

## Assessment of The Effect of Copper Coated IUCD on The Uterine Blood Flow Using The Transvaginal Colour and Pulsed Doppler Sonography

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### Abstract:

**Background:** Transvaginal colour Doppler (TVCD) Sonography is the gold standard in investigating gynecological pathologies, in addition to its close proximity to the pelvic organs that gives close view of the morphological features of the organs, it also provides an opportunity to visualize and quantify pelvic blood flow in uterine and adnexial masses. Another use of TVCD to quantify the physiological changes of the uterine and ovarian blood flow in relation to hormonal changes during the menstrual cycle. The intrauterine contraceptive device (IUCD) is a widely used measure of contraception that is not devoid of complications, and the most important one is the occurrence of menorrhagia in women using the copper coated IUCD which may be predicted by measuring both pulsatility and resistance index of uterine artery .

**Aims of the study:** The aim of this study was to evaluate the effect of copper- IUCD on uterine artery blood flow by using pulsed and colour Doppler ultrasonography.

**Patients material and method:** Sixty women were submitted to this study and after exclusion of two of them then 58 women (age range 16-45) were divided into two groups: the control group 30 women (51.72%) without IUCD and the 2<sup>nd</sup> group 28 women (48.28%) with copper coated IUCD.

The RI and PI of the uterine artery were measured by colour and pulsed Doppler TVUS, 44 women (75.86%) of them were in the proliferative and the other 14 (24.14%) were in the secretory phase of the menstrual cycle.

**Results:** the RI and the PI values of the uterine artery are changed by the phase of the menstrual cycle in both groups, the mean RI in the early proliferative phase 0.88, and in the secretory phase 0.87 of the control group, and in the IUCD group it was in the proliferative 0.85 while in the secretory was 0.86

The PI also showed differences between the two halves of the cycle in both groups: In the 1<sup>st</sup> group were 2.37, 2.13 in the early 1<sup>st</sup> and the 2<sup>nd</sup> halves of the cycle respectively, and in the 2<sup>nd</sup> was 2.15 and 2.53 in the early 1<sup>st</sup> and the 2<sup>nd</sup> halves respectively. It was evident that in women with IUCD and menorrhagia both the RI (0.81) and PI (1.78) were lower than the women with IUCD and normal menstrual flow

**Conclusions:** The IUCD does not alter the blood flow indices of the uterine arteries significantly as measured by Doppler TVUS except in susceptible women who are prone to develop menorrhagia after IUCD insertion. So it can be used to predict which women will develop menorrhagia after IUCD insertion.

### الخلاصة

ان الفحص بالامواج فوق الصائتة الملونة والنبضية المهبلية هو الطريقة المثلى للتحري عن الحالات المرضية في مجال الامراض النسائية بسبب قربه من الاعضاء التناسلية الداخلية واعطائه صورة واضحة عن تلك

الاعضاء وكذلك يمكنه قياس معدل جريان الدم في الاوعية الدموية الحوضية والرحمية بشكل خاص مما يمكن الفاحص مقارنتها مع التغيرات الطبيعية الفسلجية اثناء الدورة الشهرية للتعرف على الحالات المرضية. ان الة منع الحمل الرحمية (اللؤلؤ) هي الة واسعة الانتشار والاستعمال كمانع للحمل ولكن الكثير من النساء يشكون من زيادة النزف اثناء الدورة الشهرية مع استخدام المانع الرحمي المغطى بالنحاس الذي يعطل من قبل البعض بسبب زيادة جريان الدم في الاوعية الردموية الرحمية والذي يمكن قياسه بواسطة قياس معامل النبضية ومعامل المقاومة للجريان باستخدام السونار المهبلي الملون.

**الاهداف:** اهداف هذه الدراسة هي لتقييم تأثيرات الة منع الحمل الرحمي النحاسي على جريان الدم في الشرايين الرحمية باستخدام الفحص بالامواج فوق الصائنة الملون والنبضي المهبلي.

**طريقة العمل والنتائج:** ثمان وخمسون امرأة تم اخضاعهن للدراسة اعمارهن تتراوح بين ( 16-45) وبعد اخذ موافقتهن تم تقسيمهن الى مجموعتين: الاولى (القياسية) تتكون من 30 امرأة (لايستخدمن المانع الرحمي) والثانية 28 امرأة (يضعن المانع الرحمي النحاسي).

