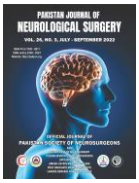

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Original Article

# A Comparison of the Use of Tranexamic Acid versus Placebo in Patients Undergoing Excision of Intracranial Meningioma

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## ABSTRACT

**Objective:** Complete surgical removal of intracranial meningiomas is curative but with significant blood loss. Tranexamic acid has been proven beneficial in reducing blood loss following major surgical procedures. Therefore, the purpose of the study was to evaluate how well tranexamic acid worked to stop blood loss in patients having an intracranial meningioma removed.

**Objective:** This study compares the effects of tranexamic acid and placebo effects on intraoperative blood loss, transfusion needs, and the frequency of surgical sites with good hemostatic quality in patients with an intracranial meningioma removed.

**Materials & Methods:** This clinical trial was carried out in the Department of Neurosurgery, unit II PGMI/ PINS, Lahore over 1 year. Two equal groups of 30 individuals each were formed from a total of 60 patients having an intracranial meningioma diagnosis. Group 1 was given TXA, whereas Group 2 was given a placebo (normal saline). Patients were assessed for intraoperative blood loss, transfusion needs, and a clean surgical area in terms of hemostasis.

**Results:** Mean blood loss in the TXA group was 803.0 ± 106.53mL while that in the placebo group was 1159.5 ± 101.79 mL which was statistically significant ($p = 0.000$). TXA also significantly reduced transfusion requirements ($p = 0.000$) and was associated with better hemostasis of the surgical field ($p = 0.000$).

**Conclusion:** This study concluded that TXA can reduce intraoperative blood loss and significantly decrease the transfusion requirements in the postoperative period compared to placebo in patients experiencing surgical intracranial meningioma excision.

**Keywords:** Tranexamic acid, Intracranial, Meningioma, Placebo, Transfusion, Hemostasis.

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## INTRODUCTION

Meningiomas, which make up 13-26% of all primary cerebral tumors, are meningeal tumors that are slow-growing, well-circumscribed, and mostly benign. Meningiomas do not invade the surrounding structures; they compress them to cause symptoms. Surgery aimed at complete tumor excision may be curative due to the reasonably clear operational plane. While complete surgical removal of intracranial meningiomas is the main therapeutic option available, it is associated with significant blood loss.[1,2] A study by Hsu et al from Taiwan in 2016 found that significant blood loss ≥ 500 ml occurred in 60.6% of all cases undergoing excision of intracranial meningiomas. The study also found that patients with significant blood loss had increased duration of intensive care unit stay, increased ventilator use, increased overall hospital stay, and delayed postoperative recovery following surgery.[3] Significant intraoperative blood loss during meningioma excision surgery can cause hemodynamic instability that can be fatal and frequently necessitates multiple transfusions. It can be challenging to achieve hemostasis during meningioma excision because of the particular blood supply to skull base meningiomas, considerable peritumoral edema in large tumors, encasement of cerebral veins, dural sinuses involvement, and invasion of the scalp via feeding vessels.[4] Preoperative autologous blood donation, intraoperative blood salvage utilizing the cell saver, normovolemic haemodilution, controlled hypotension, and the use of anti-fibrinolytics are all methods for reducing blood loss.[5] The synthetic lysine derivative tranexamic acid, which acts as an anti-fibrinolytic, inhibits the lysine binding sites on plasminogen molecules. It lessens bleeding and stops blood clots from dissolving. It was founded in 1962, making it one of the most efficient and secure medications required in a healthcare system, according to the WHO's List of Essential Medicines. It has been proven beneficial in reducing blood loss following major trauma including head injuries, post - parpostpartumdic surgery, and elective surgical procedures. The CRASH-2 and CRASH-3 trials are landmark trials showing their efficacy in preventing morbidity and mortality due to bleeding.[6-8] Effective blood loss reduction was observed with tranexamic acid during severe spine surgery.[9] In a 2017 study researchers discovered that blood loss by the intraoperative method was considerably less in the TXA group compared with the placebo group in patients undergoing cerebral meningioma excision. Both groups had similar operating times (346 minutes vs. 359 minutes). Additionally, few patients needed transfusions of blood in the TXA group as compared with the placebo group (43.3% vs. 56.7%; p = 0.46). Patients in the tranexamic acid group had better hemostasis than the placebo group. 76.7% vs. 33.3% having good hemostasis in both groups respectively.[4] Vel et al, published in 2015 studied the effect of TXA versus placebo in supra-tentorial tumors and found that the mean perioperative blood loss in the tranexamic acid group was 817 ± 423.3 ml versus 1084 ± 604.8 ml in the placebo group which was statistically significant (p = 0.01).[5] However, blood transfused between groups was comparable. 445.2 ± 229.6 ml vs. 459.68 ± 247.4 ml in TXA and placebo groups respectively (0.83). The rationale of this study was that there is limited research available on the use of TXA in the excision of intracranial meningiomas with no study available in Pakistan on this subject. Since blood loss following intracranial meningioma excision is related to significant morbidity, as it prolongs hospital stay and recovery time thereby increasing the cost. These findings will help in determining the beneficial outcomes of the use of tranexamic acid in the Pakistani population concerning intraoperative blood loss and transfusion requirements which will significantly improve the management of patients with intracranial meningiomas.

