Three dimensional and Doppler Characteristics of Subendometrium in Cases of Menorrhagia after Intrauterine Contraceptive Device Insertion

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Abstract: The intrauterine contraceptive device is one of the most frequently used method of contraception allover the world. The most important adverse effects related to copper intrauterine contraceptive device use are excessive uterine bleeding and menstrual pain which are responsible for 5-15% removal rate of IUD during the first year of its insertion. Abnormal uterine bleeding may be excessive to the extent of causing iron deficiency anemia. There are several possible mechanism that explain the cause of menorrhagia in patient using IUCD. Several studies reported that IUD insertion increase the production of prostaglandins in the endometrium which cause an increase in vascularity, vascular permeability and inhibitplatelet activity and therefore increase menstrual bleeding. With recent advances in ultrasound. Three-dimensional power Doppler ultrasound can be used to evaluate endometrial and subendometrial perfusion in cases of menorrhagia. The aim of the present study is to evaluate subendomtrial blood flow in cases of menorrhagia after copper IUCD insertion in comparison to cases using IUCD and not complaining of abnormal uterine bleeding and cases not using IUCD. This study includes 315 women divided into three groups. Group I; included 105 women using copper intrauterine device (Tcu 380A) and complaining of menorrhagia, Group II; included 105 women using copper IUD and not complaining of abnormal uterine bleeding and group III; not using any contraceptive method and not complaining of abnormal uterine bleeding. The uterus and ovaries were first visualized using conventional B-mode ultrasound to check uterine size and presence of uterine masses and the accurate placement of the device inside the uterus in first and second groups. The color pulsed Doppler was activated in the 2D mode, the right and left uterine arteries pulsatility index (PI) and resistance index (RI) were calculated. Then the ultrasound machine was switched to the 3D mode with power Doppler, subendometrial blood flow pulsatility index (PI) and resistance index were calculated then three-dimensional power Doppler vascular indices; vascularization index (VI), flow index (FI) and vacular flow index (VFI) were calculated automatically using VOCAL (virtual-organ computer aided analysis) software. As regard to Doppler findings, it was noted that PI, RI of uterine arteries and subendometrial PI and RI were significantly lower in group I incomparison to group II and group III (p-value <0.001) while subendometrial power Doppler indices VI, FI, VFI were significantly higher in group I incomparison to group II and group III. The results of our study revealed that uterine artery and subendometrial blood flow were increased in women with IUCD induced menorrhagia in comparison to women with copper IUD and not complaining of abnormal bleeding and women without copper IUD. By using ROC curves, the optimum cutoff value of VI was >4.1 and FI was >34 and VFI >0.98 with sensitivity 87.6%, 89.5% and 85.7% and specificity 96%, 95.2% and 87.6% respectively.

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1. Introduction

An intrauterine device is one of the most frequently used methods for birth control around the world ***(de Souza and Geber, 2006).***

The most important copper intrauterine contraceptive device (IUCD) related side effects are excessive uterine bleeding and menstrual pain. The menstrual blood may be excessive to the extent of causing iron deficiency anemia ***(Usama et al., 2010).***

These side effects are responsible for a removal rate of 5% to 15% during the first year after intrauterine contraceptive device (I.U.C.D) insertion ***(Jimenez et al., 2006).***

There are several possible mechanisms that explain the cause of menorrhagia in patients using

IUD. Several studies reported that I.U.D insertions 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 ***(Xin et al., 2004).***

Probably there is relation between IUD adverse effects and uterine vascularization. However, this association is neither well-known nor well-studied ***(Jimenez et al., 2006).***

Only a few studies have demonstrated an increase in subendometrial vascularization in patients with IUD induced menorrhagia ***(El-Mazny et al., 2013).***

The three-dimensional power Doppler is based on three-dimensional reconstruction of vessels image, received from power Doppler system. The intensity of three-dimensional angiography Doppler signal is directly dependent from blood flow velocity. It enables quantitative evaluation of vessels in the area studied due to the use of angiohistogram function in which 3-dimensional vascularization and blood flow indices [Vascular Index (VI)], Flow Index (FI) and Vascular Flow Index (VFI), are counted automatically ***(Dubiel et al., 2010).***

Aim of the Work

Studying subendometrial blood flow in cases after intrauterine contraceptive device insertion with and without menorrhagia compared to cases not using intrauterine contraceptive device.

