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Original Research Article

Effect of bilateral uterine artery ligation in cases of postpartum hemorrhage on ovarian reserve

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ABSTRACT

Background: Bilateral uterine artery ligation (BUAL) is a fertility-preserving procedure used in women experiencing postpartum hemorrhage (PPH). However, the long-term effects of this procedure on ovarian reserve remain unclear. Aim to investigate the effect of BUAL in cases of PPH on ovarian reserve**,**
Methods: This study was carried out at department of obstetrics and gynecology Tanta university on 40 patients divided into 2 groups: (The study group); included 20 patients underwent cesarean section with successful BUAL for intractable atonic PPH, (The control group); included 20 patients underwent cesarean section without BUAL; during a period between April 2020 and December 2021,
Results: There is no-significant difference between study and control group according to AMH (ng/ml), resistivity index (RI) and pulsatility index (PI) of right and left uterine artery and ovarian artery after 6 months of bilateral UAL**,**
Conclusions: Bilateral UAL had no negative effects on ovarian reserve or ovarian blood supply, so this treatment should be used as a fertility preservation technique to avoid hysterectomy in patients experiencing PPH**,**

Keywords: Hemorrhage, Postpartum, Ovarian blood flow, Ovarian reserve, Uterine artery ligation

INTRODUCTION

Postpartum hemorrhage (PPH) is the leading cause of maternal mortality. Its causes include placenta accreta, placental abruption, genital tract laceration, coagulation disorders and the most common cause uterine atony.[1] Management of PPH due to uterine atony during cesarean section is done by several lines, pharmacological therapies and bimanual compression is the first line, if failed BUAL, B-Lynch technique, modified compression sutures, internal iliac artery ligation and even hysterectomy.[2]

BUAL is one of the most popular fertilities preserving surgical technique to control PPH. It is easy, effective, relatively safe and rapid maneuver with success rate over 90%.[3] The blood supply to the ovaries comes from the ovarian arteries which are branches from abdominal aorta and from the uterine arteries. BUAL can decrease blood flow to the ovaries affecting ovarian reserve.[4,5] Many studies have reported that hysterectomy with preservation of both ovaries can lead to decrease ovarian reserve, elevation of FSH hormone level and early menopause.[5] Another study reported that ovarian reserve is reduced after uterine artery embolization.[6] However the effect of BUAL on ovarian blood supply and ovarian reserve has not been adequately studied.

Decrease ovarian blood flow can lead to diminished ovarian reserve which is a major cause of infertility.[7] Ovarian reserve markers include day 3 FSH level, anti-Mullarian hormone (AMH) and antral follicle count.[8] The study will investigate the effect of BUAL on ovarian reserve. The study aimed to investigate the effect of BUAL in cases of PPH on ovarian reserve.

METHODS

The study was done between April 2020 and December 2021 at department of obstetrics and gynecology Tanta university. This prospective study included 40 patients

aged between 20 and 35 years delivered by cesarean section for obstetric indications.

The study group includes 20 patients who underwent cesarean section with successful BUAL for atonic PPH.

The control group consisted of 20 patients who underwent cesarean section without BUAL or any other interventions for PPH. Fundal massage, bimanual compression, oxytocin administration, methylergonovine maleate, and rectal misoprostol were applied to all patients.

Inclusion criteria: between 20 and 35 years, 1st cesarean section, pregnant without ovulation induction.

Exclusion criteria: Patients with uterine, ovarian anomalies, blood diseases, previous uterine or ovarian surgery. Patients receiving B-Lynch or other hemostatic sutures, stepwise uterine devascularization, internal iliac artery ligation, or hysterectomy.

Patients included in the study were subdivided into 2 groups; study group includes 20 patients who underwent cesarean section with successful BUAL for atonic PPH. The control group includes 20 patients who underwent cesarean section without BUAL or any other interventions.

PPH was defined as blood loss greater than about 1,000 mL during cesarean section. Intractable PPH was defined as PPH that persisted despite standard medical treatment.

Bilateral UAL was performed 2 cm below the Kerr incision A 1-vicryl absorbable suture was placed from the anterior to posterior aspects of the myometrium 2-3 cm medial to the descending part of the uterine vessels through an avascular space in the broad ligament and tied.

