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ORIGINAL ARTICLE

Effect of Tranexamic Acid in Reducing Blood Loss during Abdominal Myomectomy

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ABSTRACT

Background: Open myomectomy remains the key alternative that has been shown to have a satisfactory outcome in terms of fertility preservation and symptom resolution, particularly when the number and size of leiomyomas do not permit any other surgical route of surgery. This work aimed to reduce blood loss during myomectomy using either intravenous or topical methods. **Methods:** This randomized controlled trial included 60 Patients who undergo abdominal myomectomy with myoma staging from (3 to 6) according to FIGO staging divided into three groups each group comprised of 20 patients. Group I: received 110 ml normal saline intravenous just before skin incision. Group II: 1g tranexamic acid intravenous just before skin incision. Group III: received 2g topical tranexamic acid applied on myoma bed after myomectomy. The primary outcome was total blood loss estimation intra-operative, and postoperative. **Results:** there was a statistically significant difference between the studied groups regarding blood loss with higher blood loss intraoperative, postoperative on control, and topical than intravenous tranexamic acid group (p-value= 0.8, 0.9 and 0.9) respectively. Regarding the need for blood transfusion where (50.0%) of the control group needed blood transfusion while only (10.0%) of intravenous and topical tranexamic acid groups needed blood transfusion (p-value= 0.003*). **Conclusions:** Intravenous and topical tranexamic acid safe and reliable method to help decrease blood loss during open myomectomy without serious side effects.
Keywords: Myomectomy, Tranexamic Acid, Uterine leiomyomas

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INTRODUCTION

Uterine Leiomyomas are the most common neoplasms in women of reproductive age in benign uterine tumors and occurrence for the general population of approximately 70% of life[1]. Roughly 20-40% of females with fibroid symptoms and gynecological treatment are consulted. Abnormal uterine bleeding, dysmenorrhoea, pelvic pain, infertility, and recurrent pregnancy loss are among the most common clinical symptoms[2].

There are currently many strategies for the treatment of fibroids, but myomectomy remains the most common and most effective uterine-saving treatment[3]. However, this technique is associated with documented complications, with excessive intraoperative blood loss, which often includes hysterectomy. However, in many cases, blood transfusions were still required to treat anemia. An allogeneic blood transfusion will raise the risk of adverse outcomes such as virus infections, immunologically induced diseases, and cardiovascular dysfunction, resulting in financial pressures and potentially life-threatening effects on patients [4,5].

Various strategies are available to minimize intraoperative bleeding, but variations in patient characteristics render the comparison of efficacy difficult. As a result, there is still no consensus on the optimal form of hemostasis [6]. There are various pharmacological and non-pharmacological methods have been tested to control hemorrhage during myomectomy. In a systematic review of the Cochrane database, misoprostol, vasopressin, bupivacaine plus epinephrine, tranexamic acid, and mechanic

tourniquet were stated to be more effective in managing myomectomy-associated bleeding compared to placebo or no care [6].

This study aimed to find out the effect of tranexamic acid (TXA) in reducing blood loss during abdominal myomectomy

METHODS

This study was a randomized controlled trial that included 60 women undergoing abdominal myomectomy for symptomatic uterine leiomyomas in the Department of Obstetrics and Gynecology, at Zagazig University Hospital during the period study year September 2019 to March 2020. Criteria for inclusion in the study were women who visited an outpatient gynecology clinic, sought care for and were scheduled to undergo abdominal myomectomy with myoma staging (3 to 6) according to FIGO staging, age 18-45, with vaginal bleeding, infertility, pelviabdominal mass no drug allergy, not complete her family i.e need uterine preservation, respiratory, hepatic, renal or thromboembolic conditions. Exclusion criteria were: patients will be undergoing vaginal or laparoscopic myomectomy. Patients were given preoperative embolization or gonadotrophin-release hormone analog. Myoma of the cervical and broad ligament. Myoma staging from (0, 1, or 2) according to FIGO staging **[7-9].** Patients with respiratory, hepatic, renal, or thromboembolic conditions. Patients have a tranexamic acid allergy.

Written informed consent was obtained from all participants, the study was approved by the research ethics committee of the Faculty of Medicine, Zagazig University. The work was carried out for studies involving humans under the World Medical Association's Code of Ethics (Helsinki Declaration) IRB number 5750. The participants who fulfilled the eligibility criteria were explained about the study with the beneficial and possible adverse effects of tranexamic acid.