# MATERIALS AND METHODS

## Study Design

This research was a randomized controlled experiment that adhered to CONSORT standards.

## Study Setting

The study was approved by the hospital's ethical review committee and 60 patients who were admitted to the neurosurgical unit II at PGMI/ Punjab Institute of Neurosciences over 12 months between July 2021 and August 2022 and were having an intracranial meningioma surgically removed were included in the study.

## Sampling Technique and Randomization

Randomization via the balloting method and non-probability purposive sampling was used. Using a random number table and an allocation ratio of 1:1 for both groups, participants were divided into two groups at random. The operating consultant/supervisor recruited participants and assigned them to the intervention, which was then put into action. Losses and exclusions following randomization may be attributable to participants who did not get the intended intervention and research protocol violations.

## Sample Size

A total of 60 (30 patients in each group) was estimated. The size of the sample was calculated as per **WHO** guidelines.

Significance level = 5%

Test power = 80%

Population proportion 1 (anticipated) = 76.7% 4

Population proportion 2 (anticipated) = 33.3% 4

Each group sample size = 30 patients.

The total number of cases (30+30) = 60 patients.

# SAMPLE SELECTION

## Inclusion Criteria

Patients of either sex with Intracranial Meningioma and ASA Grade I and II between the ages of 18 to 60 years, consenting for inclusion in the study sample at the Neurosurgical department, PGMI/ Lahore General Hospital.

## Exclusion Criteria

Patients Allergic to Tranexamic acid, with Bleeding diathesis/coagulopathies, ASA Grade III, IV, and V, Pregnant & lactating mothers, History of a thromboembolic event, Deranged renal functions(Serum creatinine of >2 mg/dL)

## Data Collection Procedure

A total of 60 patients admitted to the Neurosurgical department, PGMI/Lahore General Hospital undergoing surgical excision of intracranial meningioma meeting exclusion and inclusion criteria were included in the study after written permission from the ethical review committee of the hospital. Informed consent was taken in writing from all admitted patients of the study and attached as annexure A. Patients were randomly allocated to group A (Tranexamic acid group) and group B (Placebo group) by lottery method (30 patients in each group). Patients and the operating team were blinded regarding the group of patients undergoing surgery. All the operations were carried out under general anesthesia. The test drug was prepared by an anesthetist. In Group A (Tranexamic acid group), 2gTXA was diluted in 50 ml and injected as a loading dose of 20 mg/Kg over 20 minutes followed by a maintenance infusion of 1 mg/Kg/ hr. till completion of surgery. While in Group B (Placebo group), 50 ml of normal saline was injected as a loading dose of 20 mg/Kg over 20 minutes followed by a maintenance infusion of 1 mg/Kg/hr. till completion of surgery. The operative time was recorded by an operating

