IUDs were used by 27 percent of female contraceptive users in Asia and 17 percent of female contraceptive users in Europe. Use of IUDs has increased in the United States (US). In the decade from 2002 to 2012, IUD use rose from 2 to nearly 12 percent among US women using contraception (4). Actively informing women about benefits, risks and common side effects of IUDs appeared to improve consideration and acceptance of the method (5). The most common reasons for the discontinuation of this method were menstrual bleeding and dysmenorrhea. In the first year of use between 4% and 15% of women using a copper IUD it was removed for these reasons (6). One of the most versatile forms of a long-acting reversible method of contraception (LARC) is the levonorgestrel-releasing intrauterine system (LNG-IUS). This system is an extremely effective contraceptive and has many non-contraceptive health benefits, including suppression of menstruation, maintenance of iron stores, improvement in dysmenorrhea and endometrial protection for women on estrogen replacement therapy (7).

The LNG-IUS offers, in addition to its excellent contraceptive efficacy, further added health benefits. The immediate and intense suppression of the endometrium leads to over 90% reduction of menstrual blood loss over a period of 12 months.
Blood and ferritin levels in women who are suffering from problematic heavy menstruation increase significantly and hence, the need to preclude to hysterectomy has been reported to decline (1). A study had shown the cost-effectiveness and improvement of quality of life in women using the LNG-IUS compared to those women undergoing hysterectomy (1). The LNG-IUD was first introduced in Finland in 1990 and is currently marketed in most European countries and in the US since 2000 (1). The Levonorgestrel IUD is approved for 5 years, but lasts up to 10 years and reduced the menstrual blood loss and pelvic infection rates (7).

In this work we evaluated safety and efficacy of Levonorgestrel releasing IUS (METRAPLANT-E) in the management of copper IUD related heavy painful menstrual loss.

Metraplant-E:
A new intrauterine system recently prepared by Azzam (8). Metraplant-E design has a T-shaped frame containing Levonorgestrel hormone (60 mg), EVA "Ethylene Vinyl Acetate" (120 mg) and barium sulphate (20 mg) to make it radio-opaque. "T" frame contains: EVA, Levonorgestrel and barium sulphate. i.e. the whole system is containing Levonorgestrel which is different from other forms of LNG-IUS like Mirena or Metraplant. Poly ethylene is recently added to give Metaplant-E more strength and memory to decrease the incidence of expulsion (8).

It’s designed with release rate more than 20µg/24H which allows it to be used as a contraceptive for more 5 years, furthermore the higher initial release just post application, by more than 28µg/24H was of benefit if it used to treat Menorrhagia (8).

Expected Advantages of Metraplant-E over similar intrauterine devices (Mirena and Femilis)
- Low cost
- Easy insertion technique.
- Relatively easier manufacturing process than other levonorgestrel- releasing devices containing silicone other than polyethylene.
- Availability without obstacles and delays of importation.

EVA is used also in other forms of levonorgestrel releasing IUS e.g. (Fibroplant and Femilis) invented by Direk Wildemeerch in 2005 in Belgium.

Aim of the Work:
This study aimed to evaluate safety and efficacy of Levonorgestrel releasing IUS (METRAPLANT-E) in the management of copper IUD related heavy painful menstrual loss.

PATIENTS AND METHODS
Type of the study: prospective cohort study.
Study setting:
The study was performed in Abo-Elnomrus Hospital. Women who attended to the hospital (Family planning clinic) for IUD follow up and have complication (bleeding and dysmenorrhea) for which copper IUD is removed.

Inclusion criteria:
1. Age: 20-40 years
2. Women who have complication related to copper IUD
3. Women who did not tolerate copper IUD due to increased amount of menstrual blood loss which could lead to anemia.

