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**Assessment of the efficacy of uterine artery Doppler  
in predicting the response to Mefenamic Acid  
during treatment of women having IUCD  
associated menorrhagia**

**Thesis**

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in Obstetrics & Gynaecology

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لَسْبَدَانِكَ لَا نَعْلَمُ لَنَا  
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْعَظِيمُ

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### Abstract

**Background:** Bleeding with IUCDs is considered iatrogenic dysfunctional uterine bleeding. The bleeding associated with IUCD use may either occur during menstruation (heavy and/or prolonged) or in the form of intermenstrual bleeding and spotting. **Patients and Methods:** This study was carried out on 156 women attended the family planning out-patient clinic in the obstetrics and gynecology department, Ain Shams University Hospitals, during the period from May 2017 to May 2018. Patients were divided according to the response to treatment into two groups: Group (I): Responders to treatment with Mefenamic acid and Group (II): Non-responders to treatment with Mefenamic acid. Response to treatment was evaluated according to: Pictorial blood loss assessment chart. **Results:** Interpretation of the results of this work showed that uterine artery mean value of the PI of the women who responded to treatment with mefenamic acid (group I) ( $1.54 \pm 0.42$ ) were significantly higher than mean value of PI of women who didn't respond to treatment with mefenamic acid (group II) ( $0.96 \pm 0.28$ ), also showed that uterine artery mean value of the RI of the who responded to treatment with mefenamic acid (group I) ( $1.01 \pm 0.25$ ) were significantly higher than mean values of RI of women who didn't respond to treatment with mefenamic acid (group II) ( $0.71 \pm 0.21$ ). Doppler indices showed that Pulsatility index  $\geq 1.27$  had moderate sensitivity (75.3%) and NPV (75.3%) but high specificity (90.1%) & PPV (90.1%) in prediction of responders. Resistive index  $\geq 0.93$  had low sensitivity (69.4%) and NPV (70.8%) but moderate specificity (88.7%) & PPV (88.1%) in prediction of responders. **Conclusion:** There is a strong relationship between uterine artery Doppler indices and prediction of response to mefenamic acid.

**Key words:** uterine artery doppler, mefenamic Acid, treatment, IUCD, menorrhagia

## Introduction

A normal menstrual cycle is 21-35 days in duration, with bleeding lasting on average for 5 days and a total blood loss of 25-80 ml. Menorrhagia is defined as having menstrual period with longer duration or excessively heavy flow (total menstrual flow > 80ml per cycle, or soaking a pad/tampon every 2 hours or less)(**Munro et al., 2011**).

An intrauterine contraceptive device (IUCD) is one of the most frequently used methods for birth control around the world. However, menorrhagia is one of its side effects. Menorrhagia may cause iron deficiency anemia and usually ends by removing the IUCD in the first year after its insertion in many cases (**Mansour et al., 2017**).

Although the intrauterine contraceptive device (IUCD) has been used for more than 30 years, its mode of action as a contraceptive still remains poorly defined. It is currently believed that it acts by prevention of fertilization through a sterile inflammatory reaction produces tissue injury that is spermicidal. In copper IUCD users; the copper concentration in cervical mucus is substantial and that leads to inhibition of sperm motility. Because copper ions also result in significant endometrial changes, sperm migration, quality

and viability at the level of endometrium is hindered **(Kaneshiro and Aeby, 2010).**

There are several mechanisms that explain the cause of excessive bleeding in patients using IUCD. Several studies reported that IUCD insertion increase the production of prostaglandins in the endometrium which cause an increase in vascularity, vascular permeability, and inhibit platelet activity and therefore increase menstrual bleeding **(Mansour et al., 2017).**

Studies have reported that IUCD causes COX-2 (cyclooxygenase isoenzyme 2) up-expression, the subsequent elevated prostanoids biosynthesis and signaling can promote the expression of pro-angiogenic factors, such as VEGF (vascular endothelial growth factor), bFGF (basic fibroblast growth factor), PDGF (platelet-derived growth factor), Ang-1 (angiopoietin-1), and Ang-2 (angiopoietin-2) or down-regulate the expression of anti-angiogenic genes such as cathepsin-D **(Fouda et al., 2010).**

The resulting exaggerated inflammation within the endometrium may lead to increased and prolonged tissue damage at the time of menstruation. Therefore, limitation of the production of inflammatory mediators is helpful in the treatment of women with heavy menstrual bleeding **(Maybin and Critchley, 2016).**

The Cochrane Review states that non-steroidal anti-inflammatory drugs (NSAIDs) are the most effective treatment to reduce the bleeding with IUCD use. They are prostaglandin synthetase inhibitors acting by decreasing production of endometrial prostaglandins; thus can enhance both uterine bleeding and pain (**Ali et al., 2017**).

NSAIDs exert their anti-inflammatory effect through inhibition of cyclooxygenase, which is the enzyme that catalyses the transformation of arachidonic acid to prostaglandins and thromboxanes. Mefenamic acid is the most commonly used NSAID for treatment of heavy menstrual bleeding and results in a reported blood loss reduction of 25–50%. However, other NSAIDs show similar efficacy to the more commonly prescribed mefenamic acid (**Maybin and Critchley, 2016**). In addition, there is also a recent systematic review reported that NSAIDs are the first line used for treatment of menorrhagia and dysmenorrhea associated with Cu-IUCD (**Godfrey et al., 2013**).

However, many women respond well to NSAIDs and show high acceptability and satisfaction, on the other hand; a group of women may not respond to this line of treatment and obligated to shift to other treatment line or have IUCD removal (**Ali et al., 2017**).

For this reason; the prediction of the responsiveness to these drugs in controlling menorrhagia associated with Cu-IUCDs is challenging issue which should be addressed. The present study examines the hypothesis that usage of uterine artery power Doppler before starting mefenamic acid can help in prediction of the responsiveness for this treatment at one month. To our knowledge; no clinical trial had been registered or conducted to study the potential predictors of responsiveness for mefenamic acid in controlling the uterine bleeding with Cu-IUCDs.

## **Aim of the Study**

Is to use the uterine artery Doppler for prediction of response to Mefenamic acid as a treatment in women having IUCD-associated menorrhagia.

## **Intrauterine contraceptive Device**

*A*n intrauterine Contraceptive devices (IUCD) primarily the copper IUCD are used by more than 150 million women worldwide; making it the most widely used reversible method of contraception, with remarkably low failure rate of less than 1 per100 women in the first year of use (**Bliss and Tod, 2010**).

### **Types of intrauterine contraceptive devices (IUCDs):**

#### **1) Non-medicated (Inert) IUCD:**

The first IUCD used in humans was a ring-shaped device, developed in the early1900s by Ernst Grafenberg. However, this was not widely used because of possibility of infection and difficulty of removal. The first American IUCD was the Margulies coils, which frequently causing bleeding and cramping and had a hard, uncomfortable tail. The device was modified by Jack Lippes, who created the Lippes Loop IUCD, changed the ring to a loop for easy removal, and also attached a softer string for checking its position (**Peri, 2007**).

Lippes loop made of plastic impregnated with barium sulfate and it is still used throughout the world except in United State. Flexible stainless steel rings were widely used in China, which is then replaced by copper IUCD (**Bilian, 2006**).