theatre nurse from the start of surgery till the application of the last skin suture. Intraoperative blood loss was calculated by weighing the swabs/ sponges/patties used during the surgery. The weight of swabs/ patties before and after surgery was determined. One milliliter of blood was considered to be equal to one gram (1 g = 1 ml). By deducting the amount of irrigation fluid used during surgery, the blood that was suctioned into the drain was added to the total amount of blood lost. It was noted how much blood or blood-derived products were transfused during surgery. The degree of hemostasis/ooze in both groups was graded following Annexure "D" to determine the hemostatic quality of the surgical field. The patients were given post-operative care in the surgical ICU. A predesigned proforma of a questionnaire was used to collect data from both groups, and it is attached at the conclusion as Annexure "B". Throughout the trial, each patient was treated with respect and had their needs taken care of. Each procedure was carried out by a neurosurgeon with a minimum of three years of expertise. The exclusion criteria were strictly followed to limit confounders and bias in the study.

## DATA ANALYSIS PLAN

Data was loaded into SPSS Version 23 for analysis. Age, intraoperative blood loss, blood transfusion, tumor size, and surgery time were estimated as means with standard deviations. In terms of frequency percentages, qualitative variables like gender, ASA grade, a strong hemostatic surgical field, and tumor location were measured. The sample's male-to-female ratio was computed. Stratification was used to control effect modifiers such as age, gender, ASA grade, and tumor size. Stratification after comparing the operating time, intraoperative blood loss, and volume of blood transfused in the two groups, an independent sample T-test was utilized. A chi-square test was performed for qualitative variables i.e., good hemostatic quality of the surgical field and tumor location. P value ≤ 0.05 was taken as significant.

## RESULTS

A total of 60 patients into two equal groups consisting of 30 patients each were included.

### Age Distribution

The age range was 24 – 60 years with 41.83 ± 10.68 years of mean age. In the group, The mean age of patients was 40.46 ± 9.53 years and in the group, B was 43.21 ± 11.73 years. The difference was statistically non-significant between groups A and B (p = 0.323). The age distribution is given in Table 1.

### Gender Distribution

As regards the gender distribution of the patients, 33 patients (55%) included in the study were females and 27 patients (45%) were males. There were 17 female patients (56.67%) and 13 male patients (43.33%) in Group A. While in Group B, there were 16 female patients (53.33%) and 14 male patients (46.67%). Between both groups, the difference was statistically non-significant (P = 0.795). The gender distribution is given in Table 2.

### Distribution of Patients According to ASA Grade

Out of the total of 60 patients, 31 patients (51.67%) included in the study were ASA grade I, and 29 patients (48.33%) were ASA grade II. The difference between groups A and B was again statistically non-significant (p = 0.438). The distribution of patients according to ASA grade is given in Table 3.

### Mean Operative Time and Size of Tumor between Groups A and B

The operative time mean was 369 ± 61.72

minutes. The difference between groups A and B in terms of mean operative time was statistically significant (p = 0.0003). The mean size of the tumor was 6.13 ± 1.51 cm. The difference between groups A and B in terms of mean tumor size was statistically non-significant (p = 0.101). The operative time as well as tumor size of the two groups are given in Table 4.

## Distribution of Patients According to the Location of the Tumor

The common position of the tumor was convexity in 24 patients (40%). The frequencies of tumors among both groups according to the location are given in Table 5.

## Comparison of the Mean Intraoperative Blood Loss between the Two Groups

The overall mean intraoperative blood loss was 981.25 ± 207.32 ml. The mean blood loss in the TXA group was 803.0 ± 106.53mL while in the placebo group, it was 1159.5 ± 101.79 mL, the difference being statistically significant (p = 0.000). The distribution of patients according to intraoperative blood loss is given in Table 6.

## Distribution of Patients According to Blood Transfusion

The distribution of patients according to blood transfused during surgery is given in Table 7. The difference between the groups was also statistically significant (p = 0.000).

## Distribution of Patients According to Hemostatic Quality of Surgical Field

The difference between the two groups in terms of good hemostatic quality of the surgical field is given in Table 8. The difference between groups A and B was also statistically significant (p = 0.000).

## Stratification of Operative Time

Stratification of operative time between groups A and B according to age, gender, ASA grade, and size of the tumor is given in Table 9.

## Stratification of Intraoperative Blood Loss

Stratification of intraoperative blood loss between groups A and B according to age, gender, ASA grade, and size of the tumor is given in Table 10.

