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The efficacy of tranexamic acid for decreasing blood loss in open myomectomy

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Abstract Uterine fibroids are the most prominent benign tumor in females. Recently, attention has focused on the use of tranexamic acid to reduce blood loss if given prophylactically at myomectomy. We conducted this study to evaluate the efficacy and safety of perioperative tranexamic acid in blood loss reduction in many patients with uterine fibroids undergoing myomectomy *et al* Basrah maternity and children's hospital in Basrah. The study was conducted at Basrah maternity and child hospital for the period from the 1st of January 2020 till the 1st of January 2023. It includes 98 (48 control who received no medication before the surgery and 50 cases patients who received IV 1 g tranexamic acid at the skin incision) ladies who planned to undergo open myomectomy. The duration of surgery was calculated in minutes, Intraoperative, postoperative, and total blood loss was measured. Abdominal pain was the commonest presenting symptom of fibroid in both case and control group (56.0% and 52.1%, respectively) and followed by AUB then the infertility. Regarding the intraoperative, postoperative, and total blood loss there's a significant significant difference between case and control group. The operation time and hospital stay were significantly less among case group who received IV tranexamic acid. Tranexamic acid is a safe drug to reduce hemorrhage in women with fibroid subjected to open myomectomy and it has no major adverse effects.

Keywords: tranexamic acid, myomectomy, uterine fibroids, childbearing, basrah

1. Introduction

Uterine fibroids are the most common benign tumors in females and are also known as leiomyomas. Uterine leiomyomas are hormone-responsive tumors that develop from myocytes in the myometrium, mainly through the formation of a solitary smooth muscle cell (of monoclonal origin) (Flake et al., 2003).

Fibroids mostly afflict women during their childbearing life, are exceedingly rare before menarche, and normally retreat after menopause due to their hormonally dependent character (Marsh and Bulun, 2006). According to a study published in early 2003 by Baird et al., the calculated incidence of fibroids among women aged >50 years was 70% for white women and >80% for black women (Day Baird et al., 2003). Fibroids are far more prevalent in African-American women than in Asian and white women; they appear at an earlier age, they are more numerous, and they are larger in size [(3)]. As mentioned, fibroids are formed by uterine smooth muscle cells (myometria), whose proliferation is predominantly influenced by circulating estrogen levels (Zimmermann et al., 2012).

Being overweight, infertile, hypertensive, late menopausal, or pregnant early in age; having a family history of fibroids; and being of advanced age are all risk factors (Bulun, 2013). Diet, exercise, tobacco, alcohol consumption, stress, and other biological influences all play important roles in the pathophysiology of uterine fibroids, although the impact of these factors on the pathophysiology of uterine fibroids is unclear.

Recently, attention has focused on the use of tranexamic acid to reduce blood loss if administered prophylactically at myomectomy (Conforti et al., 2015). Tranexamic acid is an antifibrinolytic medication that is often used to treat menstruation irregularities. It inhibits the conversion of plasminogen into plasmin, which is the major degradation outcome of pro-coagulation compounds, in a competitive manner. After a cesarean section as well as a cervical operation, tranexamic acid greatly lowers hemorrhage (Gai et al., 2004).

Caglar et al. (2008) investigated the effects of intravenous tranexamic acid before myomectomy in a randomized controlled trial. They discovered that a substantial difference was found in a limited number of patients with numerous myomas.

Tranexamic acid may decrease the need for hysterectomy, lower the chance of developing severe anemia, and eliminate the need for blood transfusions; as a result, it may greatly help achieve the goal of lowering morbidity and mortality (Lakshmi, 2016). TXA should be administered at a fixed dose of 1 g in 10 mL (100 mg/mL) IV at 1 mL/min (i.e.,

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administered over 10 minutes), with a second dose of 1 g IV if bleeding continues after 30 minutes. TXA should be administered via an IV route only for the treatment of PPH (Gai et al., 2004).
Study Aim We conducted this study to evaluate the efficacy of perioperative tranexamic acid for reducing blood loss in patients with uterine fibroids who underwent myomectomy at the Basrah Maternity and Children's Hospital in Basrah.

