The Use of Levonorgestrel-Releasing Device (Metraplant-E) in the Treatment of Dysfunctional Uterine Bleeding

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BY

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List of Contents

Title ……. Page

ABSTRACT

Introduction: Heavy menstrual bleeding (HMB), or menorrhagia, is subjectively defined as a "complaint of a large amount of bleeding during menstrual cycles that occurs over several consecutive cycles" and is objectively defined as menstrual blood loss of more than 80 ml per cycle that is associated with an anemia status (defined as a hemoglobin level of <10 g/dl). The levonorgestrel-releasing intrauterine system (LNG-IUS) has a variety of non-contraceptive benefits including treatment for menorrhagia, endometriosis, and endometrial hyperplasia. *Metraplant-E*, which is a new levonorgestrel-releasing intrauterine system used in this study, a new intrauterine system produced by *Azzam* 2013. **Objective:** to evaluate the therapeutic effect of the intrauterine system (Metraplant-E) in the treatment of dysfunctional uterine bleeding. **Patients and Methods:** 61 women attending the outpatient gynecology clinic at Ain Shams University Maternity hospital or the Early Cancer Detection Unit (ECDU) for hysteroscopy. Steps taken to include women in this study (women who are selected according to inclusion and exclusion criteria) by 1) taking thorough personal, menstrual and medical past history, 2) Pelvic ultrasonographic scan ordered for candidate women, 3) office hysteroscopy and endometrial biopsy done, 4) obtaining endometrial biopsy result, 5) treating cervicitis or PID or any suspected genital infection, 6) Metraplant-E insertion, 7) follow-up of women and 8) obtaining a second endometrial biopsy. **Results**: Metraplant-E, a new levonorgestrel-releasing intrauterine device made by **Azzam, 2013** in its first clinical trial. At the end of the study: Total success rate was **49.18% (30 cases).** The assessment of blood

loss using pictorial assessment bleeding chart (PBAC) showed a decrease of the mean blood loss from 228.44 before insertion to 6.87 six months after Metraplant-E insertion (***p***=0.000), using bleeding index the mean was 22.94 before which decreased to reach 2.3 six months after insertion (***p***=0.000) and using the total bleeding score was 28.97 before insertion which decreased to reach 2.33 at six months after Metraplant-E insertion (***p***=0.000). The mean of the affection of quality of life scale (Likert scale) was 9.1 which improved six months after Metraplant-E insertion reaching 4.93 (***p***=0.000). All 15 cases who returned for follow-up has progesterone effect in histo-pathologic examination of follow-up endometrial biopsies The rate of spontaneous expulsion was 15 cases out of 61 participants equals about **24.59%**.

Conclusions: "**Metraplant-E**" is a modified form of LNG-IUS (modified by **Azzam** from Metraplant) liberating ~ 20 micrograms per day. In this study Metraplant-E was found to be effective in managing dysfunctional menorrhagia on both clinical and histopathologic levels. However, further studies needed to be carried out to improve the efficacy and eliminate the side effects of the newly developed device (Metraplant-E). The greater risk for expulsion of intra-uterine device can be attributed to the severity of cases of dysfunctional uterine bleeding with the great amount of blood loss causing flushing out of the device, physical properties of the new device or late timing of insertion during the menstrual cycle.

Key words: Metraplant-E - LNG-IUS - Azzam - Menorrhagia – Contraceptives

LIST OF ABBREVIATIONS

- ADUB … Anovulatory dysfunctional uterine bleeding.
- ANGPT ……... Angiopoietin.
- ANGPT1 ……... Angiopoietin1.
- ANGPT2 ……... Angiopoietin2.
- AUB …….. Abnormal uterine bleeding.
- AUB-C …… AUB caused by coagulation disorders.
- AUB-E ……..…. AUB caused by endometrial primary dysfunction.
- AUB-O …… AUB caused by ovulation disorder.
- BTB ……. Breakthrough bleeding.
- CMTs ……. Conventional medical therapies.
- COCs …… Combined oral contraceptives.
- COX-2 ……. Cyclo-oxygenase enzyme-2.
- DC ……... Decidual cell.
- DMPA ……... Depot medroxy-progesterone acetate.
- DUB …… Dysfunctional uterine bleeding.
- ECM ……. Extracellular matrix.
- ER …… Estrogen receptor.
- ESCs …… Endometrial stromal cells.
- EVA …….. Ethelene vinyl acetate.
- FBLN-1…….. Fibulin-1.
- FoxO1 …….. Forkhead box O1.
- FP-LNG-IUS ……... Fibroplant levonorgestrel-releasing intrauterine system.
- GEA …… Global endometrial ablation.
- GnRH …… Gonadotrophin-releasing hormone.
- GnRHa ……. Gonadotrophin-releasing hormone analogue.