## Stratification of Intraoperative Blood Transfusions

Stratification of blood transfusions done between groups A and B according to age, gender, ASA grade, and size of tumor are given in Tables 11, 12, 13, and 14 respectively.

## Stratification of Good Quality of Surgical Field

Finally, the stratification of good hemostatic quality of surgical field between the two groups according to age, gender, ASA grade, and size of tumor are given in Tables 15, 16, 17, and 18 respectively.

**Table 1:** Age distribution for both groups (n=60).

| Age (Years) | Group A (n = 30) | | Group B (n = 30) | | Total (n = 60) | |
|---|---|---|---|---|---|---|
| | No. of Patients | % age | No. of Patients | % age | No. of Patients | % age |
| 18 – 40 | 17 | 56.67 | 12 | 40 | 29 | 48.33 |
| 41 – 60 | 13 | 43.33 | 18 | 60 | 31 | 51.66 |
| **Mean ± SD** | **40.46 ± 9.53** | | **43.21 ± 11.73** | | **41.83 ± 10.68** | |

(p = 0.323) Not significant.

**Table 2:** Distribution of patients according to Gender (n=60).

| Gender | Group A (n = 30) | | Group B (n = 30) | | Total (n = 60) | |
|---|---|---|---|---|---|---|
| | No. of Patients | % age | No. of Patients | % age | No. of Patients | % age |
| Female | 17 | 56.67 | 16 | 53.33 | 33 | 55 |
| Male | 13 | 43.33 | 14 | 46.67 | 27 | 45 |

(p = 0.795), Not significant

**Table 3:** Distribution of patients according to ASA Grade (n = 60).

| Gender | Group A (n = 30) | | Group B (n = 30) | | Total (n = 60) | |
|---|---|---|---|---|---|---|
| | No. of Patients | % age | No. of Patients | % age | No. of Patients | % age |
| ASA I | 14 | 46.67 | 17 | 56.67 | 31 | 51.67 |
| ASA II | 16 | 53.33 | 13 | 43.33 | 29 | 48.33 |

(p = 0.438), Not significant

**Table 4:** Comparison of the mean operative time and size of tumor between the two groups (n = 60).

| | Group A (n = 30) | | Group B (n = 30) | | Total (n = 60) | | p-value |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | |
| **Operative Time (Minutes)** | 341.40 | 50.12 | 396.60 | 60.52 | 369.00 | 61.72 | 0.0003* |
| **Size of Tumor (cm)** | 6.45 | 1.52 | 5.81 | 1.45 | 6.13 | 1.51 | 0.101 |

*significant result

**Table 5:** Distribution of patients according to the location of the tumor (n = 60).

| Location | Group A (n = 30) | | Group B (n = 30) | | p-value |
|---|---|---|---|---|---|
| | No. of Patients | %age | No. of Patients | %age | |
| Convexity | 13 | 43.33 | 11 | 36.67 | |
| Parasagittal | 5 | 16.67 | 7 | 23.33 | |
| Skull base | 2 | 6.67 | 5 | 16.67 | 0.581 |
| Infratentorial | 7 | 23.33 | 6 | 20.0 | |
| Others | 3 | 10.0 | 1 | 3.33 | |

**Table 6:** Comparison of the mean intraoperative blood loss between the two groups (n = 60).

| | Group A (n = 30) | | Group B (n = 30) | | Total (n = 60) | |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD |
| Intraoperative Blood loss (mL) | 803.0 | 106.53 | 1159.5 | 101.79 | 981.25 | 207.32 |

(p = 0.00), Statistically significant.