2. Patients and Methods

2.1. Study Setting

A prospective case–control randomized clinical trial is needed to study the efficacy of tranexamic acid in decreasing blood loss during open myomectomy. The study was conducted at Basrah Maternity and Child Hospital, which is the main referral center that serves the southern part of Basrah city from the 1st of January 2020 until the 1st of January 2023. A total of 98 (48 controls and 50 patients) women who planned to undergo open myomectomy were included.
All our patients were women who attended the outpatient gynecology clinic of Basrah Maternity and Child Hospital; all were seeking treatment for symptomatic fibroids and planned to undergo open abdominal myomectomy.

2.2. Study population

The studied population was divided into two groups. Group 1 included 50 patients who received 1 g of tranexamic acid (made by Pfizer) (2 ampoules of 500 mg of kapron in 5 ml, AMOUN) just before the skin incision. All patients received the same type of injection. Group 2 included 48 patients in the control group who did not receive tranexamic acid before surgery.

All patients underwent U/s or MRI imaging to assess the number, location, and diameter of the fibroids and classify them according to FIGO staging. The duration of surgery was calculated in minutes from the time of incision on the uterus to the time of the last uterine stitch applied by the doctor.

2.3. Blood loss estimation

Intraoperative blood loss was measured by the volume of blood in the suction bottle and the difference in weight between the dry and soaked operation packs of the same type used and the covering sheets and towels (1 g = 1 ml). Postoperative blood loss was estimated through the use of an intraperitoneal drain, which was maintained for 24 hours postoperatively. Total blood loss was subsequently calculated by summing the intraoperative and postoperative blood loss. The secondary outcome measures included the need for blood transfusion, operative time, and hospitalization duration.
The hemoglobin concentration was measured in all patients preoperatively and 24 hours postoperatively, and the change in concentration was measured. Any side effects such as nausea, vomiting, or diarrhea were recorded. All participating patients were informed about the study, and they were signed and asked for permission to be part of the study. All personal information was kept anonymous.

2.4. Statistical analysis

The data set was checked for any missing data and subsequently entered into the Statistical Package for the Social Sciences (SPSS) version 26, which was used to code and analyze the data. The X2 test and Fisher's exact test were used to evaluate associations between groups, and a P value ≤ 0.05 was considered to indicate statistical significance.

3. Results

Our study starts with 128 patients at Basrah maternity and child hospital, from the 1st of January 2020 till the 1st of January 2023 for open abdominal myomectomy who were asked to participate in the study.22 patients were excluded because they didn't meet the inclusion criteria and 8 patients refused to participate so the remaining patients were 98. Patients were divided into two groups. Group 1: The case group included 50 patients who received 1 g of tranexamic acid IV at the time of skin incision, whereas group 2 (the control group) did not receive any drugs in the form of IV fluid at the time of skin incision. There was no significant difference between the two groups with respect to age, BMI, parity, or other demographic characteristics. Table 1 shows that there was no significant difference among the studied groups regarding demographic characteristics.

Table 2 shows that approximately 56% of the patients presented with abdominal pain, followed by 42% with AUB, whereas 52.1% and 39.5% of the patients in the control group presented with abdominal pain.

Table 3 shows that the total blood loss among the patients was 718± 196.3 ml in comparison to 1102±120.7 ml in the control group, and this difference was statistically significant.

Table 4 shows that there was a significant reduction in Hb levels in the control group compared to those in the case group; these patients needed more time to stay at the hospital, and the difference was statistically significant.

Table 1 Patient demographic and preoperative data.