All participants underwent a detailed history, general examinations, body mass index (BMI) was calculated, abdominal and vaginal examinations and pelvic ultrasound examinations were undertaken for all participants to assess the number and location of myomas and the largest myoma diameter. Investigations, CBC, PT, PTT, ALT, AST, and serum creatinine, were performed preoperatively for all groups, and CBC was repeated on the first and third postoperative day.

Randomization was done using a computer program by randomized 60 patients in 3 groups each group comprised of 20 patients. Group I: 20 patients received 110 ml of normal saline intravenous just before the skin incision. Group II: 20 patients received 1g tranexamic acid (2 ampoules of kapron 500mg 5ml) intravenous just before skin incision. Group III: 20 patients received 2g topical tranexamic acid (4 ampoules of kapron 500 mg 5ml) applied on the myoma bed after myomectomy.

Intervention:

All participants received general anesthesia immediately before surgery and immediately before the skin incision. The abdomen was exposed through a midline or Pfannensteil incision, the subcutaneous fat and abdominal fascia was opened crosswise after the skin incision, and the midline rectal muscle was opened. The uterus was examined for the number, place, and shape of myomas and the related pathology of other pelvic organs. Uterine incisions were performed using monopolar diathermy at the top of the myoma vertical incision. Myomas were intracapsular nucleated by gently dissecting between the myoma and the pseudo capsule. Collins forceps grabbed the myoma and gently enucleated it out.

The 3rd group was given a gauze soaked with 2 gm tranexamic acid (20 ml) diluted in 100 ml of 0.9 percent sodium chloride or placebo (120 ml of 0.9 percent sodium chloride) to compress the myoma bed for 5 minutes. [7]. Myoma bed was then closed by 1 or 2 layers of interrupted vicryl sutures (Vicryl 1–0 polyglactin 910; Egycryl, Taisier CO, Egypt). At the end of the surgery, 1 intraperitoneal suction drain was regularly used in all patients on the second postoperative day, unless otherwise stated. The number and size of myomas have been reported. The size of the myoma was the mean size of each myoma. Enucleated myomas have been submitted to histopathology.

Blood loss estimation:

Intraoperative blood loss was measured by applying the volume of the suction bottle and the difference in weight (in grams) between the dry and the soaked operating sheets and the towels (1g = 1ml). Postoperative blood loss was measured through an intra-peritoneal suction drain which was measured every 12 hours and upon removing the drain. After that, the total blood loss was calculated by the addition of intraoperative and postoperative blood loss, Hb, and Hct levels were measured on the first and third postoperative day for require of blood transfusion. The number of transfusion requirements was recorded according to intraoperative blood loss and postoperative Hb and Hct.

Study outcome:

The primary outcome was to estimate the efficacy of tranexamic acid in reducing blood loss during abdominal myomectomy. Including total blood loss level, amount of blood transfusion, and drainage volume.

Secondary outcomes; were estimating the efficacy of tranexamic acid either intravenous or topical in reducing blood loss after myomectomy, Amount of blood transfusion, and Change in preoperative and postoperative Hb.

STATISTICAL ANALYSIS

Data were entered checked and analyzed using Epi-Info version 6 and SPP for Windows version 8 [8].

RESULTS

There was no statistically significant difference between the studied groups in age, BMI, gravidity, parity and age grouping, previous scar, largest myoma size, stage, and a total number of myomas **table (1)**.

There was a statistically significant difference between the studied groups regarding blood loss with higher blood loss either intraoperative, postoperative, and overall blood loss on control than topical than intravenous tranexamic acid group **table (2)**.

There was a statistically significant difference between the studied groups in hemoglobin postoperative with higher levels among group11 than the group control group1. But regarding preoperative hemoglobin, there was no statistically significant difference between the studied groups. There was a statistically significant difference decrease in hemoglobin postoperatively in the three studied groups but this decrease was more among control than topical than intravenous tranexamic acid groups **Figure (1)**.

Additionally, there was a statistically significant difference between the studied groups regarding the need for blood transfusion where (50.0%) of the control group needed blood transfusion while only (10.0%) of intravenous and topical tranexamic acid groups needed blood transfusion **Figure (2)**.

There was a high statistically significant difference between the studied groups regarding operative time where the intravenous tranexamic acid group had the least operative time followed by a topical group than the control group had the longest operative time. Regarding hospital stay where control group stayed more than topical than intravenous tranexamic acid groups **Table (2)**.

There was no statistically significant difference between the studied groups regarding side effects like nausea, vomiting, and diarrhea **Table (2)**.

Table (1): Demographic criteria of the study groups.