**Table 7:** Distribution of patients according to Blood Transfusion (n = 60).

| No. of Transfusion | Group A (n=30) | | Group B (n = 30) | | p-value |
|---|---|---|---|---|---|
| | No. of Patients | % age | No. of Patients | % age | |
| None | 13 | 43.33 | 0 | 0.0 | |
| 1 Pint | 17 | 56.67 | 8 | 26.67 | 0.000* |
| 2 Pints | 0 | 0.0 | 18 | 60.0 | |
| > 2 Pints | 0 | 0.0 | 4 | 13.33 | |

*significant result

**Table 8:** Distribution of patients according to hemostatic quality of surgical field (n = 60).

| Grade of Ooze | Group A (n=30) | | Group B (n=30) | | p-value |
|---|---|---|---|---|---|
| | No. of Patients | %age | No. of Patients | %age | |
| Bloodless | 2 | 6.67 | 0 | 0.0 | |
| Minimal | 21 | 70.0 | 2 | 6.67 | |
| Moderate | 6 | 20.0 | 17 | 56.67 | 0.0001* |
| Severe | 1 | 3.33 | 8 | 26.67 | |
| Unsatisfactory | 0 | 0.0 | 3 | | |

*significant result

**Table 9:** Stratification of operative time.

| Variable | Groups | Group A (n=30) Operative Time (min) | | Group B (n=30) Operative Time (min) | | p-value |
|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | |
| Age Groups (Years) | 18 – 40 | 331.29 | 53.72 | 386.92 | 59.23 | 0.000 |
| | 41 – 60 | 354.62 | 43.48 | 403.06 | 62.19 | 0.000 |
| Gender | Female | 338.77 | 40.47 | 400.07 | 63.26 | 0.000 |
| | Male | 343.41 | 57.57 | 393.56 | 59.93 | 0.000 |
| ASA Grade | ASA I | 334.14 | 52.78 | 397.71 | 57.69 | 0.000 |
| | ASA II | 347.75 | 48.48 | 395.15 | 66.41 | 0.000 |
| Size of Tumor | < 5 cm | 301.33 | 35.44 | 377.80 | 68.81 | 0.000 |
| | > 5 cm | 351.42 | 48.69 | 406.00 | 55.39 | 0.000 |

**Table 10:** Stratification of intraoperative blood loss.

| Variable | Groups | Group A (n = 30) Intraoperative Blood Loss (mL) | | Group B (n = 30) Intraoperative Blood Loss (mL) | | p-value |
|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | |
| Age Groups (Years) | 18 – 40 | 822.06 | 108.54 | 1171.67 | 111.99 | 0.000 |
| | 41 – 60 | 778.08 | 102.62 | 1151.39 | 96.88 | 0.000 |
| Gender | Female | 780.29 | 104.59 | 1167.50 | 106.77 | 0.000 |
| | Male | 832.69 | 105.63 | 1150.36 | 98.93 | 0.000 |
| ASA Grade | ASA I | 748.57 | 98.03 | 1147.06 | 115.46 | 0.000 |
| | ASA II | 850.62 | 91.81 | 1175.77 | 82.21 | 0.000 |
| Size of Tumor | < 5 cm | 780.00 | 55.86 | 1110.50 | 109.91 | 0.000 |
| | > 5 cm | 808.75 | 116.01 | 1184.00 | 90.53 | 0.000 |

**Table 11:** Stratification of blood transfusion done according to age groups.

| Variable | Groups | Blood Transfusion | Group A | | Group B | | p-value |
|---|---|---|---|---|---|---|---|
| | | | No | %age | No | %age | |
| Age Groups (Years) | 18 – 40 | None | 7 | 23.3 | 0 | 0.0 | 0.000* |
| | | 1 pint | 10 | 33.3 | 2 | 6.6 | |
| | | 2 pints | 0 | 0.0 | 6 | 20.0 | |
| | | More | 0 | 0.0 | 4 | 13.3 | |
| | 41 – 60 | None | 6 | 20.0 | 0 | 0.0 | 0.000* |
| | | 1 pint | 7 | 23.3 | 6 | 20.0 | |
| | | 2 pints | 0 | 0.0 | 11 | 36.7 | |
| | | More | 0 | 0.0 | 1 | 3.3 | |

*significant result

**Table 12:** Stratification of blood transfusion done according to gender.

| Variable | Groups | Blood Transfusion | Group A | | Group B | | p-value |
|---|---|---|---|---|---|---|---|
| | | | No | % age | No | % age | |
| Gender | Male | None | 9 | 30.0 | 0 | 0.0 | 0.000* |
| | | 1 pint | 8 | 26.7 | 4 | 13.3 | |
| | | 2 pints | 0 | 0.0 | 8 | 26.7 | |
| | | more | 0 | 0.0 | 4 | 13.3 | |
| | Female | None | 4 | 13.3 | 0 | 0.0 | 0.001* |
| | | 1 pint | 9 | 30.0 | 4 | 13.3 | |
| | | 2 pints | 0 | 0.0 | 9 | 30.0 | |
| | | more | 0 | 0.0 | 1 | 3.3 | |

