Role of Uterine Artery Doppler in Assessment of Abnormal Uterine Bleeding in Females Using Copper Contraceptive Intrauterine Device

ZEINAB AZKOUL, M.Sc.; SAMY ABDEL-AZEEM, M.D.; ASHRAF NASSIF, M.D. and AMR SHARAF EL-DEEN, M.D.

The Department of Obstetrics & Gynecology, Faculty of Medicine, Benha University, Egypt

Abstract

Objectives: To evaluate the role of uterine artery Doppler in assessment of abnormal uterine bleeding in females using copper contraceptive intrauterine device.

Methods: Forty women who were using copper IUCD (TCU380A) were enrolled in the study. They were classified into two groups. Group I (control) who were using IUCD and not complaining of abnormal uterine bleeding and group II (bleeding) who were using IUCD and complaining of AUB. All under went transvaginal pulsed uterine artery doppler analysis in early follicular phase. The Pulsatility Indices (PI) and resistance indices of both right and left uterine arteries were measured. Doppler parameters were compared between both groups.

Results: There were no significant differences between the control group and bleeding group as regarding resistance and pulsatility indices (p>0.05).

Conclusion: Neither the presence of an IUCD (TCU 380A), nor the associated AUB seem to cause any change in uterine blood flow assessed by pulsed Doppler ultrasound.

Key Words: Copper intrauterine device – Uterine artery doppler – Abnormal uterine bleeding.

Introduction

AN Intrauterine Device (IUD) is a very common contraceptive method of family planning used world wide [1].

Tcu 380A, is non hormonal contraceptive device and its mechanism of action is based on the release of copper ions, which alone are spermicidal. Additionally the device causes an inflammatory action leading to hostile uterine environment [2].

The most common side effects related to the use of IUD are abnormal uterine bleeding, pelvic pain and dysmenorrhea. So, premature discontinuation affects large numbers of women. Each year, an estimated 40 million women insert IUD, from 5% to 15% of these women discontinue IUD within one year because of bleeding or pain [3].

The IUD increases menstrual bleeding by its impact on several aspects of endometrial haemostasis. IUD may increase prostaglandins (PGI2 "Prostcyclin", PGE1). These prostaglandins increase vascularity, vascular permeability and inhibit platelet activity. IUD induce menorrhgia with poor contractility of spiral arterioles in spongeous layer of endometriume. Also there is increase of fibrinolysis with IUD as a result of damage of capillary plexus causing increase and prolonged menstrual bleeding [4].

Many studies were done to evaluate the role of uterine artery doppler in assessment of abnormal uterine bleeding in females using copper intrauterine device [5]. Nuray found the mean PI to have significantly decreased with IUCD induced bleeding whereas the RI was unchanged.

[6] Kucur reported both Pulsatility Index (PI) and Resistance Index (RI) of uterine arteries to be significantly lower in patients with IUCD induced bleeding in their studies.

However, [7] Iknur Mutlu found that no statistically significant changes in PI and RI values in their studies.

Abbreviation:

IUCD : Intrauterine Contraceptive Device.
AUB : Abnormal Uterine Bleeding.
PI : Pulsatility Index.
RI : Resistance Index.
These contradictory results urged us to probe the subject.

Patients and Methods

This is a case control study, it included 40 women who were using copper IUCD (TCU380A). They were selected from Outpatient Gynecology Clinic at Benha University Hospital, during the period from November 2015 to November 2016.

40 women were divided into two groups:

Group I: 20 women using IUCD and not complaining of abnormal uterine bleeding, as a control group.

Group II: 20 women using IUCD and complaining of abnormal uterine bleeding, as bleeding group.

Inclusion criteria were:
- Age between 20 and 45 years.
- Regularly menstruating women before IUCD insertion.
- No hormonal treatment at least 3 months before the study.
- No non steroidal anti-inflammatory 24 hours before the examination.
- Body Mass Index (BMI) ≤ 30kg/m².