Follow up of both groups was done 6 months after cesarean section by; The ovarian reserve markers including anti-Mullerian hormone level (AMH ng/ml). Doppler screening for PI and RI of both uterine and ovarian arteries on both sides. Measurement of serum AMH quantitative measurement of serum AMH, name: Ultra-sensitive AMH/MIS ELISA.

Principle of the test

AMH ELISA assay kit is designed, developed and produced for quantitative measurement of human AMH in serum or heparin plasma samples. AMH assay utilizes the two-site "sandwich" technique with two selected antibodies that bind to different epitopes of human AMH.

In this AMH Assay, calibrators, controls and patient samples are added directly to wells of a microtiter plate that is coated with antibody to N-terminal AMH along with another AMH specific antibody labeled with horseradish peroxidase. After an initial incubation period, the plate is washed a sandwich of solid-phase antibody-human AMH-HRP-conjugated monoclonal antibody is formed. The unbound monoclonal antibodies and buffer matrix are removed in the subsequent washing step. For the detection of this immunocomplex, the well is then incubated with a substrate solution in a timed reaction and then measured in spectrophotometric microplate reader. Enzymatic activity of immunocomplex bound to wall of each microtiter well is directly proportional to amount of human calprotectin in test sample. A standard curve is generated by plotting absorbance verse respective human calprotectin concentration for each standard on cubic/ point-to-point curve fitting. Concentration of human AMH in test samples is determined directly from this calibration curve.

Table 1: Normal range of AMH.

Interpretation (women under age 35 Years)	AMH blood level (hg/ml)
High (often PCOS)	Over 4.0
Normal	1.5-4.0
Low normal range	1.0-1.5
Low	0.5-1.0
Very low	Less than 0.5

Transvaginal USG measurements

For ultrasonographic evaluation we used transvaginal 7.5 MHz (KAIXIN KX2000E+) in obstetrics and gynecology department Tanta University hospital. Transvaginal USG was carried out at any time regardless time of menstruation by the same observer.

The ultrasound settings were standardized, with a pulse repetition frequency of 1.3 kHz for the uterine and ovarian arteries and 1.1 kHz for the spiral artery to evaluate a minimum flow velocity of 5 cm/sec, gain of 3.4, a low wall motion filter (1), the harmonic setting at low, and power at 100%. The same procedure was applied to all patients.

Transverse and sagittal imaging of uterus and ovaries was performed using an endovaginal probe. Spiral arteries were assessed within a 1-mm area parallel to myometrium-endometrium border by color Doppler. Descending branches of uterine artery were measured at the level of the internal OS of cervix uteri. Ovarian arteries were evaluated as the large vessels at the level of the ovarian hilum. PI and RI of right and left uterine and ovarian arteries on both sides were calculated. Average values were recorded.

Statistical analysis

Statistical analysis was done by SPSS v25 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean, standard deviation (SD) and range and were compared between the two groups utilizing unpaired Student's t test. Categorical variables were presented as frequency and percentage and were analysed utilizing the Chi-square test or Fisher's exact test when appropriate. Pearson or Spearman coefficient correlation (r) was used to estimate the degree of correlation between two variables. $P<0.05$ was considered statistically significant.

RESULTS

Gravidity in study group ranged from 1 to 3 with mean ± SD (1.65±0.75) and control group ranged from 1 to 3 with mean ± SD (1.70±0.80). There is no-significant difference between study and control group according to gravidity. Parity in study group ranged from 0 to 2 with mean ± SD (0.50±0.76) and control group ranged from 0-2 with mean ± SD (0.55±0.69). No significant difference between study and control group according to parity. Age in study group ranged from 21 to 32 with mean ± SD (26.80±3.37) and control group ranged from 21-34 with mean ± SD (26.70±3.92). No significant difference between study and control group according to age. BMI in study group ranged from 21-24 with mean ± SD (22.95±0.89) and control group ranged from 21-24 with mean ± SD (22.85±0.99). No significant difference between study and control group according to BMI (Table 2).

AMH in study group ranged from 1.8-2.8 with mean ± SD (2.25±0.28) and control group ranged from 2.1 to 2.98 with mean ± SD (2.37±0.24). No significant difference between study and control group according to AMH (Table 3).

The right UA RI in study group ranged from 0.75 to 0.86 with mean ± SD (0.80±0.03) and control group ranged from 0.71 to 0.83 with mean ± SD (0.78±0.04) with no-significant difference between the studied groups (p=0.170). Likewise, there is no-significant difference between the studied groups regarding LT UA RI (p=0.851) as left UA RI in study group ranged 0.69-0.81with mean ± SD (0.75±0.04) and control group ranged from 0.74 to 0.8 with mean ± SD (0.75±0.03) (Table 4).