*significant result

**Table 13:** Stratification of blood transfusion done according to ASA grade.

| Variable | Groups | Blood Transfusion | Group A | | Group B | | p-value |
|---|---|---|---|---|---|---|---|
| | | | No | %age | No | %age | |
| ASA Grade | ASA I | None | 9 | 30.0 | 0 | 0.0 | 0.000* |
| | | 1 pint | 5 | 16.7 | 6 | 20.0 | |
| | | 2 pints | 0 | 0.0 | 8 | 26.7 | |
| | | More | 0 | 0.0 | 3 | 10.0 | |
| | ASA II | None | 4 | 13.3 | 0 | 0.0 | 0.000* |
| | | 1 pint | 12 | 40.0 | 2 | 6.7 | |
| | | 2 pints | 0 | 0.0 | 9 | 30.0 | |
| | | More | 0 | 0.0 | 2 | 6.7 | |

*significant result

**Table 14:** Stratification of blood transfusion done according to the size of the tumor.

| Variable | Groups | Blood Transfusion | Group A | | Group B | | p-value |
|---|---|---|---|---|---|---|---|
| | | | No | %age | No | %age | |
| Size of tumor in cm | less than 5 cm | None | 2 | 6.7 | 0 | 0.0 | 0.016* |
| | | 1 pint | 4 | 13.3 | 2 | 6.7 | |
| | | 2 pints | 0 | 0.0 | 6 | 20.0 | |
| | | more | 0 | 0.0 | 2 | 6.7 | |
| | more than 5 cm | None | 11 | 36.7 | 0 | 0.0 | 0.000* |
| | | 1 pint | 13 | 43.3 | 6 | 20.0 | |
| | | 2 pints | 0 | 0.0 | 11 | 36.7 | |
| | | more | 0 | 0.0 | 3 | 10.0 | |

*significant result

**Table 15:** Stratification of good quality of surgical field according to age groups.

| Variable | Groups | Hemostatic Quality | Group A | | Group B | | p-value |
|---|---|---|---|---|---|---|---|
| | | | No | %age | No | %age | |
| Age Groups (years) | 18 – 40 | Adequate | 1 | 3.3 | 0 | 0.0 | 0.046* |
| | | Minimal | 10 | 33.3 | 2 | 6.7 | |
| | | Moderate | 5 | 16.7 | 4 | 13.3 | |
| | | Severe | 1 | 3.3 | 4 | 13.3 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | Unsatisfactory | 0 | 0.0 | 2 | 6.7 | |
| | | Adequate | 1 | 3.3 | 0 | 0.0 | |
| | | Minimal | 9 | 30.0 | 0 | 0.0 | |
| | 41 – 60 | Moderate | 3 | 10.0 | 13 | 43.3 | 0.000* |
| | | Severe | 0 | 0.0 | 4 | 13.3 | |
| | | Unsatisfactory | 0 | 0.0 | 1 | 3.3 | |

*significant result

**Table 16:** Stratification of good quality of surgical field according to gender.

| Variable | Groups | Hemostatic Quality | Group A | | Group B | | p-value |
|---|---|---|---|---|---|---|---|
| | | | No | % age | No | % age | |
| Gender | Male | Adequate | 2 | 6.7 | 0 | 0.0 | |
| | | Minimal | 12 | 40.0 | 2 | 6.7 | |
| | | Moderate | 3 | 10.0 | 6 | 20.0 | 0.001* |
| | | Severe | 0 | 0.0 | 6 | 20.0 | |
| | | Unsatisfactory | 0 | 0.0 | 2 | 6.7 | |
| | Female | Adequate | 0 | 0.0 | 0 | 0.0 | |
| | | Minimal | 7 | 23.3 | 0 | 0.0 | |
| | | Moderate | 5 | 16.7 | 11 | 36.7 | 0.014* |
| | | Severe | 1 | 3.3 | 2 | 6.7 | |
| | | Unsatisfactory | 0 | 0.0 | 1 | 3.3 | |