Exclusion criteria:
- Pregnancy.
- Nulligravida.
- Presence of systemic cause of abnormal bleeding (e.g. hypertension and thrombocytopenia).
- Present or past history of pelvic inflammatory disease.
- Presence of pelvic pathology as fibroids, ovarian cysts, pelvic endometriosis, or endometrial polyps.
- Displaced IUCD from its position, detected by ultrasound.
- Benign or malignant gynecological tumours.

The study protocol will be approved by the hospital research ethics board. Study participants will be counselled, and informed consent will be obtained.

All females were submitted to the following:

1- Full clinical history taking from the patient including age, parity, menstrual history (frequency, duration and amount), history of other contraceptive methods used before insertion of IUD, history of any drug intake, blood disease and any medical disorders.

2- Clinical examination would be done including general, abdominal and pelvic examination which include bimanual examination to detect any abnormal findings and speculum examination to exclude any local cause of bleeding as polyp or erosion, as shown in (Appendix 1).

After instructing the patients to empty their bladders, transvaginal ultrasound (Voluson 730-D, Toshiba with frequency 7.5 MHz) will be done for both groups.

Ultrasound examinations was done on day 3 or 4 of cycle to exclude possible effect of menstrual cycle phase with pulsed doppler on both right and left uterine arteries. A coupling gel was applied to the vaginal probe which was introduced into a rubber glove and another layer of coupling gel was applied to the glove. The probe was introduced into the vagina for systematic scanning. All the ultrasound measurements was measured between 9:00 am and 2:00 pm to eliminate diurnal variation.

Blood flow indices of the uterine artery were be calculated to obtain the Pulsatility Index (PI) and the Resistance Index (RI) according to the following equations:

\[ PI = \frac{S-D}{\text{mean}} \]
\[ RI = \frac{S-D}{S} \]

Where S is the peak systolic, D is the end-diastolic doppler shift, and the mean is the maximum doppler shift frequency taken over the cardiac cycle. The mean PI and RI were be calculated by combining three waveforms of the left and right uterine arteries and were be used for subsequent statistical analysis (Appendix 1).


- Doppler Indices: Rt Lt - PI - PI - RI - RI

...
A $p$-value $<0.05$ was considered statistically significant (*) while $>0.05$ statistically insignificant. $p$-value $<0.01$ was considered highly significant (**) in all analyses.

### Results

#### Table (1): Comparison between the control group who use copper IUCD and not complaining of AUB and bleeding group who use copper IUCD and complaining of AUB as regarding age distribution.

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Bleeding group</th>
<th>Test $t$</th>
<th>$p$-value</th>
<th>Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>32.1±</td>
<td>30.55±</td>
<td>$t=0.87$</td>
<td>0.39</td>
<td>Non</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>6.18</td>
<td>4.99</td>
<td></td>
<td></td>
<td>Significant</td>
</tr>
</tbody>
</table>

$p$-value $>0.05$.

So there were no significant differences between the control group and bleeding group as regarding age distribution.

#### Table (2): Comparison between the control group who use copper IUCD and not complaining of AUB and bleeding group who use copper IUCD and complaining of AUB as regarding parity.

<table>
<thead>
<tr>
<th>Parity $n$ (%)</th>
<th>Control group</th>
<th>Bleeding group</th>
<th>Test FET</th>
<th>$p$-value</th>
<th>Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primipara</td>
<td>0 (0.0)</td>
<td>4 (20.0)</td>
<td></td>
<td>0.089</td>
<td>Non</td>
</tr>
<tr>
<td>Multipara</td>
<td>20 (100)</td>
<td>16 (80.0)</td>
<td>2.89</td>
<td></td>
<td>Significant</td>
</tr>
</tbody>
</table>

$p$-value $>0.05$.