Variable	Group (A) No. (20)	Group (B) No. (20)	Group (C) No. (20)	F-test	P
Age (years) Mean ± SD (range)	35.1±4.6 (27-41)	35.8±6.6 (23-43)	35.0±4.5 (27-41)	0.1	0.8
BMI Mean ± SD (range)	27.2±3.8 (23.3-36)	27.3±3.1 (23-33)	27.1±3.9 (23.3-36)	0.1	0.9
GravidityMean ± SD (range)	3.1±1.3 (1-5)	3.6±1.2 (1-6)	3.5±1.1 (1-6)	0.3	0.6
Parity Nulliparous Multiparous	2 (10.0%) 18 (90.0%)	4 (20.0%) 16 (80.0%)	2 (10.0%) 18 (90.0%)	χ^2= 1.1	0.6
Age grouping <35 years 35-39 years >39 years	10 (50.0%) 4 (20.0%) 6 (30.0%)	4 (20.0%) 10 (50.0%) 6 (30.0%)	6 (30.0%) 10 (50.0%) 4 (20.0%)	χ^2= 6.3	0.2
Largest myoma diameter (cm) Mean ± SD (range)	8.9±2.4 (4-10)	8.7±2.1 (3-10)	9.1±2.7 (3-12)	1.5	0.3
Largest myoma diameter ≤6 cm (13) >6 cm (47)	2 (10.0%) 18 (90.0%)	5 (25.0%) 15 (75.0%)	6 (30.0%) 14 (17.0%)	χ^2= 2.5	0.3

Variable	Group (A) No. (20)	Group (B) No. (20)	Group (C) No. (20)	F-test	P
Myoma stage Mean ± SD (range)	4.2±0.6 (3-5)	4.6±0.5 (4-5)	4.1±1.1 (3-6)	0.4	0.7
Myoma stage 3 4 5 6	2 (10.0%) 12 (60.0%) 6 (30.0%) 0.0 (0.00%)	0.0 (00.0%) 8 (40.0%) 12 (60.0%) 0.0 (0.00%)	2 (10.0%) 8 (40.0%) 8 (40.0%) 2 (10.0%)	χ^2= 2.5	0.3
Previous scar Yes No	6 (30.0%) 14 (70.0%)	2 (10.0%) 18 (90.0%)	7 (35.0%) 13 (65.0%)	χ^2= 3.7	0.1
Total n. of myomas Single Multiple (2-3)	14 (70.0%) 6 (30.0%)	16 (80.0%) 4 (20.0%)	17 (85.0%) 3 (15.0%)	χ^2= 0.8	0.6

Table (2): Mean and standard deviation of blood loss, operative time, and Frequency and percentage of side effects pre and postoperative in the three studied groups

Blood loss	Group (A) No. (20)	Group (B) No. (20)	Group (C) No. (20)	t-test	P
Intraoperative blood loss (ml) Mean ± SD (range)	1032±128.6 **(850-1350)**	790±245.8 (100-950)	805±138.5 **(500-1000)**	5.7	**0.005***
Postoperative blood loss Mean ± SD (range)	105±42.6 (50-150)	62±27.4 (30-100)	76±49.4 (20-200)	11.4	**0.001****
Approximate total blood loss (ml) Mean ± SD (range)	1137±144.4 **(1000-1500)**	852±241.1 **(170-1000)**	881±136.4 **(600-1050)**	15.9	**0.001****
Variable	Group (A) No. (20)	Group (B) No. (20)	Group (C) No. (20)	F-test	**P**
Operative time (minutes) **Mean ± SD** **(range)**	111±19.7 (90-145)	72.5±7.3 (60-85)	110±19.1 (90-135)	7.6	**0.001****
Hospital stay (days) **Mean ± SD** **(range)**	4.4±0.5 (4-5)	3.6±0.8 (4-5)	3.9±0.6 (3-5)	7.9	**0.001****

Side effects	Group (A) No. (%)	Group (B) No. (%)	Group (C) No. (%)	test χ^2	P
Nausea	3 (15.0%)	5 (25.0%)	4 (20.0%)	1.9	0.3
Vomiting	1 (5.0%)	2 (10.0%)	1 (5.0%)		
Diarrhea	1 (5.0%)	2 (10.0%)	1 (5.0%)		
Absent	15 (75.0%)	11 (55.0%)	14 (70.0%)		