*significant result

**Table 17:** Stratification of good quality of surgical field according to ASA grade.

| Variable | Groups | Hemostatic quality | Group A | | Group B | | p-value |
|---|---|---|---|---|---|---|---|
| | | | No | % age | No | % age | |
| ASA Grade | ASA I | Adequate | 2 | 6.7 | 0 | 0.0 | |
| | | Minimal | 7 | 23.3 | 2 | 6.7 | |
| | | Moderate | 5 | 16.7 | 10 | 33.3 | 0.024* |
| | | Severe | 0 | 0.0 | 3 | 10.0 | |
| | | Unsatisfactory | 0 | 0.0 | 2 | 6.7 | |
| | ASA II | Adequate | 0 | 0.0 | 0 | 0.0 | |
| | | Minimal | 12 | 40.0 | 0 | 0.0 | |
| | | Moderate | 3 | 10.0 | 7 | 23.3 | 0.001* |
| | | Severe | 1 | 3.3 | 5 | 16.7 | |
| | | Unsatisfactory | 0 | 0.0 | 1 | 3.3 | |

*significant result

**Table 18:** Stratification of good quality of surgical field according to the size of the tumor.

| Variable | Groups | Hemostatic quality | Group A | | Group B | | p-value |
|---|---|---|---|---|---|---|---|
| | | | No | % age | No | % age | |
| Size of Tumor | less than 5 cm | Adequate | 0 | 0.0 | 0 | 0.0 | |
| | | Minimal | 4 | 13.3 | 1 | 3.3 | |
| | | Moderate | 2 | 6.7 | 7 | 23.3 | 0.114 |
| | | Severe | 0 | 0.0 | 1 | 3.3 | |
| | | Unsatisfactory | 0 | 0.0 | 1 | 3.3 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| More than 5 cm | Adequate | 2 | 6.7 | 0 | 0.0 | 0.000* |
| | Minimal | 15 | 50.0 | 1 | 3.3 | |
| | Moderate | 6 | 20.0 | 10 | 33.3 | |
| | Severe | 1 | 3.3 | 7 | 23.3 | |
| | Unsatisfactory | 0 | 0.0 | 2 | 6.7 | |

*significant result

## DISCUSSION

Meningiomas are the commonest variety of primary intracranial tumors and comprise one-third of all central nervous system neoplasms. Most of these mitotic lesions are benign, however, approximately 20% of the tumors have atypical or malignant features.[10] Complete excision of the tumor is the choice of treatment but because of the extensive blood supply of the brain, surgical resection is associated with considerable morbidity due to blood loss.[1,2] Significant blood loss during surgery of meningioma can be life-threatening and multiple transfusions are required. It is because of the extensive blood supply of tumors, encasement of cerebral blood vessels, and involvement of dural sinuses that make hemostasis a challenging task.[4] Several options are available in the armamentarium of neurosurgeons to reduce blood loss such as preoperative autologous blood donation, intraoperative blood salvage using the cell saver, controlled hypotensive anesthesia, and use of anti-fibrinolytics. [5] TXA has been used with considerable success in orthopedics, trauma, obstetrics, and spinal surgery. The mean age of patients included in our study was 41.83 ± 10.68 years. The mean age was 40.46 ± 9.53 years in the TXA group and 43.21 ± 11.73 years in the placebo group respectively. A similar study by Hooda et al reported a mean age of 39.3 ± 11.4 years in the TXA group and 41.6 ± 11.2 years in the placebo group respectively.[4] Azeemuddin et al, reported a mean age of 55.2 ± 13 years.[10] Another study from Lahore by Malik et al published in 2015 reported a mean age of 48.3 years.[11] While a study by Hsu et al reported a much higher mean age of 60.9 ± 13.8 years.[2] As regards the gender distribution, 33 patients (55%) included in our study were females and 27 patients (45%) were males. Hsu et al also reported that meningioma was more common in female patients with a frequency of 59.6%, while 40.4% of patients included in their study were males.[2] Hooda et al reported a higher percentage of 65% comprising female patients.[4] The mean operative time was 369.0 ± 61.72 minutes with a range of 255 to 525 minutes in our study. The mean operative time was reported to be 346 ± 124 minutes in the TXA group and 359 ± 120 minutes in the placebo group in a study by Hooda et al.[4] While Hsu et al reported a much higher mean operative time of 9.6 ± 3.4 hours in their study.[2] Nania et al, reported that the mean operative time was 256.1 ± 51.76 minutes in patients undergoing surgical excision of meningioma.[12] Mostly the location of the tumor in our study was convexity in 24 patients (40%) followed by an infra-tentorial location in 12 patients (20%). Hooda et al reported infra-tentorial and convexity as the most common location in 28.3% of patients each.[4] While Hsu et al, reported convexity as the most common site of a tumor in 38.4% of patients.[2] Bhatt et al reported that the most common location of meningioma was supratentorial in 50.34% of patients.[13] There was a significant reduction in blood loss between the TXA group and placebo in our study (p = 0.000). The mean blood loss in the TXA group was 803.0 ± 106.53 ml while that in the placebo group was 1159.5 ± 101.79 ml. Hooda et al, also reported that the mean blood loss was 830 mL in the TXA group versus 1124 ml in the placebo group which was statistically significant (p = 0.03).[4] A similar result was obtained by Krishnan et al, in 2015 who