So there were no significant differences between the control group and bleeding group as regarding parity.
Table (3): Comparison between the control group who use copper IUCD and not complaining of AUB and bleeding group who use copper IUCD and complaining of AUB as regarding Body Mass Index (BMI).

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Bleeding group</th>
<th>Test</th>
<th>P-value</th>
<th>Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI:</td>
<td>25.1±3.73</td>
<td>26.05±4.03</td>
<td>t=0.77</td>
<td>0.44</td>
<td>Non Significant</td>
</tr>
</tbody>
</table>

p-value >0.05

So there were no significant differences between the control group and bleeding group as regarding Body Mass Index (BMI).

![Mean BMI of control and bleeding group.](image)

Fig. (3): Mean of BMI of control and bleeding group.

Table (4): Comparison between the control group who use copper IUCD and not complaining of AUB and bleeding group who use copper IUCD and complaining of AUB as regarding duration of IUCD insertion.

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Bleeding group</th>
<th>Test</th>
<th>P-value</th>
<th>Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of IUCD insertion</td>
<td>5.22±3.32</td>
<td>1.48±1.88</td>
<td>t=4.38</td>
<td>0.001**</td>
<td>Highly Significant</td>
</tr>
</tbody>
</table>

p-value <0.01.

So there were highly significant differences between the control group and bleeding group as regarding duration of IUCD insertion.

![Mean of duration of IUCD insertion of control and bleeding group.](image)

Fig. (4): Mean of duration of IUCD insertion of control and bleeding group.

Table (5): Comparison between the control group who use copper IUCD and not complaining of AUB and bleeding group who use copper IUCD and complaining of AUB as regarding Pulsatility Index (PI).

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Bleeding group</th>
<th>Test</th>
<th>P-value</th>
<th>Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler</td>
<td>1.94±0.63</td>
<td>2.28±0.61</td>
<td>t=1.73</td>
<td>0.092</td>
<td>Non Significant</td>
</tr>
<tr>
<td>Lt PI:</td>
<td>2.43±0.72</td>
<td>2.37±0.74</td>
<td>t=0.27</td>
<td>0.79</td>
<td>Highly Significant</td>
</tr>
</tbody>
</table>

p-value >0.05

So there were no significant differences between the control group and bleeding group as regarding Pulsatility Index (PI).

![Mean of Pulsatility Index (PI) of control and bleeding group.](image)

Fig. (5): Mean of Pulsatility Index (PI) of control and bleeding group.

Table (6): Comparison between the control group who use copper IUCD and not complaining of AUB and bleeding group who use copper IUCD and complaining of AUB as regarding Resistance Index (RI).

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Bleeding group</th>
<th>Test</th>
<th>P-value</th>
<th>Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler</td>
<td>0.98±0.41</td>
<td>0.91±0.21</td>
<td>t=0.73</td>
<td>0.47</td>
<td>Non Significant</td>
</tr>
<tr>
<td>Lt PI:</td>
<td>0.90±0.18</td>
<td>0.95±0.31</td>
<td>t=0.67</td>
<td>0.51</td>
<td>Highly Significant</td>
</tr>
</tbody>
</table>

p-value >0.05.

So there were no significant differences between the control group and bleeding group as regarding Resistance Index (RI).
An Intrauterine Contraceptive Device (IUCD) is a highly effective and prevalent form of birth control with a low failure rate. If without complications (including irregular uterine bleeding, pelvic pain, perforation, expulsion, infection, and pregnancy). Investigation of the symptomatic patient and routine follow-up of asymptomatic women with IUCDs include transvaginal ultrasonography to rule out IUCD malposition and other complications [8].

Although the use of an IUCD is a very common practice for family planning, and it has been used worldwide for many decades, many side effects are still being reported after its insertion consequently, a large number of patients have dysmenorrhea and abnormal uterine bleeding that might lead to a high prevalence of withdrawal from the method [9].

Abnormal uterine bleeding is one of the most undesirable effects of use of IUCDs. Approximately 20% of IUCD users choose to have the device removed for this reason [10].