Exclusion criteria:
1. Hypersensitivity to any component of this product.
2. Uterine abnormality (septum-polyp…..)
3. Previous ectopic pregnancy
4. Vaginal infection at time of insertion
5. Pregnancy
6. Acute liver disease or liver tumor (benign or malignant).
7. Conditions associated with increased susceptibility to infections with microorganisms. Such conditions include, but are not limited to, leukemia, acquired immune deficiency syndrome (AIDS), and I.V. drug abuse.
8. A previously inserted IUD that has not been removed.
9. Known or suspected carcinoma of the breast.
All women participating in this study were subjected to the following:

- Personal history.
- Obstetric history.
- Menstrual history (with assessment of blood loss and dysmenorrhea).
- General examination.
- Abdominal examination and
- Pelvic examination. (to exclude any contraindication of hormonal IUD)

Investigations:
- CBC
- Vaginal Ultra sound

Assessment of the menstrual blood loss:
- Pictorial blood loss assessment chart (PBAC).
- Bleeding index (BI).
- Total bleeding score / month.

Levonorgestrel-releasing device insertion technique:
Exactly like insertion of copper T380A (withdrawal technique).

Patient counseling:
After thorough clinical assessment of the women included and if the patient fulfills the inclusion and exclusion criteria the Metraplant-E IUS was inserted by the usual withdrawal method at any time during the menstrual cycle. The device side effects and the health benefits were explained after women agreement and informed consent were obtained.

Follow up of the patients:
All women were followed up for 1-3 and 6 months after IUD insertion for menstrual history as amenorrhea, spotting, menorrhagia, metrorrhagia, premenstrual syndrome, mastalgia, mood changes or development of acne. All patients were followed up for at least 6 months from insertion date with CBC level tested. All data were documented on informed case “record form”

Patient satisfaction:
Satisfaction questionnaire was designed including three questions:
1) Are you satisfied with the IUD you use?
2) Do you prefer to keep using this device?
3) Do you want to suggest these IUDs to the others? *(9)

Ethics:
The study was approved from the Ethical Committee of the Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University.

Statistical Methods
Data were analyzed using IBM® SPSS® Statistics version 23 (IBM® Corp., Armonk, NY). Continuous numerical data were presented as mean and SD, and categorical data as number and percentage. Paired comparison of continuous numerical data was done using the paired t test. Repeated-measures analysis of variance (ANOVA) was used to compare multiple within-group measures. The Bonferroni correction was used to adjust the p-value for multiple within-group comparisons.

-Time to event analysis was done using the Kaplan-Meier method.
- Two-sided p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Hemoglobin level before IUS insertion and at 6 months post-insertion.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before insertion</th>
<th>6 months after insertion</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>10.0 ± 1.3</td>
<td>10.5 ± 1.2</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are mean ± SD, *Paired t test.
Hemoglobin level increased from a mean baseline value of 10.0 ± 1.3 at baseline controls to a mean level of 10.5 ± 1.2 after 6 months of Metrapearl-E use. Differences in hemoglobin levels were highly significant P <0.0001.

Table 2: PBAC before IUS insertion and at 1 month, 3 months and 6 months post-insertion.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time</th>
<th>Mean ± SD</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBAC</td>
<td>Before insertion</td>
<td>213.4 ± 54.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>1 month after insertion</td>
<td>15.4 ± 33.1†</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 months after insertion</td>
<td>7.0 ± 18.5†</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 months after insertion</td>
<td>15.6 ± 40.3†</td>
<td></td>
</tr>
</tbody>
</table>

*Repeated-measures analysis of variance (ANOVA), †p-value <0.0001 versus baseline (Bonferroni-corrected).
Levonorgestrel Releasing IUS…

In our study results of the menstrual blood loss (MBL) were detected by using the pictorial chart scoring system. All women reported a marked reduction in MBL, which started from the first menstrual period following insertion of the Metraplant -E. Bleeding reduced further over the next months until the 6th month. Menstrual blood loss was reduced from a mean baseline of 213.4 ± 54.8 to a mean volume of 15.6 ± 40.3† after 6 months. The difference in menstrual bleeding was highly significant (P < 0.0001).