تم قياس معامل المقاومة ومعامل النبضية للشرايين الرحمية لكل امرأة وكانت النتائج كالتالي:

كان معامل المقاومة يتغير باختلاف وقت الفحص بالنسبة للدورة الشهرية ومعامل المقاومة في النصف الاول للدورة الشهرية هو (0.88) بينما في النصف الثاني للدورة كان (0.87) في المجموعة القياسية بينما في المجموعة الثانية كان في النصف الاول (0.85) و في النصف الثاني (0.86) وكذلك معامل النبضية كان كالتالي و للمجموعتين على التوالي:

في الاولى كان (2.73) و (2.13) على التوالي وفي المجموعة الثانية كان (2.15) و (2.53) على التوالي والملاحظ ان هناك فرق في المعاملين لكن لم يصل الى حد الاهمية الاحصائية لكن وجد ان النساء اللواتي لديهن زيادة في النزف الشهري مع استخدام المانع الرحمي كان معامل المقاومة (0.81) و معامل النبضية (1.78) اقل وبشكل واضح من النساء اللواتي لا يعانين من النزف الشهري مع استخدام المانع الرحمي.

**الاستنتاجات:** ان الة منع الحمل الرحمية لا تسبب زيادة في معاملات جريان الدم للشرايين الرحمية الا في النساء اللواتي لديهن الاستعداد لزيادة النزف في الدورة الشهرية عند استخدامه لذلك فان الفحص بالامواج فوق الصائنة الملون و النبضي المهبلي يمكن استخدامه للتحري والتنبؤ عن استعداد المرأة لزيادة النزف في الدورة الشهرية فيما اذا تم وضع الة منع الحمل الرحمية النحاسية لها.

## Introduction

Transvaginal colour Doppler (TVCD) sonography is the gold standard in investigating a gynecological pathology, in addition to its close proximity to the pelvic organs that gives close view of the morphological features of the organs, it also provides an opportunity to visualize and quantify pelvic blood flow in uterine and adnexial masses. Another use of TVCD to quantify the physiological changes of the uterine and ovarian blood flow in relation to hormonal changes during the menstrual cycle.

The follicle and corpus luteum of the ovary and endometrium are the only areas in the normal adult where angiogenesis occur, Girling JE and Rogers PA.(2005)<sup>(1)</sup>, Kurjak A.et al (1991)<sup>(2)</sup>.

During the menstrual cycle the hormonal changes of ovarian origin

play an important role in the regulation of menstruation mainly via their effects on the endometrium and its histological structure throughout the cycle. Jabbour H N. et al (2008)<sup>(3)</sup>.

Apparently there are complex relations between concentrations of ovarian hormones in peripheral blood and uterine artery blood flow parameters. Goswamy R.K. et al<sup>(4)</sup>.

In most women there is a small amount of end diastolic flow in the uterine artery during the proliferative phase.

Collins and co-workers (1991) reported that diastolic flow in the uterine artery disappeared during the day of ovulation<sup>(5)</sup>.

During the normal MC there is a sharp increase in the end diastolic velocity between the proliferative and secretory phases of the menstrual cycle.

It is particularly interesting that the lowest impedance to blood flow occur at the time of peak luteal function, during which time implantation is most

likely to occur as reported by Kurjak (1991), Steer (1991), Battaglia, and their colleagues (1990) <sup>(2, 6, 7)</sup>.

The uterine artery waveform analysis shows high to moderate flow velocity as shown in figures (1 and 2) below. the resistance index (RI) depends on the patients age, the phase of the menstrual cycle, and specific conditions such as pregnancy and uterine tumors.

The blood flow resistance is even higher in patients with dysmenorrhoeic pain during the first day of menstruation than in eumenorrhoeic patients

(Pirhonen and Pulkkinen, 1995)<sup>(8)</sup>, indicating that decreased blood flow is involved in the pathophysiology of primary dysmenorrhoea (Dawood, 1993)<sup>(9)</sup>.

Studies with TVCDS have shown that the uterine artery pulsatility index (PI), measuring arterial flow impedance, is higher in amenorrhoeic and climacteric than in menstruating women. On the other hand, PI is reduced by hormone replacement therapy and the restoration of cyclic withdrawal bleeding (De Ziegler *et al.*, 1991)<sup>(10)</sup>.