Right UA PI in study group ranged from 0.8 to 2.7 with mean ± SD (1.64±0.56) and control group ranged from 0.79 to 2.69 with mean ± SD (1.68±0.59) with no-significant difference between studied groups (p=0.861). Left UA PI in study group ranged from 1.5-2.9 with mean ± SD (2.07±0.44) and control group ranged from 0.89 to 2.72 with mean ± SD (1.77±0.55) with no-significant difference between studied groups (p=0.066) (Table 5).

The right OA RI in study group ranged from 0.60 to 0.69 with mean ± SD (0.65±0.03) and control group ranged from 0.61 to 0.67 with mean ± SD (0.63±0.02) with no-significant difference between the studied groups (p=0.079). Likewise, there is no-significant difference between the studied groups regarding LT OA RI (p=0.807) as left OA RI in study group ranged 0.64 to 0.77 mean ± SD (0.71±0.03) and control group ranged from 0.66 to 0.77 with mean ± SD (0.71±0.03) (Table 6).

Table 2: Comparison between the two studied groups regardingclinical and demographic characteristics.

Variables		Study	Control	T test	P value
Gravidity	Range	1±3	1±3	0.204	0.839
	Mean ± SD	1.65±0.75	1.70±0.80		
Parity	Range	0±2	0±2	0.218	0.828
	Mean ± SD	0.50±0.76	0.55±0.69		
Age	Range	21±32	21±34	0.087	0.931
	Mean ± SD	26.80±3.37	26.70±3.92		
BMI (Kg/m^2)	Range	21±24	21±24	0.337	0.738
	Mean ± SD	22.95±0.89	22.85±0.99		

Table 3: Comparison between the two studied groups regarding AMH (ng/ml).

AMH	Study	Control	T test	P value
Range	1.8±2.8	2.10±2.98	1.456	0.154
Mean ± SD	2.25±0.28	2.37±0.24		

Table 4: Comparison between the two studied groups regarding right and left UA RI.

Variables		Study	Control	T test	P value
Right UA RI	Range	0.75±0.86	0.71±0.83	1.397	0.170
	Mean ± SD	0.80±0.03	0.78±0.04		
Left UA RI	Range	0.69±0.81	0.71±0.8	0.189	0.851
	Mean ± SD	0.75±0.04	0.75±0.03		

Table 5: Comparison between the two studied groups regarding right and left UA PI.

Variables		Study	Control	T test	P value
Right UA PI	Range	1.5±2.9	0.89±2.72	1.894	0.066
	Mean ± SD	2.07±0.44	1.77±0.55		
Left UA PI	Range	0.8±2.7	0.79±2.69	0.176	0.861
	Mean ± SD	1.64±0.56	1.68±0.59		

Table 6: Comparison between the two studied groups regarding right and left OA RI.

Variables		Study	Control	T test	P value
Right OA RI	Range	0.6±0.69	0.61±0.67	1.807	0.079
	Mean ± SD	0.65±0.03	0.63±0.02		
Left OA RI	Range	0.64±0.77	0.66±0.77	0.246	0.807
	Mean ± SD	0.71±0.03	0.71±0.03		

DISCUSSION

PPH is a life-threatening complication. Uterine atony is considered to be the most common cause. The other known risk factors for PPH include placenta accrete, placental abruption, retained placenta, genital tract lacerations, uterine rupture, and coagulation disorders.[9]

Bimanual uterine compression, pharmacological therapies, and intrauterine balloon tamponade are the first-line therapies for atonic PPH. If these therapies fail, surgery may be needed to control the hemorrhage. Hysterectomy is the definitive surgical procedure for blood loss; however, it is a radical procedure, especially in young women. For this reason, several fertility-preserving surgical techniques have been developed, such as uterine artery ligation (UAL), internal iliac artery ligation, the B-Lynch technique, and modified compression sutures.[10]

In accordance with our results, study of Samy et al as they included in the BUAL group, women underwent BUAL before placental delivery; in the control group, women had cesarean delivery without BUAL. They found that there were no significant differences in age, BMI, number of previous cesarean deliveries or parity (all p>0.05).[11]