**Statistically highly significant difference ($P \leq 0.001$).

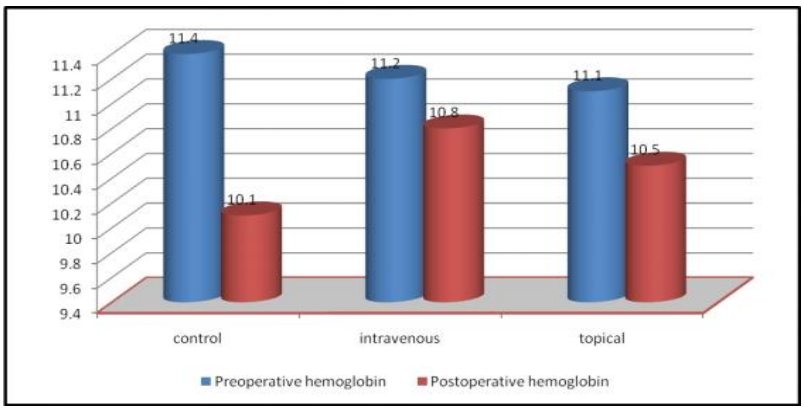

Figure (1): Bar chart for comparing mean hemoglobin level pre and post-operative between the studied groups

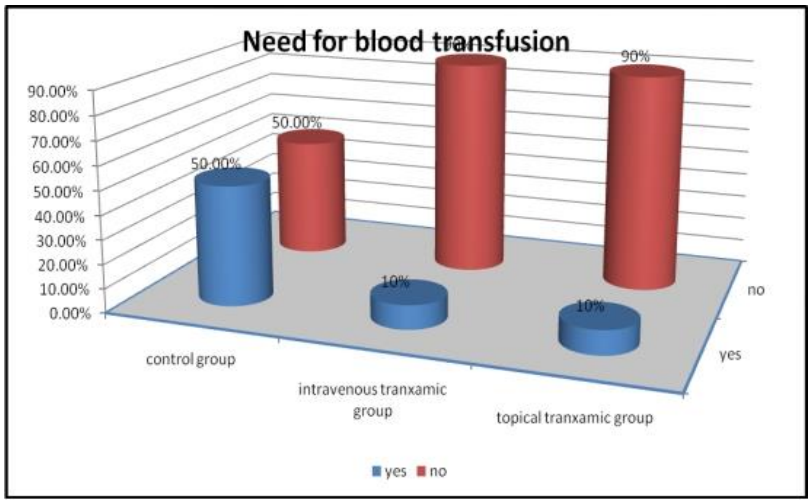

Figure (2): Bar chart for comparing the need for blood transfusion among the studied groups

DISCUSSION

The current study showed that there was no statistically significant difference between the studied groups as regard age, BMI, gravidity, and parity Also there was no statistically significant difference between the studied groups regarding the presence of previous scar myoma size, stage, and a total number of myomas, this was in consistence with many previous studies as **Shady et al. [10]** in the study, 105 patients were randomized to 3 groups of 35 patients in each group. Group I: (received 1 g IV normal saline), Group II: (received 1 g tranexamic acid IV) and found that there was no significant difference between the three groups concerning their age, weight, Hight, body mass index (BMI) parity, myoma number, myoma stage, uterine size, initial hemoglobin and history of the previous

Also, the present study was in agreement with **Sallam and Shady**[11] where 129 patients were included in their study and randomized to three groups: Group I (43) patients received 110 ml normal saline IV just before skin in scion], Group II [43 patients received 1 g tranexamic acid (2) ampoules of kapron 500 mg 5ml. Amoun company) IV just before skin in scion], and Group III [43 patients received 2 g topical tranexamic acid (4 ampoules of kapron 500 mg 5ml) and reported that there was no significant difference between the three groups concerning their age, weight, height, body mass index (BMI), uterine size, an indication of hysterectomy, initial hemoglobin, and history of previous scar, diabetes mellitus (DM), and hypertension (HTN).

Shaaban et al. [12] The research was close to our findings as the mean age of patients in both tranexamic acid and control groups was 35 years and 34.6 years. No statistical difference was observed concerning the mean number of myomas or the mean size of myomas.

Concerning blood loss as a primary outcome of our study, the current study reported that there was a statistically significant difference between the studied groups regarding blood loss with higher blood loss either intraoperative, postoperative, and overall blood loss on control than topical than an intravenous tranexamic acid group. This was in similarity **to Shaaban et al.** [12] who reported lower overall blood loss (407 mL) relative to the control group (677 mL). This overall blood loss was the amount of blood lost during the surgery and postoperative period.

Finally, tranexamic acid was compared with a placebo in a randomized study performed by Wang et al. [13] in patients undergoing open-label myomectomy. Tranexamic acid is associated with decreased overall blood loss.