Fig 1. Uterine artery and vein visualized by TVCDS

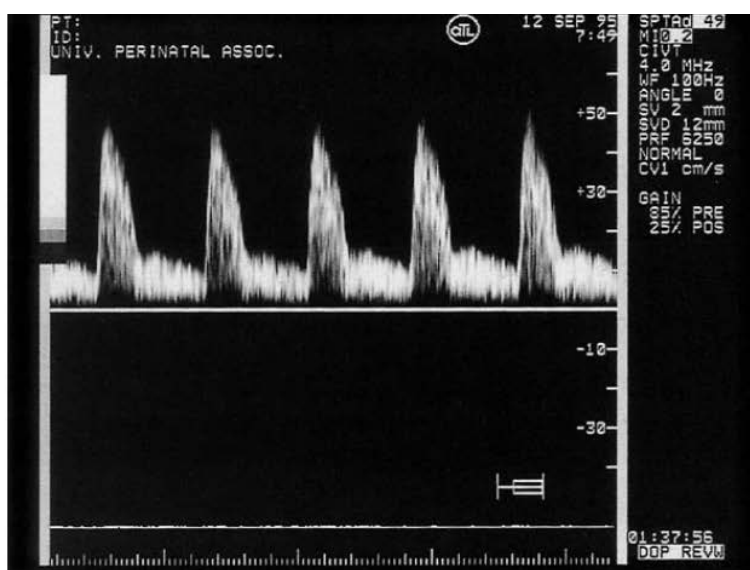


Fig 2. Typical pulsed wave Doppler waveform of the uterine artery during luteal phase of a normal menstrual cycle

The intrauterine contraceptive device (IUCD) is a widely used measure of contraception that is not devoid of complications, it induces changes in endometrial activity, and in the composition of uterine fluid, resulting in the inhibition of sperm function and blastocyst implantation and, at times, resulting in side-effects (e.g. menorrhagia and dysmenorrhoea) because of its traumatic and inflammatory effects on the endometrium (Johannisson, 1987; Ortiz and Croxatto, 1987; Kulier R et al, 2007).<sup>(11, 12, 13)</sup>

The LNG-IUS is an alternative contraception for woman with heavy period prior to IUCD use because of its local effect on the endometrium by inducing endometrial atrophy and reduced bleeding, Stewart A et al (2001)<sup>(14)</sup>

The morphological features of endometrium exposed to an IUCD (copper coated) are manifestations of localized mechanical trauma, foreign body response and impaired haemostasis, Salamonsen LA (2003)<sup>(15)</sup>.

### **Aim of the study**

The aim of this study was to evaluate the effect of copper- IUCD on uterine blood flow using pulsed and colour Doppler ultrasonography.

### **Patients and methods**

This prospective study was performed in a private ultrasound clinic in Al-Hilla city, from the period between February 2010 and October 2010.

sixty women were selected to enter this study after excluding two cases (one of them because of painful examination so it was not completed, and the 2<sup>nd</sup> one because of discovering a large ovarian mass that lead to excluding it from the study) then 58 women their

age ranging between (16-45) years, after taking their consent orally,.

Women were divided into two groups for studying purposes

(Group 1) (30) 51.72% women were non IUCD users, and (group 2) (28) 48.28% women were with copper coated IUCD fitted in place for a period ranging between (2- 72) months with a mean duration (21.3 ± 17.6) months.

### **The exclusion criteria**

Pregnancy, acute or chronic pelvic inflammatory disease, cervicitis, genital tumour, copper allergy, abnormalities in blood clotting and severe dysmenorrhoea. Also contraceptive pills had not been taken during the previous 3 months and any previous IUCD had been removed at least 1 month earlier in the 1<sup>st</sup> group. The patients were not allowed to use non-steroidal anti-inflammatory drugs (NSAID) within 24h of any examination.

### **Procedure**

The patients were examined using a pulsed colour Doppler ultrasound machine (Siemens versa plus. 6.5 MHz vaginal probe).

Women were examined in dorsal position, a coupling transonic gel was applied to the probe then a condom was put to prevent transmission of infection and another layer of the gel was applied on the condom, the uterus and the ovaries were first visualized using conventional B-mode ultrasound to rule out any pathology.

The flow velocity waveforms of the main uterine artery were obtained on both sides at the level of the inner cervical os just beside the cervix. Three similar and optimal consecutive waveforms were analyzed.

All examinations were performed between 04.00 and 07.00 hr p.m. to

reduce the effect of circadian variation in PI.