- HAND2 …….. Heart and neural crest derivatives expressed transcript 2.
- 17-h HSD …… 17 Human hydroxysteroid dehydrogenase.
- HMB …….. Heavy menstrual bleeding.
- HEEC …….. Human endometrial endothelial cell.
- Hoxa-10 ……... homeobox A10.
- HRT ……. Hormone replacement therapy.
- HTA…… HydroThermAblator.
- Hx ……... Hypoxia.
- IGF-1 ……... insulin growth factor 1.
- IGFBP-1……..….. Insulin-like growth factor-binding protein 1.
- IL …… Interleukin.
- IUCD ……... Intrauterine contraceptive device.
- IUD …… Intrauterine device.
- LH …… Lutenizing hormone.
- LNG ……. Levonorgestrel.
- LNG IUD …….. Levonorgestrel-releasing intrauterine device.
- LNG IUS ……... Levonorgestrel-releasing intrauterine system.
- MBL ……... Menstrual blood loss.
- MEA …… Microwave endometrial ablation.
- MMP…… Matrix metalloproteinase.
- MPA …… Medroxy-progesterone acetate.
- N …… Newton (unit of measuring force).
- NET ……. Norethisterone acetate.
- Ng-mT …….. El Mahgoub mini-T intracervical device.
- Ng-T …….. El Mahgoub intrauterine levonorgestrel devices.

- NSAIDs ……..... Non-steroidal anti-inflammatory drugs.
- ODUB …….…….. Ovulatory dysfunctional uterine bleeding.
- PBAC …… Pictorial bleeding assessment chart.
- PIPs …… Progestasert intrauterine progesterone devices.
- PMS …… Premenstrual syndrome.
- PR …….. Progesterone receptor.
- PRL …….……... Prolactin.
- PRMs …….. Progesterone receptor modulators.
- SAA ……. Serum amyloid protein A.
- SDF-1 …….…… Stromal cell derived factor-1.
- TBEA ……... Thermal balloon endometrial ablation.
- TCRE ….. Transcervical resection of the endometrium.
- TF …… Tissue factor.
- TIMP ……. Tissue inhibitor metalloproteinase.
- TVS ……... Transvaginal ultrasound.
- UAE ……. Uterine artery embolization.
- uNK …… Uterine natural killer cells.
- VEGF …….. Vascular endothelial growth factor.
- VK …….. Vitamin K.
- VKOR …….. Vitamin K epoxide reductase.
- VSMC …….. Vascular smooth muscle cells.

LIST OF FIGURES

by 3 methods: 2 numerical (bleeding index and total bleeding score) and 1 chart (PBAC).

- Figure (35)……. shows PBAC (Pictorial bleeding assessment chart) before Metraplant-E insertion, after 1 month, 2 months, 3 months, 4 months, 5 months and 6 months after insertion in both groups 1 and 2.
- Figure (36)…… curve representing comparison between PBAC in both groups before Metraplant-E insertion and monthly during the study period up to 6 months.
- Figure (37)…….. Histopathology slide representing proliferative endometrium (40 H.P.F) obtained in endometrial sampling prior to Metraplant-E insertion
- Figure (38-a) …… Histopathology slide representing simple endometrial hyperplasia without atypia obtained in endometrial sampling prior to Metraplant-E insertion
- Figure (38-b) ……...Histopathology slide representing simple endometrial hyperplasia without atypia (100 H.P.F) obtained in endometrial sampling prior to Metraplant-E insertion.
- Figure (39) ……..... Histopathology slide representing short term exposure to levonorgestrel-releasing intra-uterine device (Metraplant-E) (40 H.P.F) obtained in endometrial sampling after Metraplant-E insertion.
- Figure (40-a)…….Histopathology slide representing long term exposure to Metraplant-E (100 H.P.F).
- Figure (40-b)…… Histopathology slide representing long term exposure to Metraplant-E showing stromal decidualization, inactive endometrial glands (atrophic) and lymphocytic infiltration.
- Figure (41-a) …….. Histopathology slide representing long term exposure to Metraplant-E (40 H.P.F) showing