

# 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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## Introduction:

Transvaginal colour Doppler (TVCD) sonography is the gold standard in investigating a 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 follicle and corpus luteum of the ovary and endometrium are the only areas in the normal adult where angiogenesis occur, Findlay J.K.(1986)(1), Kurjak A.et al (1991)(2).

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.

Apparently there are complex relations between concentrations of ovarian hormones in peripheral blood and uterine artery blood flow parameters Goswamy R.K. et al (3, 4), .

*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(5).

During the normal MC there is a sharp increase in the end diastolic velocity between the proliferative and secretary 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), Goswamy(1988), Steer (1991), Battaglia, and their colleagues (1990) (2, 3, 6, 7).

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)(8), indicating that decreased blood flow is involved in the pathophysiology of primary dysmenorrhoea (Dawood, 1993) (9).

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)(10).

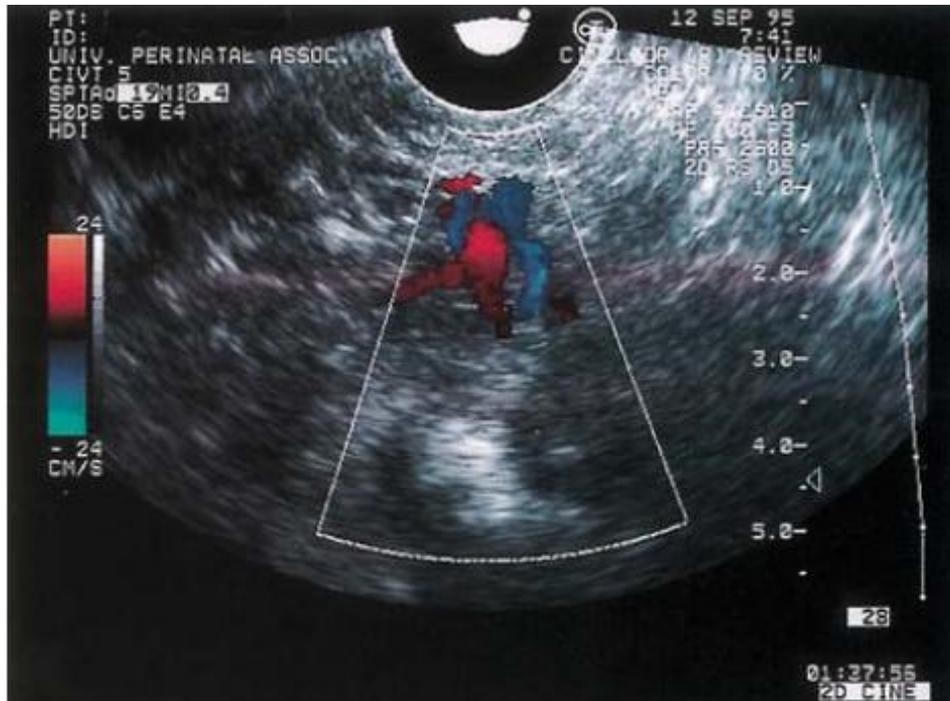


Fig 1: Uterine artery and vein visualized by TVCDS

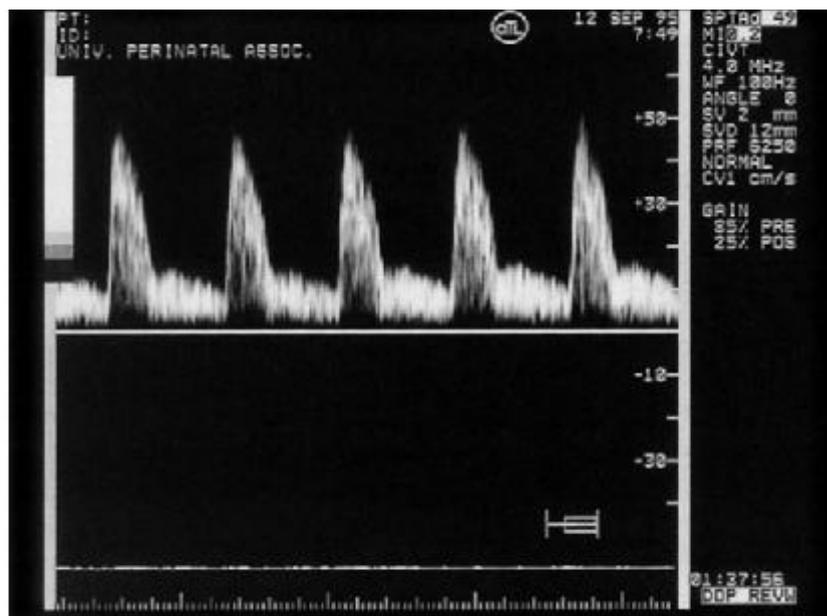


Fig 2: Typical pulsed wave Doppler waveform of the uterine artery during luteal phase of a normal menstrual cycle

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) (Johannisson, 1987; Ortiz and Croxatto, 1987; Alvarez *et al.*, 1988; Mandelin *et al.*, 1997(11, 12, 13, 14)

The morphological features of endometrium exposed to an IUCD are manifestations of localized mechanical trauma, foreign body response and impaired haemostasis (Sheppard, 1987) (15).

Many workers suggested that menorrhagia accompanying the IUCD may happen as a result of a lowered blood flow impedance caused by the IUCD itself.

### **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.

### **Women, materials, and method:**

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 leading 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 24 h 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 the 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 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.

**Table (1): women groups characteristics:**

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

**CD = cycle day of examination**

When comparing the (mean ± 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 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:

