

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

*Thesis Submitted for Partial Fulfillment of Master Degree in
Obstetrics and Gynecology*

BY

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2016

ACKNOWLEDGMENT

I give thanks first and mainly to my great mentors who enabled me to accomplish this work.

Gratitude and full appreciation to **Prof. Dr. Mohamed Ezz El-Din Aly Azzam** , Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University. Thanks for his valuable advice, continuous encouragement and honorable supervision throughout this thesis. Thanks are also to him for donating the time for the very accurate and thorough reading and revision of the thesis despite his countless obligations.

My deepest heart-felt gratitude and appreciation to Prof. Dr. **Magd Eldin M. Mohamed**, Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University .

I would like to express my sincere gratitude and thanks for Dr. **Laila Aly Farid**, Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University.

I would like to thank Prof. Dr. **Mohamad Amer**, Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University & head of the Early Cancer Detection Unit (ECDU), Ain Shams Maternity Hospital. I would like to express my appreciation and I am indebted to Dr. **Alaa Rashed**, Gynecologist at ECDU, Faculty of Medicine, Ain Shams Maternity Hospital.

ACKNOWLEDGMENT

I am much obliged to Dr **Reem Abdel- Azeem**,
Assisstant Consultant of Clinical Pathology at ECDU, Ain
Shams Maternity Hospital.

I am much obliged to Prof. Dr. **Magdy Ibrahim
Mostafa**, Professor of Obstetrics and Gynecology, Faculty
of Medicine, Cairo University for organizing my statistical
results.

Last but not least, I am most thankful to my amazing
family for their outstanding support.

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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.

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