Similarly, Mohamed et al demonstrated that there was no significant difference between their studied groups regarding demographic characteristics.[12]

BUAL is a quick and easy surgical procedure that can be coupled with uterotonics to prevent PPH in high-risk cases such as placenta previa. It is also the first step in a uterine devascularization approach that can bring about bleeding control in established cases of PPH, and it can be used prophylactically to reduce the incidence of PPH in high-risk cases. A recent retrospective study concluded that, for women with placenta accreta, BUAL before placental delivery can effectively reduce intraoperative blood loss, incidence of PPH, and the risk of complications such as hysterectomy. Uterine artery ligation does not harm the uterus and does not seem to affect subsequent reproductive function. It has also been reported that BUAL is a safe and easy method to control bleeding during cesarean delivery among women with, or at increased risk for, perioperative blood loss because it decreases uterine bleeding by reducing perfusion pressure in the myometrium.[13]

Our results were in agreement with study of Verit et al as they included 49 women aged between 21 and 36 years.[14] Of the 49 participants, 25 received uterine bilateral UAL by the same surgeon to control intractable atonic PPH. The control group consisted of 24 healthy women who had not undergone bilateral UAL or any other interventions for PPH. They revealed that there were no differences in terms of AMH levels between the groups (p>0.05).

Our results were in agreement with study of Verit et al as they reported that the results for uterine PI and RI are shown.[14] Likewise, no-significant differences were observed in uterine PI and RI among patients who underwent bilateral UAL and those who did not (p>0.05).

In the previous study, they found that the uterine artery blood supply was not compromised after bilateral UAL.[14] The result is especially important for young women who are expecting future pregnancies, because it is widely known that uterine blood flow is essential for promoting a receptive endometrium, embryo implantation, trophoblast invasion, and successful pregnancy.[15] Chang et al reported that bilateral UAL through laparoscopic myomectomy did not decrease uterine artery PI and RI values at 3 months after surgery.[16] Moreover, other studies have also demonstrated that uterine artery PI and RI values did not change after bilateral internal iliac artery ligation.[17]

Our results were in line with study of Verit et al as they reported that the results for ovarian artery PI and RI are shown.[14] Likewise, no-significant differences were observed in ovarian artery PI and RI among patients who underwent bilateral UAL and those who did not (p>0.05 for all).

Preserving ovarian blood supply during surgical procedures is important, especially in young women of reproductive age. Bilateral UAL is one of the most important fertility-preserving techniques in patients experiencing PPH, and Verit et al study showed that it did not compromise ovarian blood supply and ovarian reserve in those patients, suggesting that UAL should be used to avoid hysterectomy in cases of PPH.[14]

There may be some explanations for why uterine blood flow was restored 6 months after surgery. They used absorbable suture material and the recanalization rate of the uterine artery was found to be high at 6 months after surgery. Studies have also documented the possibility of increased collateral blood flow after bilateral UAL. The patients were re- evaluated at 6 months after surgery in this study because Vicryl theoretically undergoes complete absorption within 6 months.[18]

Been proposed as factors associated with ovarian failure.[19] However, ovarian artery embolization has not been clearly

demonstrated to affect ovarian reserve, and multiple studies have indicated that it does not seem to increase the risks of permanent amenorrhea, premature menopause, or menopausal symptoms compared with UAE. Moreover, the natural flow of the embolic agent is not towards the ovaries, and flow to the ovaries may not be present under normal conditions during embolization.[20]

Recent studies demonstrated that UAE had no effect on ovarian reserve markers in patients younger than 40-45 years of age. No significant differences in AMH and FSH levels were found in women younger than 45 years at 12 months after UAE. Furthermore, no cases of amenorrhea were observed in that group.[21] It was also reported that UAE did not affect ovarian reserve in women younger than 40 years and that ovarian reserve tests did not show any statistically significant differences in those subjects; those findings are similar to our results.[22]

However, there were some limitations of this study. First, the study size was relatively small. Second, we were not able to evaluate the ovarian reserve markers of the patients before pregnancy and surgery, because it was impossible to determine which patients would become pregnant, undergo cesarean sections, develop PPH, and undergo bilateral UAL.

CONCLUSIONS

It was concluded that bilateral UAL had no negative effects on ovarian reserve or ovarian blood supply, so this treatment should be used as a fertility preservation technique to avoid hysterectomy in patients experiencing PPH.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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