**Table (3): comparison of RI and PI between the two subgroups ( CD 1-5)**

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

**CD = cycle day of examination**

In comparison of the (mean  $\pm$  SD) of the pulsatility index and the resistance index in group 1 and 2 in CD (6-14) the difference was statistically not significant. Table (4) below.

**Table (4): comparison of RI and PI between the two subgroups ( CD 6-14)**

	<b>GROUP 1(23) (CD 6-14) (mean<math>\pm</math>SD)</b>	<b>GROUP 2(11) (CD 6-14) (mean<math>\pm</math>SD)</b>	<b>P-VALUE</b>
<b>RI</b>	<b>0.87<math>\pm</math> 0.06</b>	<b>0.88<math>\pm</math> 0.06</b>	<b>0.64</b>
<b>PI</b>	<b>2.38<math>\pm</math> 0.33</b>	<b>2.40<math>\pm</math> 0.42</b>	<b>0.88</b>

**CD = cycle day of examination**

And finally when comparing the (mean  $\pm$  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)**

	<b>GROUP 1 (3) (CD 15-28) (mean<math>\pm</math>SD)</b>	<b>GROUP 2 (11) (CD 15-28) (mean<math>\pm</math>SD)</b>	<b>P-VALUE</b>
<b>RI</b>	<b>0.87<math>\pm</math> 0.08</b>	<b>0.86<math>\pm</math> 0.04</b>	<b>0.81</b>
<b>PI</b>	<b>2.13<math>\pm</math> 0.30</b>	<b>2.53<math>\pm</math> 0.30</b>	<b>0.056</b>

**CD = cycle day of examination**

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). (16)

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) (17) and (Davies.A.J. et al (1981) (18), also inhibition of PS can reduce the resistance to blood flow in uterine arteries during menstruation I.JARVELA. et al (1998)(19) 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)(20). 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 ± SD 0.9) (Steer *et al.*, 1990) (21), (2.4 ± SD 0.7) (Momtaz *et al.*, 1994) (20), and (3.0 ± SD 0.6) (Sholtes *et al.*, 1989) (22) and in this study it was (2.37 ± 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) (23) 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.(2, 3, 6, 7) respectively.

### **conclusions:**

The presence of IUCD in the uterus did not cause a statistically significant changes 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!

### **REFERENCES:**

1. Findlay JK; angiogenesis in reproductive tissue; journal endocrinol(1986) **111**: 357-361
2. Kurjak A , kupesic Urek S, Shulman H, Zalud I, Transvaginal colour flow Doppler in the assessment of ovarian and uterine blood flow in infertile women. Fertility sterility (1991); **56**: 870-873.
3. Goswamy RK, William G, Steptoe PC; Decreased uterine perfusion – a cause of infertility : hum reprod (1988); **3**: 955-959.