The statistical analysis was performed on a personal computer using the analysis tool pack provided with the Excel (with the ANOVA – single factor test) The  $P \leq 0.05$  was considered significant. All values given are (means  $\pm$  SD).

## Results

Fifty eight women, their age range between (16-45) years, with a mean of (28.7 $\pm$  6.5) years. And the parity is ranging between (0-8) with a mean of (2.9 $\pm$  2.1), the menstrual bleeding days duration ranging between (4-10) days with a mean of (6.13 $\pm$  1.56) days, as

Table 1. Women groups characteristics:

Character	Group 1(30) (mean) $\pm$ SD	Group 2 (28) (mean) $\pm$ SD	Total (mean) $\pm$ SD	P- VALUE
Age (years)	27.9 $\pm$ 7.2	29.6 $\pm$ 5.2	28.7 $\pm$ 6.5	NS
parity	2.7 $\pm$ 1.7	2.9 $\pm$ 1.6	2.8 $\pm$ 1.6	NS
Menstrual bleeding duration (days)	5.7 $\pm$ 1.2	6.6 $\pm$ 1.8	6.1 $\pm$ 1.6	0.02

Table 2. Cycle day examination for each women group and subgroups:

CD examination	Group 1 (n & %)	Group 2 (n & %)	Total (n & %)
CD (1-5)	4 (13.3%)	6 (21.4%)	10 (17.2%)
CD (6-14)	23 (76.7%)	11 (39.3%)	34 (58.6%)
CD (15-28)	3 (10%)	11 (39.3%)	14 (24.1%)
Total	30 (100%)	28 (100%)	58 (100%)

When comparing the (mean  $\pm$  SD) of the pulsatility index and the resistance index in group 1 and 2 in early follicular days (1-5), it is evident that there is difference in the RI and PI

Table 3. Comparison of RI and PI between the two subgroups (CD 1-5)

	GROUP 1(4) (CD 1-5) (mean $\pm$ SD)	GROUP 2(6) (CD 1-5) (mean $\pm$ SD)	p-value
RI	0.88 $\pm$ 0.07	0.85 $\pm$ 0.05	0.12
PI	2.37 $\pm$ 0.38	2.15 $\pm$ 0.31	0.09

In comparison of the (mean  $\pm$  SD) of the pulsatility index and the resistance index in group 1 and 2 in CD (6-14)

shown in table 1, it is evident that the mean menstrual bleeding days is higher in the 2<sup>nd</sup> group (IUCD users) than in the 1<sup>st</sup> group (non-IUCD users) with a p-value of 0.02 which is statistically significant (<0.05).

The parity in the 1<sup>st</sup> and the 2<sup>nd</sup> groups were comparable with no statistically significant difference.

Table 2 below show the two main groups and the subgroups according to the examination day:

Group 1 (30) 51.72% women were non IUCD users, and

Group 2 (28) 48.28% women were with copper coated IUCD fitted in place for a period ranging between (2-72) months with a mean duration (21.3  $\pm$  17.6) months.

between the two subgroups in (CD 1-5) and it is lower in the 2<sup>nd</sup> than in the 1<sup>st</sup> group but it is statistically not significant. Table (3) below:

the difference was statistically not significant. Table (4) below.

Table 4. Comparison of RI and PI between the two subgroups (CD 6-14)

	GROUP 1(23) (CD 6-14) (mean±SD)	GROUP 2(11) (CD 6-14) (mean±SD)	P-VALUE
RI	0.87± 0.06	0.88± 0.06	0.64
PI	2.38± 0.33	2.40± 0.42	0.88

And finally when comparing the (mean ± SD) of the pulsatility index and the resistance index in group 1 and 2 in the luteal phase days CD(15-28) the difference in RI was not significant but

the value of PI was higher in the second group although it did not reach the significant level. as shown in table (5) below:

Table 5. Comparison of RI and PI between the two subgroups (CD 15-28)

	GROUP 1 (3) (CD 15-28) (mean±SD)	GROUP 2 (11) (CD 15-28) (mean±SD)	P-VALUE
RI	0.87± 0.08	0.86± 0.04	0.81
PI	2.13± 0.30	2.53± 0.30	0.056

In table (6) below the mean of PI between women using the IUCD for less or equal to 12 months is significantly lower than in those using it for more than 12 months, while the

mean of RI inspite of its lower values in the 1<sup>st</sup> subgroup than in the second but it does not reach the statistical significance.