Variables		Case (50)	Control (48)	p value
Age in years		39.3 (25-45)	38.6 (24-45)	0.456
Body mass index		27.6 (24-31.2)	28.2(25-32.3)	0.723
Parity	Nullipara	12(24%)	14 (29.1%)	0.652
	P1-4	20 (40%)	15 (31.3%)	
	≥ P5	18 (36%)	19 (39.6%)	
Level of education	Illiterate	22 (24%)	19 (39.6%)	0.572
	Medium	10(20%)	14 (29.1%)	
	High	18 (36%)	15 (31.3%)	
Preoperative Hb%		10.3 ±1.2	10.4±1.4	0.96
No. of myoma	1	6 (12%)	5 (10.4%)	0.925
	2-4	28 (56%)	26(54.2%)	
	≥5	16 (32%)	17(35.4%)	
Size of myoma	<5 cm	27(54%)	25 (52.8%)	0.849
	≥5 cm	23 (46%)	23(47.2%)	
	3	9 (18%)	7 (14.4%)	0.938
	4	11 (22%)	10 (20.1%)	
	5	16 (32%)	18 (37.4%)	
	6	14 (28%)	13(27.1%)	
Uterine size in weeks		22.6 ± 3.4	21.0 ± 3.8	0.334

Table 2 Comparison of symptoms between the two groups.

Variables	Case (50)		Control (48)		p value
	No.	%	No.	%	
Infertility	13	26%	11	22.9%	0.722
Abdominal pain	28	56%	25	52.1%	0.697
Abdominal mass	7	14%	5	10.4%	0.588
AUB	21	42%	19	39.5%	0.807
No symptoms	3	6%	1	2.1%	0.327

Table 3 Primary outcomes in the two study groups.

Variables	Case (50)	Control (48)	p value
Intraoperative blood loss (ml)	244 ± 35.1	389 ± 48.8	0.001
postoperative blood loss (ml)	474 ± 118.9	713 ± 36.2	0.001
Total blood loss (ml)	718± 196.3	1102 ±120.7	0.001

Table 4 Secondary outcomes in the two study groups.

Variables	Case (50)	Control (48)	p value
Operation time (min.)	50.1 ± 2.3	65± 2.1	0.001
Postoperative Hb (mg/dl)	9.6±0.8	8.1± 0.6	0.001
Hb reduction (mg/dl)	0.7 ±0.5	2.3 ±0.4	0.002
Blood transfusion	7 (14%)	16 (33.3%)	0.001
Hospital stays (days)	2.3 ±1.1	4.2 ± 0.5	0.001
	Postoperative complication		
Nausea	7(14%)	12 (25%)	0.168
Diarrhea	2(4%)	3(6.2%)	0.612
Vomiting	1(2%)	3 (6.2%)	0.287
Wound infection	3(6%)	2 (4.1%)	0.680
Fever	7 (14%)	9(18.7%)	0.524

4. Discussion

From the literature review. Bleeding or hemorrhage are the most important issues associated with open abdominal myomectomy and depend largely on the size and number of fibroids that should be removed during the operation, and the surgical technique should be used during myomectomy (Kongnyuy and Wiysonge, 2014).

Although fibroids have a poor blood supply, the adjacent myometrium has a rich network of blood vessels. Additionally, the fibroid creates a mechanical obstruction to the venous drainage of the myometrium and endometrium with obvious dilatation and venous congestion of the surrounding venous plexus, and fibroid enucleation per second from its

pseudocapsule might result in brisk bleeding from nearby blood vessels. The dead space created by enucleation is a potential cavity for the accumulation of oozing blood and hematoma formation (Neelanjana Mukhopadhaya, Chaminda De Silva and Manyonda, 2008). The role of tranexamic acid in preventing blood loss has been well established in medicine. Early administration of tranexamic acid significantly decreases the mortality rate due to head injury and hemorrhage after a significant head injury (Crash T., 2019). Worldwide, maternal antifibrinolytic agent (WOMAN) contributes to the role of tranexamic acid in reducing maternal mortality due to bleeding. Additionally, this approach reduces the need for a laparotomy to control bleeding after C.S. and vaginal bleeding if given within three hours after childbirth. Therefore, in 2017, the WHO updated their guidelines for the routine use of tranexamic acid in the management of PPH irrespective of the cause of hemorrhage (WHO, 2017).