Several factors have been suggested to explain IUD-induced bleeding. These include local vascular changes in the endometrium, with defects in the capillaries of the superficial stroma and eroded vessels at the surface, increased vascularity of the superficial endometrium in tissue adjacent to the IUCD [11].

In addition, many studies suggest that increased prostaglandin synthesis by the IUCD exposed endometrium may cause changes in endometrial vascularization and uterine blood flow and capillary permeability, and that these changes, in turn, lead to bleeding, however, none of these theories are conclusive [12].

US has a major role in the evaluation of female internal genital organs, and it provides valuable information about the vascular characteristics of these organs using Colour Doppler Sonography (CDS), particularly by transvaginal approach. There are some changes in uterine blood flow during menstrual cycle. During the normal menstrual cycle, a sharp rise of end-diastolic blood flow velocities can be demonstrated between the proliferative and secretory phases.

The blood flow resistance in the uterine artery is lowest in the mid- and late luteal phase, whereas the highest blood flow resistance in the uterine artery is on the first day of menstruation [13].

Many studies were done using doppler ultrasonography to analyze the effects of the copper T380A IUD on the uterine arteries to evaluate whether its presence could modify the uterine vasculature or not in the form of AUB [14].

In this study transvaginal pulsed doppler sonography was done in folliculare phase in day 3-4 of menstrual cycle to 40 women dividing into two groups, group (I) 20 women who were using TCU380A IUD and not complaining AUB, as control group, and group (II) 20 women who were using TCU380A IUD and complaining of AUB as bleeding group.

The result of this study showed that there were no significant differences in pulsitility index (p>0.05) and resistance index (p>0.05) in both control and bleeding groups and this means that neither the presence of IUCD (TCU380A) nor the associated abnormal uterine bleeding seem to cause any change in uterine blood flow assessed by uterine artery doppler ultrasonography.

The results of this study agreed with the results reported by Jarvela [15] who evaluated the effects of a copper IUCD on uterine artery blood flow in 21 women with regular menstrual cycles using copper IUCDs. The patients had transvaginal sonography with color Doppler flow imaging to measure the PI in the uterine arteries during the midluteal phase and on the first day of menstruation, after which the IUCD was inserted. Three months later, the patients were examined again on the corresponding cycle days. The authors did not find significant changes in uterine artery blood flow after the insertion of the IUCD during menstruation or in the midluteal phase.
The results of the present study are in agreement with that reported by deSouza and Geber [16], who reported that, the effects of the copper T380A IUCD on the uterine arteries of 100 patients were evaluated at least 30 days before IUCD insertion, and the second was performed 30 days after, patients were allocated in 2 groups according to whether they were lactating (group 2) or were not lactating (group 1) based on if there is any effect of delivery on uterine artery blood flow; however, because both groups had similar results in the first Doppler examination, they did not consider it as a bias factor. Moreover, because no difference was found between the two phases, they thought that delivery did not interfere with vascular resistance they showed that the presence of an IUCD does not interfere with the vascular resistance of the uterine arteries that can be shown by Doppler flow assessments before and 1 month after the insertion. There results were also not statistically significant when they compared the PI and RI before and after IUCD insertion for both groups.

The results of this study agreed with the results by Jamenez et al., [17] who reported that were no statistically significant differences in PI and RI between women with IUD-induced bleeding and women using IUD with normal menstruation Jamenez et al., measured PI and RI immediately before IUCD insertion in mide luteal phase and three months later after controlling age, parity and type of IUCD (TCU 380A).

The same results were found by O. Shen [18] who found no significant change in blood flow Doppler indices in 23 regular menstruating women before and after 2 months has been detected as a result of the presence of the copper-medicated IUCD in either the large pelvic vessels (uterine and ovarian arteries) or in the small ones (arcuate, radial and subendometrial artery).