The most likely reason for the effect of tranexamic acid to be pronounced only in this community is that severe tissue trauma associated with multiple myomas dissecting causes excessive fibrinolysis that can be enhanced by the use of tranexamic acid. It is well known that the concentration of plasminogen activator increases 30 minutes after the start of the activity and the suppression of plasminogen elevation by tranexamic acid enhances the effectiveness of the patient's hemostatic mechanisms. As a consequence, fibrinolysis is inhibited and severe or repeated bleeding is minimized. This effect is likely to be exaggerated by severe tissue trauma associated with dissecting multiple uterine fibroids [14]**.**

On the other hand, the only randomized controlled trials comparing the impact of preoperative intravenous tranexamic acid and placebo on women undergoing myomectomy and found no significant difference were **Caglar et al.,** [**15**] included 100 women and found that Intra-operative blood loss (ml) = 654 ± 460 **(81–2005)** versus 820 ± 558 **(213–2544)** P =0 .12 with no significant difference between preoperative intravenous tranexamic acid and placebo groups, and **Ngichabe et al.** [**16**] Adjunctive use of tranexamic acid along with intramyometrial or nipressin during open myomectomy was investigated to determine intraoperative blood loss. A total of 34 patients were randomized into two groups, with 17 receiving only ornipressin and 17 receiving both tranexamic acid and ornipressin. There was no difference in blood loss between ornipressin (n = 17) median blood loss groups and ornipressin plus tranexamic acid.

Regarding secondary outcomes such as hemoglobin and hematocrit levels, the need for blood transfusion, operative time and the hospital stay; this study found that there was a statistical significance between the studied groups in hemoglobin and Hct postoperatively with higher levels among the intravenous group than topical tranexamic acid group than control group groups. But regarding preoperative hemoglobin and Hct, there was no statistically significant difference between the studied groups .women in tranexamic acid groups had a smaller drop in hemoglobin and Hct levels after surgery compared with the control. Also, there was a statistically significant difference between the studied groups regarding the need for blood transfusion where (50.0%) of the control group needed blood transfusion while only (10.0%) of intravenous and topical tranexamic acid groups needed a blood transfusion**,** this was in agreement with **Shaaban et al.** [12] Who found that there were significantly higher levels of postoperative Hb and hematocrit in the study groups.

Similarly, **Sallam and Shady** [11] were consistent with our study and reported that the mean postoperative hemoglobin concentration was higher in topical and intravenous tranexamic acid than in the control group, similarly, women in tranexamic acid groups had a smaller drop in hemoglobin levels after surgery compared with control but there was no significant difference in the incidence of blood transfusion.

Shady et al. [10] found that the incidence of blood transfusion was significantly increased in the control group, 19 patients compared with 6 patients in group II, and 7 patients in group III. However, no significant difference in the incidence of blood transfusion between topical and intravenous tranexamic acid (p = 0.759). But regarding postoperative Hb, there was no statistically significant difference (9.83 ± 0.63 versus 10.02 ± 0.81 versus 10.03 ± 0.797 p=0.4).

Oppositely, **Caglar et al.** [15] found no significant difference between tranexamic acid and control groups regarding post-operative Hb and Blood transfusion.

On concern with operative time and hospital stay, the following study found that there was a highly statistically significant difference between the studied groups regarding operative time and hospital stay where the intravenous tranexamic acid group had the least operative time followed by the topical group than the control group had the longest operative time and the control group stayed more than topical more than intravenous tranexamic acid groups**.** with no statistically significant difference between the studied groups regarding side effects such as nausea, vomiting, and diarrhea, this was similar to the findings of **Shaaban et al.** [12] and also **Caglar et al.** [15].

In contrast to our results**, Sallam and Shady** [11] found that there was no significant difference was observed in operation time, duration of hospital stay, nausea, vomiting, and diarrhea between the groups and also **Ngichabe et al.** [16] showed no significant change in operative time between the groups.

Shady et al. [10] It was found that there was a substantial reduction in operating time in Group II relative to Group I and Group III. However, there was no substantial difference between Group I and Group III in terms of operating time (p=0.911) with no significant difference between the three classes associated with a hospital stay, postoperative hemoglobin, nausea, vomiting, and

diarrhea (P=0.752,.446,.102,.87, and 1.00, respectively).

CONCLUSIONS

Intravenous and topical tranexamic acid are safe and reliable methods for decreasing blood loss during open myomectomy without serious side effects. Further prospective studies with different protocols are required to validate these findings with a larger sample size.

Conflict of Interest: Nothing to declare.

Financial Disclosures: Nothing to declare

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