Table 6. Comparison of mean RI and PI among IUCD users when correlated to the duration of its use

	IUCD ≤12 months	IUCD > 12 months	p-value
RI (mean)	0.86 ±0.05	0.88 ±0.06	0.44
PI(mean)	2.25 ±0.33	2.54 ±0.35	0.03

## Discussion

Several studies were reviewed but non of them dealing with women with IUCD at different cycle days to perform TVDS in order to assess the changes in the uterine artery blood flow as a result of IUCD insertion, but most of them concentrate on the early (follicular) proliferative days (CD1-5) of the menstrual cycle.

In this study we took different women groups and divided them into subgroups according to the IUCD use or not and according to the cycle day examination to be more precise in results.

In this study the mean menstrual bleeding days is higher in the 2<sup>nd</sup> group (IUCD users) than in the 1<sup>st</sup> group (non-IUCD users) with a p-value of 0.02 which is statistically significant (<0.05), several factors have been suggested to explain that, these include local vascular changes in the endometrium, with defects in the capillaries of the superficial stroma, and eroded vessels at the surface that cause prolonged bleeding (Faundes, A et al, 1980).<sup>(16)</sup>

Several studies have claimed the important role of prostaglandin in genesis of IUCD induced abnormal uterine bleeding, particularly menorrhagia and in therapeutic effect of Prostaglandin synthetase inhibitors

(Roy.S. and Shaw. S.T.(1981)<sup>(17)</sup> and (Lethaby A et al (2007)<sup>(18)</sup>, also inhibition of PS can reduce the resistance to blood flow in uterine arteries during menstruation I.JARVELA. et al (1998)<sup>(19)</sup> so in this study the women were advised not to take any NSAID at least 24 hrs before examination.

In this study it was found that in women with IUCD induced heavy menstrual loss (two cases), the blood flow indices of the uterine arteries in (CD1-5) are much lower (low impedance to flow) (PI was 1.78) when compared with the women without menorrhagia, with or without IUCD (PI > 2) this is in agreement with results of (Momtaz *et al.*, 1994)<sup>(20)</sup>. These data imply a possible association between uterine blood flow and menstrual blood loss (MBL).

In studies of uterine artery PI as measured during period days (1–5) in women with normal menstruation, the mean values of PI have been ( $3.8 \pm SD 0.9$ ) (Steer *et al.*, 1990)<sup>(20)</sup>, ( $2.4 \pm SD 0.7$ ) (Momtaz *et al.*, 1994)<sup>(21)</sup>, and ( $3.0 \pm SD 0.6$ ) (Sholtes *et al.*, 1989)<sup>(22)</sup> and in this study it was ( $2.37 \pm 0.38$ ), the results of different studies are not fully comparable because of interobserver variability caused by different measuring devices and observer experience.

Steer and his co-workers (1990)<sup>(23)</sup> using the TVDS proved that the uterine blood flow is changing during the phases of the menstrual cycle so in this study the two main groups of women are further subdivided into subgroups according to the day of examination to avoid these cyclical changes.

The IUCD use although it causes lower means of RI and PI than in the non- users but these does not reach the statistically significant difference from the non-users, therefore IUCD causes elevation in the uterine blood flow and increased menstrual blood loss in a

high number of its users, and some users may develop menorrhagia.

In this study the mean PI of the IUCD users when examined in the luteal phase was higher (2.53) than that in the non users (2.13) which may indicate the poor receptivity (poor vascularity?) of the endometrium to the blastocyst by the effect of the IUCD, because in normal fertile women who is not using any contraception the mean PI in the luteal phase is lower than the follicular phase in preparation for implantation (Kurjak, Goswamy, Steer, Battaglia, and their colleagues.<sup>(2, 4, 6, 7)</sup> respectively.

## Conclusions

The presence of IUCD in the uterus did not cause a statistically significant change in the uterine blood flow unless it was associated with abnormal uterine bleeding.

The result of this study showed that the blood flow indices are influenced by the duration of the IUCD insertion Doppler ultrasound may be used for patient selection (to identify women who are prone to develop menorrhagia after IUCD insertion by measuring the blood flow indices before its insertion (if the woman has low PI < 2.0 she may develop menorrhagia after IUCD insertion!

## Recommendations

It is recommended to continue with this study in a prospective manner with larger number of women, and women with menorrhagia before and after IUCD insertion doing the Colour and Pulsed Doppler to assess the changes before and after IUCD insertion.

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