### Table 3: bleeding index before IUS insertion and at 1 month, 3 months and 6 months post-insertion.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time</th>
<th>Mean ± SD</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding index</td>
<td>Before insertion</td>
<td>38.7 ± 8.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>1 month after insertion</td>
<td>6.1 ± 6.3†</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 months after insertion</td>
<td>3.9 ± 5.5‡</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 months after insertion</td>
<td>5.5 ± 7.1†</td>
<td></td>
</tr>
</tbody>
</table>

*Repeated-measures analysis of variance (ANOVA).
† p-value <0.0001 versus baseline (Bonferroni-corrected).
‡ p-value <0.0001 versus 1 month (Bonferroni-corrected).

Menstrual blood loss (Using bleeding index) was reduced from a mean baseline of 38.7 ± 8.7 to a mean volume of 5.5 ± 7.1†after 6 months. The difference in menstrual bleeding was highly significant (P < 0.0001).

### Table 4: total bleeding score before IUS insertion and at 1 month, 3 months and 6 months post-insertion.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time</th>
<th>Mean ± SD</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bleeding score</td>
<td>Before insertion</td>
<td>29.6 ± 6.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>1 month after insertion</td>
<td>2.6 ± 3.5†</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 months after insertion</td>
<td>1.7 ± 3.2‡</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 months after insertion</td>
<td>2.6 ± 5.4†</td>
<td></td>
</tr>
</tbody>
</table>

*Repeated-measures analysis of variance (ANOVA).
† p-value <0.0001 versus baseline (Bonferroni-corrected).
‡ p-value <0.0001 versus 1 month (Bonferroni-corrected).

Menstrual blood loss (Using total bleeding score) was reduced from a mean baseline of 29.6 ± 6.4 to a mean volume of 2.6 ± 5.4†after 6 months. The difference in menstrual bleeding was highly significant (P < 0.0001).

### Table 5: incidence of adverse outcomes in the study population.

<table>
<thead>
<tr>
<th>Adverse outcome</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent menorrhagia</td>
<td>2 (3.3%)</td>
</tr>
<tr>
<td>Pregnancy on top of IUS</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Simple IUS expulsion</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>IUS expulsion with severe bleeding</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>IUS expulsion with severe bleeding ending up with hysterectomy</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Overall IUS expulsion</td>
<td>3 (5.0%)</td>
</tr>
</tbody>
</table>

Data are number (%).

The total observation period was six month only one pregnancy occurred, within the third months after insertion, giving an overall pregnancy rate of this LNG-IUS of 1.7% at 6 month. There were three cases of expulsion of Metraplant –E giving an overall expulsion rate of this LNG-IUS of 5% at 6 month.

All women in our study reported a marked reduction in MBL, which started from the first menstrual period following insertion of Metraplant –E except two cases.
Mohamed Azzam et al.

Table 6- Kaplan-Meier table for occurrence of IUS expulsion.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Time after insertion (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 month</td>
</tr>
<tr>
<td>Number at risk</td>
<td>60</td>
</tr>
<tr>
<td>Number experiencing failure event (expulsion)</td>
<td>1</td>
</tr>
<tr>
<td>Number censored (no expulsion till end of or loss to follow-up)</td>
<td>0</td>
</tr>
<tr>
<td>Proportion with expelled IUS (failed proportion)</td>
<td>0.017</td>
</tr>
<tr>
<td>Proportion with retained IUS (censored proportion)</td>
<td>0.983</td>
</tr>
<tr>
<td>Survival (IUS retention) distribution function</td>
<td>0.983</td>
</tr>
<tr>
<td>SE for survival function</td>
<td>0.017</td>
</tr>
<tr>
<td>Lower 95% CI bound</td>
<td>0.951</td>
</tr>
<tr>
<td>Upper 95% CI bound</td>
<td>1.000</td>
</tr>
</tbody>
</table>

DISCUSSION

Intrauterine devices (IUDs) are among the most widely used contraceptive methods in the world and are used by more than 2 million women in the United States (US) (10). Copper-containing IUDs (Cu-IUDs) were introduced into worldwide markets in the late 1960s and they are available in a variety of types, most of which are named for their shape and amount of copper on the device. Currently, the Copper 380A (TCu380A) is the most Cu-IUD available in the US and approved for use for 10 years, although effectiveness for up to 20 years has been shown (6). The TCu380A is considered as the most effective Cu-IUD (11). Complaints of bleeding irregularities are common with Cu-IUD use and can lead to increased rates of discontinuation (6).