2. Patients and Methods

This cross sectional case control study was performed in Al Galaa Maternity Teaching Hospital, during the period between February 2016 and September 2016. Three hundred and fifteen women attending Gynecology and family planning outpatient clinics were included in the study.

Women were divided into three groups as follows:

Group (I): included 105 women using copper T380 IUCD and complaining of menorrhagia.

Group (II): included 105 women using CuT380 IUCD and not complaining of abnormal uterine bleeding. They attended the outpatient clinic complaining of vaginal discharge or inability to feel the threads of IUCD or requesting IUCD removal.

Group (III): was a control group which included 105 women without IUCD who attended outpatient clinic complaining of vaginal discharge or requesting copper IUCD insertion and not complaining of abnormal uterine bleeding.

Inclusion criteria:

1) Age from 25 to 40 years old.
2) Regular menstrual cycle.
3) Body mass index < 30 kg/m^2.

Exclusion criteria:

1) Pregnancy.
2) Acute or chronic pelvic inflammatory disease.
3) The presence of pelvic pathology as benign or malignant genital tumors or any uterine congenital anomalies.
4) Patients on hormonal treatment in the last three months before the study.
5) Bleeding tendencies and general causes as von Willebrand disease… etc.
6) Patients on anti–coagulant and non-steroidal antinflammatory drugs.

The study protocol was approved by the hospital research ethics board. Study participants were counseled and informed consent was obtained.

3. Discussion

The use of copper IUD is a very common practice for family planning and although it has been used worldwide for many decades, many side effects are still being reported after its insertion, the most common copper IUD related side effect is extensive uterine bleeding that might lead to a high prevalence of discontinuation of the method**(Pinter, 2002)**.

One of the major problems related to the side effects of the IUD is the incapacity to anticipate weather the patient is or is not likely to have these effects mainly because their pathogenesis is still unknown**(De Souza and Geber, 2006)**.

There are several possible mechanisms that explain the cause of excessive bleeding in some patients using copper IUD, several studies reported that IUD insertion increase the production of prostaglandins in the endometrium which cause increased vascularity, vascular permeability and inhibit platelet activity and therefore increase menstrual bleeding **(Xin et al., 2009)**.

This study is one of few studies the effect of copper IUD on sub-endometrial microvascularization as measured by 3D power Doppler ultrasound.

According to the results obtained in this study, it seems that the uterine arteries and subendometrial blood flow is significantly higher in women with copper IUD and complaining of menorrhagia than women using copper IUD with normal menstrual flow or women with normal menstruation and not using any contraceptive method.

There were no significant differences between patients in the three groups with respect to age, parity, and body mass index. Using strict inclusion criteria, there were no demographic characteristic difference between women who had IUD induced menorrhagia and those without menorrhagia.

The result of the current study showed that women in group I with menorrhagia had a significant

increase in subendometrial vascularization index (VI), flow index (FI) and vascular flow index (VFI), and a significant decrease in subendometrial pulsitility index (PI), resistance index (RI) and uterine artery (PI) and (RI), in comparison with women in group II using copper IUD and not complaining of abnormal uterine bleeding and women in group III (control group).

In addition, the results of the current study revealed that there were no statistically significant differences in subendomatrial PI, RI, VI, FI, VFI, and uterine arteries PI and RI between women using copper IUD and not complaining of abnormal uterine bleeding and women in control group who not using copper IUD.

The ROC curves were used to detect the optimum cut off of subendometrial VI, FI, VFI for discrimination between women with IUCD-induced abnormal uterine bleeding and women using IUCD with normal menstrual bleeding. The ROC curves reveal that VI $\geq$4.1 with sensitivity 87.6% and specificity 96% and FI $\geq$34 with sensitivity 89.5% and specificity 95.2% and VFI $\geq$0.98 with sensitivity 85.7% and specificity 87.6% in detecting women with IUCD induced menorrhagia.