reported that the blood loss was 616.42 ± 393.42 mL in the TXA group versus 1150.02 ± 416.1 mL in the placebo group which was significant statistically (p = 0.02).[14] TXA significantly reduced transfusion requirements in our study (p = 0.000) with none of the patients in the TXA group requiring more than 1-pint transfusion. On the contrary, Hooda et al reported a mean transfusion volume of 554 ml in the TXA group versus 645 ml in the statistically insignificant placebo group (p = 0.46).[4] Finally, the use of TXA was associated with better hemostatic quality in the surgical field. Studies by Hooda et al and Krishnan et al reported similar results with better hemostasis of surgical field achieved using TXA acid.[4,14] Bukhari et al, reported that TXA may be used prophylactically in intracranial meningioma surgery to reduce absolute blood loss but the risk of transfusion may not be significantly reduced.[15] Brown NJ et al, did a systemic review and suggested that TXA may be effective for reducing blood loss and the need for blood transfusion while also having minimal reported complications. Significant P-values in our study results also supported TXA group results and or hypothesis. Our study is the first of its kind comparing TXA versus placebo in meningioma surgery. There is a paucity of literature comparing TXA with placebo or with other hemostatic modalities worldwide in general and locally in Pakistan in particular. Our study evaluated a smaller group of 60 patients. We recommend further research on the topic with bigger trials as hemostasis is a pivotal aspect of neurosurgery. In the present era of evidence-based practices, our study will pave the way for further research on this topic. Thus, the hypothesis that "Tranexamic acid is better than placebo for reducing intraoperative blood loss, transfusion requirements, and good hemostatic quality of the surgical field in patients undergoing excision of intracranial meningioma" stands true.

## CONCLUSION

Our study concluded that in the patients undergoing surgical intracranial meningioma excision, tranexamic acid was significantly better than placebo in terms of intraoperative blood loss reduction and lesser need for blood transfusion during surgery. Tranexamic acid use was also associated with better hemostatic quality in the surgical field. Thus, we strongly recommend the use of intravenous tranexamic acid in all patients undergoing surgical resection of intracranial meningiomas.

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## Additional Information

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In compliance with the ICMJE uniform disclosure form, all authors declare the following:
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## AUTHOR CONTRIBUTIONS

| Sr. No. | Author's Full Name | Intellectual Contribution to Paper in Terms of |
|---|---|---|
| 1. | Adnan Khalid | Study Design, Methodology, and Paper Writing. |
| 2. | Muhammad Usman Nazir | Paper Writing |
| 3. | Naeem Raza | Data collection and calculations |
| 4. | Muhammad Sheraz Aslam | Analysis of data and interpretation of results |
| 5. | Zohaib Hassan | Literature Review and referencing |
| 6. | Muhammad Naveed Majeed | Literature Review and Quality Insurer. |