World Health Organization (WHO) trial conducted in South America demonstrated that women receiving the multiload Cu-IUDs had significantly higher mean menstrual blood loss (MBL) for at least 12 months following insertion, whereas those who received the Cu-T200 or Cu-7 IUDs, which are more similar to the TCu380A, had an increase in MBL during the first 6 months of use that returned to preinsertion levels by 12–24 months (11). Increased menstrual bleeding in the presence of a Cu-IUD is thought to be due to excessive prostaglandin release in the endometrial cavity. Nonsteroidal anti-inflammatory drugs (NSAIDs) act as inhibitors of prostaglandin synthetase and help decrease the endometrial prostaglandin release, thereby potentially reducing MBL, even in the presence of Cu-IUDs (12). In 34 randomized controlled trials involving more than 50,000 women and 16 different comparisons between devices, copper IUDs were highly effective in preventing pregnancy, with protection lasting up to 12 years for the TCu380A (12). It is probable that about 10% of women with IUDs risk secondary anemia, especially those who bleed more than 80 mL per period. It has been suggested that an increased risk of iron deficiency exists even with a 40-mL blood loss (13). Levonorgestrel-releasing intrauterine systems (LNG IUS) have an additional major health benefit because they markedly reduce the volume and duration of menstrual bleeding. In cases of anemia attributable to menorrhagia, the LNG IUS reduces blood loss within 1 month and by more than 90% after 6 months (14). A study that compared copper devices and the levonorgestrel intrauterine system (LNG-IUS), pregnancy rates were lower with the LNG-IUS than with copper devices (15). Side effects and device-related complications such as expulsions and perforations are comparable between copper IUDs and the LNG-IUS.

Proper insertion is the key to preventing complications including perforations, expulsions and pain. Expulsion of an IUD occurs in 1 in 20 women and is most common in the first 3 months after insertion, often during menstruation. The most important adverse effects are dysmenorrhea and bleeding, which lead to the removal of copper IUDs in 10% of women in the first year of use (16). Up to 50% of women stop using IUDs within 5 years, most often because of unacceptable vaginal bleeding or pain. The frequency of removals for bleeding problems (including amenorrhea) is similar for copper IUDs and the LNG-IUS: 14% in copper T users and 11% in LNG-IUS users after 36 months of use (17).

The irregular bleeding or spotting that does occur with the LNG-IUS is usually limited to the initial months of use. Once the endometrial effects are established, the bleeding pattern with the LNG-IUS turns gradually to oligomenorrhea or amenorrhea. Using strict criteria for amenorrhea (90 consecutive
days with no bleeding or spotting), 20% of the LNG-IUS users are defined to be in amenorrhea after one year of use. Given the comparable effectiveness between the LNG-IUS and the high dose copper devices, the reduction in menstrual flow with the LNG-IUS, and its 5-fold higher cost, the LNG-IUS, might be reserved for women who have excess menstrual bleeding or pain. IUD/IUS continuation rates are within the range of continuation rates for other methods of contraception. In a systematic review of the literature for a national guideline on long-acting reversible contraceptives, the National Institute for Health and Clinical Excellence in the UK reported cumulative discontinuation rates as high as 17% after 1 year and 28% after 2 years for the Cu-IUD. For the LNG-IUS, discontinuation rates were as high as 24% after 1 year and 33% after 2 years. Discontinuation rates were up to 50% for all types of IUDs by 5 years. Women used copper IUDs were most likely to discontinue because of bleeding and/or pain. Although these were also common reasons for discontinuation of use of the IUS, almost 1 in 4 women stop using the LNG-IUS because of amenorrhea, which other women consider a benefit. Overall, the most common reason for discontinuation of a Cu-IUD or LNG-IUS is unacceptable bleeding patterns.