On comparing the results of current study with the results of other studies **El-Mazny et al. in 2013,** measured PI and RI of uterine arteries, endometrial and subendometrial VI, FI, VFI in 120 women before and three months after the copper IUD insertion concluded that there was a significant increase in the endometrial and subendometrial VI, FI and VFI in 47 women who had menorrhagia after IUD insertion compared to 73 women who were not complaining of abnormal uterine bleeding after insertion. Whereas the uterine artery PI and RI were not significantly different before and after IUD insertion.

Jamenez et al. in 2006 concluded that the copper IUD increases the subendometrial microvascularization of those patients who presented with IUD induced side effects (menorrhagia or dysmenorrhea) before and 3 months after IUD insertion, However uterine artery PI and RI were not altered after IUD insertion.

These two studies were prospective studies measured subendometrial microvascularization before and after insertion of Copper IUD but the current study was cross-sectional study measured subendometrial microvascularization in selected groups of patients after IUD insertion.

In agreement with the results of the current study:

Usama Fouda et al. in 2010 measured PI and RI of uterine arteries in 93 women divided into three groups, group I 32 women were complaining of menorrhagia, group II 30 women with CIUD and not complaining of abnormal uterine bleeding group III control group. 31 women without CIUD. The uterine artery PI and RI were significantly lower in group I compared to group II and group III. However there were not statistically difference in PI and RI between women in group II and women in group III.

Frajndlich et al. in 2000 measured uterine artery RI and PI in 101 women, 74 women who were using copper IUCD and 27 controls who were not using any contraceptive method.

The intrauterine contraceptive device users were divided into three groups; those with normal bleeding n=34, those with abnormal uterine bleeding without medication n=16 and those with abnormal bleeding corrected with use of prostaglandin inhibitors n=24. PI and RI were significantly lower in the group of women using intrauterine contraceptive devices who had abnormal bleeding than in all other groups.

Momtaz et al. in 1994, measured PI and RI of uterine arteries in 68 women, including 44 using intrauterine contraceptive device and 24 control women who were not using a method of contraception. Both PI and RI were significantly lower in women with copper IUD-induced bleeding than in those using IUCD and not complaining of abnormal vaginal bleeding. In addition, there were no statistically significant differences in PI and RI in women using IUCD without complaining of abnormal vaginal bleeding and women in control group.

Yigit et al. found that the PI and systole/diastole ratio in the uterine artery increased significantly 3-5 month after the insertion of a copper IUD. However, patients with increased bleeding scores had significantly lower uterine artery PI compared with those without increased bleeding scores.

In contrast to results of this study, **desauza and Geber in 2006** measured the uterine artery PI and RI in both sides in 100 patients before and 30 days after insertion of Copper IUD, no statistically significant changes in PI and RI values were detected.

Jamenez et al. in 2008 reproted that were no statistically significant differences in uterine artery PI and RI between women with IUD induced bleeding and women using IUD with normal menstruation.

El-Mazny et al. also reported that were no statistically significant differences in uterine artery PI and RI before and after Copper IUD insertion in patients with IUD induced menorrhagia.

Several hypotheses regarding the mechanism of bleeding induced by the IUD have been proposed. Among the main suggested theories is the local inflammatory reaction in the endometrium, which is associated with increased prostaglandin synthesis and local vascular changes responsible for the development of menorrhagia. **El-Sahwi et al.** observed a significant rise in both PGF2α and PGE2 concentrations in the uterine wash 3 months after IUD insertion but not in users who had used an IUCD for at least 2 years; the temporary post-insertion rise in

prostaglandin concentration coincided with the phase of increased bleeding and pain. **Xin et al.** found that there was over expression of mRNA and protein of COX-2 enzyme leading to over production of prostaglandins in the endometrium after the insertion of IUCD.

From the current study and previous studies, the copper IUD modified subendometrial mcirovascularization of those patients who presented with IUD-induced menorrhagia, through changes in the production of prostaglandins leading to increase in subendometrial, endometrial and uterine artery blood flow.

Conclusion

- 3D power Doppler vascular indices (VI, FI, VFI) were significantly higher in women with IUD induced menorrhagia than women of group II and III.
- Uterine arteries RI and PI were significantly lower in women with copper IUD induced menorrhagia.
- Subendometrial blood flow RI, PI were significantly lower in women with Copper IUD induced menorrhagia than women of group II and III.

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