4. Goswamy RK, Steptoe PC; Doppler ultrasound study of uterine artery in spontaneous ovarian cycle; *Hum reprod* (1988) ; **3**: 721-726.
5. Collin W, Jurkovic D, Bourne T, Kurjak A, Campbell S, Ovarian morphology, endocrine function and intrafollicular blood flow during the peri-ovulatory period. *Hum reprod* (1991); **3**: 319-322.
6. Steer CV, Mills CV, Campbell S, vaginal color Doppler assessment on the day of embryo transfer accurately predicts patients in an invitro fertilization programme with suboptimal uterine perfusion who fail to be pregnant. *Ultrasound obstet gynecol* (1991) ; **1**: 79-83.
7. Battaglia C, Larocca E, Lanzani A, Valentini M, Genazani AR, Doppler ultrasound studies of the uterine arteries in spontaneous and IVF cycles. *Gynecol endocrinol* (1990); **4**: 245-248.
8. Pirhonen, J. and Pulkkinen, M. The effect of nimesulide and naproxen on the uterine and ovarian arterial blood flow velocity. A Doppler study. *Acta Obstet. Gynecol. Scand.* (1995), **74**: 549–553.
9. Dawood, M.Y. Nonsteroidal antiinflammatory drugs and reproduction. *Am. J. Obstet. Gynecol.* (1993), **169**: 1255–1265.
10. De Ziegler, D., Bessis, R. and Frydman, R. Vascular resistance of uterine arteries: physiological effects of estradiol and progesterone. *Fertil. Steril.* (1991), **55**: 775–779.
11. Johannisson, E. Mechanism of action of intrauterine devices: biochemical changes. *Contraception* (1987), **36**: 11–22.
12. Ortiz, M.E. and Croxatto, H.B. The mode of action of IUDs. *Contraception* (1987), **36**: 37–53.
13. Alvarez, F., Brache, V., Fernandez, E. *et al.* New insights on the mode of action of intrauterine contraceptive devices in women. *Fertil. Steril.* (1988), **49**: 768–773.
14. Mandelin, E., Koistinen, H., Koistinen, R. *et al.* Levonorgestrel releasing intrauterine device-wearing women express contraceptive glycodeilin A in endometrium during midcycle: another contraceptive mechanism? *Hum. Reprod.* (1997), **12**: 2671–2675.
15. Sheppard, B.L. Endometrial morphological changes in IUD users: a review. *Contraception* (1987), **36**: 1–10.
16. Faundes, A., Segal, S.J., Adejuwon, C.A. *et al.* The menstrual cycle in women using an intrauterine device. *Fertil. Steril.* (1980), **34**: 427–430.

17. Roy, S. and Shaw, S.T. Role of prostaglandins in IUD-associated uterine bleeding—effect of a prostaglandin synthetase inhibitor (ibuprofen). *Obstet. Gynecol*(1981)., **58**: 101–106.
18. Davies, A.J., Anderson, A.B. and Turnbull, A.C. Reduction by naproxen of excessive menstrual bleeding in women using intrauterine devices. *Obstet. Gynecol.* (1981), **57**: 74–78.
19. I.Jarvela, A.Tekay, and P.Jouppila ; the effect of diclofenac on uterine artery blood flow resistance during menstruation in patients with and without a copper intrauterine device. *Hum reprod* (1998) **13**: 2480-2483.
20. Momtaz, M., Zayed, M., Rashid, K. *et al.* Doppler study of the uterine artery in patients using an intrauterine contraceptive device. *Ultrasound Obstet. Gynecol.* (1994), **4**: 231–234.
21. Steer, C.V., Campbell, S., Pampiglione, J.S. *et al.* Transvaginal colour flow imaging of the uterine arteries during the ovarian and menstrual cycles. *Hum. Reprod* (1990)., **5**, 391–395.
22. Sholtes, M., Wladimiroff, J., van Rijen, H. *et al.* Uterine and ovarian flow velocity waveforms in the normal menstrual cycle: a transvaginal Doppler study. *Fertil. Steril.* (1989), **52**: 981–985.
23. Steer CV, Campbell S, Pampiglione JS, Kingsland CR, Mason BA and Collins WP Transvaginal colour flow imaging of the uterine arteries during the ovarian and menstrual cycles. *Hum Reprod* (1990) **5**: 391-395.