In the present study, to recognize IUD induced menorrhagia we measured the bleeding rate by using pictorial blood assessment chart (PBAC). PBAC is an objective and suitable criterion for measuring the amount of bleeding. This method showed blood association for percentage change in blood (Intraclass Correlation Coefficient {ICC} of 0.86, 95% CI, 0.80-0.91) with a sensitivity and specificity of 96 and 92% respectively.

Study on 60 Metraplant-E users women, covers a period of 6 months of IUS use. All cases were suffering from severe bleeding with copper intrauterine device. Assessment of menstrual blood loss was done by using PBAC, bleeding index and total bleed score before insertion of Metraplant –E and 1,3 and 6 months after insertion. Hemoglobin level was done before insertion of Metraplant –E and 6 months after insertion. The total observation period was six months. Only one pregnancy occurred, within the third months after insertion, giving an overall pregnancy rate of this LNG-IUS of 1.7% at 6 months. There were three cases of expulsion of Metraplant –E giving an overall expulsion rate of this LNG-IUS of 5% at 6 months. All women in the present study reported a marked reduction in MBL, which started from the first menstrual period following insertion of Metraplant –E. Bleeding reduced further over the next months until the 6th month except two cases. Amenorrhea occurred in 38 cases and the bleeding decreased in most of cases from the first cycle. The difference in menstrual bleeding was highly significant (P <0.0001). In the present study the cumulative pregnancy rate of 1.7% in 6 months. This could be explained by the limited experience of the investigator as it occurred during the training period.

Interim results from the WHO international multicentre RCT (n = 3815 insertions) reported a significantly higher cumulative pregnancy rate among users of TCu 380A IUD when compared to LNG-IUS users at 6 years (2.0% versus 0.5%). [EL = 1+]

Another studies reported similar result on different forms of Copper IUCD.

In the present study, expulsion rates (partial and complete) were three cases (5% of all cases). Transvaginal sonographic follow up at 1,3,6 months was done to diagnose cases of expulsion.

In another study expulsion of an IUD occurred in approximately 1 in 20 women and it was most common in the first three months after insertion. Expulsion commonly occurred during menstruation.

One multinational RCT (n = 2246 women in Singapore, Brazil, Egypt and the USA) reported no significant differences between LNG-IUS users and TCu 380A users in cumulative discontinuation rates due to expulsion (6.0% versus 5.5%, 7.3% versus 6.1%, 11.8% versus 7.4% and 11.8% versus 8.4% at 1, 2, 5 and 7 years, respectively).

Interim results from the international multicentre RCT (n = 3815 insertions) reported no significant difference between LNG-IUS users and TCu 380A IUD users in cumulative discontinuation rates due to expulsion (7.5% versus 8.2%) after 6 years.

One UK non-comparative study (n = 678) undertaken to determine the performance of LNG-IUS reported cumulative discontinuation rates due to expulsion of IUS of 4.5%, 5.2%, 5.5%, 5.5% and 5.9% at 1.2, 3, 4 and 5 years, respectively. However in a recent study on Metraplant-E expulsion (partial and complete) rate was much higher, this was attributed to selection of high risk patient.

Youn et al. estimated the risk factor for spontaneous expulsion of Levonorgestrel-releasing intrauterine system pre-insertion characteristics for 481 women who received the LNG-IUS at a single
institution in the Republic of Korea between 2003 and 2011, they were analyzed retrospectively. The median duration of follow up was 13.4 months. The overall crude incidence of spontaneous LNG-IUS expulsion was 9.6%. The cumulative incidence was 7.9%, 9.1%, and 9.6% at 1, 2, and 3 years respectively. It was significantly higher in women with Adenomyosis (9.1%, 10.6%, and 11.1%) or uterine leiomyoma (14.5%, 15.8%, and 15.8%) than in those with a normal uterus (3.6%, 4.1%, and 4.6%) \( (P=0.008) \) \(^{(21)} \).