Fibroids are the most common benign muscular tumors of the uterus and affect women during their reproductive life. It was estimated that 20-50% of women of childbearing age have fibroids, and surgical removal of these fibroids by abdominal myomectomy is still the main surgical option and treatment (Cheng et al., 2018).

Although tranexamic acid has shown a risk for side effects such as thrombus and embolism due to its antifibrinolytic effect, thromboembolic events have not been reported in many studies, and it has been widely used in Scandinavian and European countries in general as the first-line management option for massive bleeding since 1970. Additionally, all studies have shown no increase in the frequency of abnormal clotting disorders (Follrud, Lethagen and Berntorp, 2001).

Table 1 shows that there was no statistically significant difference between the two studied groups regarding demographic factors such as age, BMI, parity, size, number of fibroids, and other factors. This approach might help strengthen the ability of tranexamic acid to reduce blood loss during open abdominal myomectomy.

Table 2 also shows no statistically significant difference between the two studied groups regarding the presence of symptoms; approximately 56% of the patients in the case group and 52.1% of the patients in the control group presented with abdominal pain. In addition, 42% of the patients in the case group and 39.5% of the patients in the control group presented with AUB, followed by infertility (26% vs 22.9%, respectively).

Table 3 shows that there was a statistically significant difference between the two studied groups regarding the primary outcome, such as intraoperative blood loss, postoperative blood loss, and total blood loss. Therefore, in our study, there was a positive impact of I.V. tranexamic acid intraoperatively on reducing the amount of bleeding, which was consistent with the findings of previous studies (Caglar et al., 2008).

Therefore, according to our findings in this study, tranexamic acid is a safe drug for reducing hemorrhage in women with fibroids subjected to open myomectomy, and it has no major adverse effects (Fusca et al., 2019). Intraoperative blood loss was significantly lower in women who received tranexamic acid than in those in the control group who had undergone open myomectomy due to fibroids.

Finally, Table 4 shows that there was a significantly shorter operation time in the case group than in the control group (p value =0.001) (50.1±2.3 vs 65.0 ± 2.1).

Additionally, we found a significant reduction in hospital stay in the case group compared to the control group (p value =0.001), and we found a significant reduction in postoperative Hb levels in the control group and a decreased need for blood transfusions in the case group. These differences were statistically significant and were confirmed by other studies, which showed the advantageous role of tranexamic acid in reducing blood loss and Hb levels following surgery and hospital stay, as well as in facilitating blood transfusion in patients who underwent open myomectomy with iv tranexamic acid at the time of skin incision (Caglar et al., 2008, Wang et al., 2017, Shaaban et al., 2016).

5. Conclusions

From the current study, we conclude the following: abdominal pain was the most common presenting symptom among both studied groups, followed by AUB and infertility. Regarding the primary outcomes, such as intraoperative, postoperative, and total blood loss, there was a statistically significant difference between the two studied groups. There was less blood loss in the patient group. Regarding the secondary outcome, there was a significant reduction in operation time, postoperative hospital stay, and the need for blood transfusion in the patient group. Tranexamic acid is a safe drug for reducing hemorrhage in women with fibroids subjected to open myomectomy, and it has no major adverse effects.

We recommend the use of IV tranexamic acid just before the skin incision reduces the amount of intraoperative and postoperative blood loss. A more thorough study with a larger sample size is recommended to yield better statistical results.

Ethics Considerations

This was an observational study. The Research Ethics Committee has confirmed that no ethical approval is needed.

Conflict of interest

The authors confirm that there are no conflicts of interest.

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