The results of this study are in agreement with that reported by Ilkuner Mutlu et al., [19] in which 120 women enrolled, 13 women requested removal of the IUD before completion of the study; eight because of excessive menstrual bleeding, two whose, IUDs became dislocated, and three due to their partner’s displeasure. Three more women did not submit to a post insertion doppler examination of uterine blood flow and were lost to follow-up.

Any change in the duration of menstrual flow or the number of pads that the patient used were be considered arelevant change in menstrual status.

The uterine artery blood flow of the remaining 104 patients was evaluated using transvaginal pulsed doppler sonography by analysing the PI and the RI of the uterine arteries just before and six months after TCU380A IUD insertion.

To eliminate the influence of intercycle changes, both uterine artery doppler measurements were performed in early follicular phase.

There were no significant differences between the pre and post insertion. Copper T380A IUCD. (p-value in both >0.05).

In contrast to our results Momtaz et al., [20] measured the 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 the PI and RI were significantly lower in women with CIUD-induced bleeding than in those using CIUD and not complaining of abnormal vaginal bleeding. In addition, there were no statistically significant differences in PI and RI between women using CIUD without complaining of abnormal vaginal bleeding and women in the control group. They reported that the PI was less than 2 in women with CIUD-induced bleeding, while the mean PI in women using IUD without complications was 2.38.

The results in the present study are not in agreement with Frajndlich et al., [21] who measured resistance and pulsatility indices in 101 women, 74 of whom were using an intrauterine contraceptive device, 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).

The resistance and pulsatility values were significantly lower in the group of women using intrauterine contraceptive devices who had abnormal bleeding than in all other groups. A pulsatility index of less than 2 may be associated with a higher risk for development of intra-uterine contraceptive device-induced bleeding.

The result of these study not agreed to a study performed by Nuray et al., [22] in which a total of 28 women, 14 women (group I) had increased menstrual bleeding scores after IUCD (TCU380A) insertion, whereas 14 (group II) had no increase bleeding scores were included in the study. Colour doppler sonography with 3-5 MHZ was done to both groups before and 3-5 months after the insertion of IUCD, on the 3rd or 4th day of the menstrual cycle. No significant difference was detected be-
tween the PI and RI values for the women (group I) with increased bleeding and (group II) without increased bleeding scores recorded during their first visit. However, PI values of the women with increased bleeding scores during their second visit were significantly lower than those of women without increased scores (p<0.05).

The divergence between the results of the present study and those reported by the different authors previously mentioned, might be attributed to many variables as the patient cooperation during the examination time, the skills of the examiner, method of the study, time of follow-up of patient using IUCD in relation to cycle days, the sample size, variation in the angle of insonation of the Doppler beam which cannot be standardized or precisely determined, type of Doppler beam used, frequency used and machine resolution that affect the result of study. So, we might need more specified studies regarding patients using IUCD with abnormal uterine bleeding to confirm whether these results would be the same or not.

Conclusion:

Neither the presence of an IUCD (TCU 380A), nor the associated abnormal uterine bleeding seem to cause any change in uterine blood flow assessed by pulsed doppler ultrasonography; as there were no statistically significant differences in PI and RI between control group who were using IUCD and not complaining of AUB and bleeding group who were using IUCD and complaining of AUB, and hence, there is no role of utrine artery doppler in evaluation and prediction of abnormal uterine bleeding in female using copper (TCU30A) IUCD.

Recommendations:

Because we only analysed uterine artery doppler velocimetry. Other branches of the uterine vasculature like subendometrial microvessels could be analysed.

Endometrial, subendometrial microvascularization could be also evaluated using three-dimensional power doppler ultrasound.

It is suggested that further research should be done on this topic to confirm or negate these results.

References


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3036 Role of Uterine Artery Doppler in Assessment of Abnormal Uterine Bleeding

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دور دوردلنر الربن الربن في تكريم التزيف الفيبر طبيعي
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