In the present study, menstrual blood loss scores dropped significantly during the observation period in all women except two cases. Menstrual blood loss was reduced from a mean baseline of 213.4 ± 54.8 to a mean volume of 15.6 ± 40.3\(^{†} \) after 6 months and hemoglobin level increased from a mean baseline value of 10.0 ± 1.3 at baseline controls to a mean level of 10.5 ± 1.2 after 6 months of Metraplant-E use. Differences in menstrual blood loss and hemoglobin levels were highly significant \( P <0.0001 \); twenty five cases were with hemoglobin level between 7 to 9.5mg before insertion of Metraplant-E and it improved significantly 6 months after insertion. Metraplant-E was inserted in two cases with uterine fibroid the menstrual blood loss (MBL) was decreased significantly.

The present study confirmed the promising therapeutic value of the LNG IUS (Metraplant-E). Being an effective contraceptive, together with the strong reduction of MBL, makes it a very attractive method for many women in the developed and developing countries. Our results are in accordance with another results \(^{(14,29)} \).

**Metraplant-E**, is designed without any surface coat membrane as in Mirena, which helps in more rise in Levonorgestrel level (Higher initial release). The high initial release of Levonorgestrel may help in early cessation of bleeding in patients who suffer from menorrhagia. Subsequent release will depend on the concentration gradient between the endometrial environment and the intrauterine system \(^{(8)} \).

**Conclusion and Recommendations**

The copper IUD is the most commonly used method of reversible contraception worldwide, and is used by an average of 23 percent of female contraceptive users. The copper IUD is associated with increased menstrual flow both in length of menses and in amount of blood loss. The most common reasons for the discontinuation of this method are menstrual bleeding and dysmenorrhea. We removed the copper IUD if the woman complains of menorrhagia and experiences a clinically significant fall in hemoglobin. These patients may consider another method of contraception or insertion of a LNG IUS. The Levonorgestrel-releasing intrauterine system is associated with a reduction in menstrual blood loss; LNG IUS users report fewer bleeding or spotting days per month compared to noncontraceptors and users of copper IUD. The Levonorgestrel-releasing intrauterine system is a safe, effective and accepted form of contraception being used worldwide.

The Levonorgestrel-releasing intrauterine system also has a multiple non contraceptive benefits including improvement in menorrhagia, decreased pelvic pain associated with endometriosis and adenomyosis, as well as a treatment of endometrial hyperplasia. Metraplant- E co-polymer is made of ethylene vinyl acetate (EVA) instead of polymethylsiloxane (silicone) used in Mirena IUS which is easier in manufacturing so it will be cheaper instead of more expensive other LNG-IUS. Metraplant- E is effective in significantly reducing the amount of menstrual blood loss in women with heavy painful menstrual loss related to copper IUD. Strong endometrial suppression is the principal mechanism, explaining both the effect on menstrual blood loss and the contraceptive performance of the IUS.

The present study confirmed the promising therapeutic value of the LNG IUS (Metraplant- E). Being an effective contraceptive, together with the strong reduction and managing of copper IUD related heavy painful menstrual loss, makes it a very attractive method for many women. It is importance of the follow-up the patients and their reassurance especially regarding breakthrough bleeding. Timing of insertion of the Metraplant-E device is better to be done within the first 21 days of the menstrual cycle and no later to decrease the incidence of expulsion. Evaluating the uterus by vaginal ultrasound before insertion and conducting a vaginal ultrasound evaluation after insertion of the IUS, to visualize the position of the IUS, is recommended. Proper treatment of the chronic endometritis prior to Metraplant-E insertion is recommended. Actively informing women about benefits, risks, and common side effects of IUS appears to improve consideration and acceptance of the method. The availability of relatively inexpensive form of Levonorgestrel-releasing intrauterine system (Metraplant-E) would benefit large group of women who need it for different indication.
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