# Effect of Tranexamic Acid on Blood Loss in Brain Tumour Resection Surgery

**Rameesa Batul[1], Meryem Juwhyreeyeh[1], Bashir Ahmad Dar[2], Rahid Rasool[3], Ouber Qayoom[4]**

[1]Senior Resident, Department of Anaesthesia, SKIMS Soura, J&K, India
[2]Professor, Department of Anaesthesia, SKIMS Soura, J&K, India
[3]Medical Officer, J&K Health and Family Welfare Department, India
[4]Senior Resident, Department of Cardiology, GMC Jammu, J&K, India

Corresponding Author: Ouber Qayoom

## ABSTRACT

**INTRODUCTION:** Intraoperative blood loss is considered to be one of the major complications in neurosurgical operations and neurosurgical procedures and is directly related to the postoperative morbidity and mortality. Administration of Tranexamic acid [TXA] by reducing blood loss has resulted in survival benefits in Traumatic Brain Injury [TBI] population, as shown in two recent meta-analysis.

**AIMS AND OBJECTIVES:** To study the effect of tranexamic acid on blood loss in brain tumor resection surgery.

**MATERIAL AND METHODS:** Patients of either sex, aged 18-65 years who were undergoing brain tumour resection were randomly allocated to either group - the study group and the control group (30 patients in each group). Patients in the study group received tranexamic acid intravenously @10 mg/kg body weight over 10 minutes after induction and then maintenance of continuous infusion @ 1mg/kg/hr intraoperatively till skin closure. Patients in the control group received the same volume of saline per kg body weight as the volume of tranexamic acid in study group.

**RESULTS:** The average drop in haemoglobin and HCT was significantly lower in TXA group. Accordingly, amount of blood loss was less in TXA group compared to saline group. (332ml vs 576 ml; $p = 0.011$).

**CONCLUSION:** From our study, it was concluded that the administration of TXA resulted in a significant reduction in blood loss. TXA can thus be suggested as a cost effective method of reducing mortality due to hemorrhage in brain tumor surgery.

*KEYWORDS:* Tranexamic acid [TXA], Traumatic Brain Injury [TBI].

## Ⅰ. INTRODUCTION

Brain tumor resection has been associated with increased blood loss and a significant increase in the incidence of intravascular disseminated coagulopathy. The development of coagulopathy in the context of tumor resection is associated with poor results. Transfusion decision during the course of neurosurgical surgery offers benefits such as increased oxygen carrying capacity but may increase the risk associated with transfusions such as blood infections, hemolysis, lung injury and immunosuppression. Tranexamic acid is an antifibrinolytic agent that blocks the binding of plasminogen to the fibrin surface. It has been used to reduce blood loss during coronary revascularization, liver resection, obstetrics and orthopedic procedures intraoperatively up to 45% [1]. The primary concern when administering an antifibrinolytic drug is the potential increased incidence of thromboembolic events. Reduction in transfusion requirements lead to reduction in complications of blood transfusion and perioperative incidents.

In neurosurgery, haemorrhagic abnormalities and postoperative haematomas uniformly result in poor outcome, with one recent series reporting 55% severe disability or mortality at six months, and only 13% with good outcome [2]. Intraoperative blood loss is considered to be one of the major complications in neurosurgical operations and is directly related to the postoperative morbidity and mortality of the patients [3] .Most investigators currently think that hyperfibrinolysis, either primary or secondary to a disseminated intravascular coagulation type condition, is the mechanism responsible for these haemostatic abnormalities [2,4] .The pathophysiology is thought to involve release of plasminogen activator factors from tumour cells, or tissue factors from injured brain parenchyma during surgery [5,6] .

The substantial intraoperative bleeding that occurs often needs to be replaced with many units of blood and blood products in addition to the infusion of large volume of crystalloids and colloids. However, allogeneic red blood cell transfusion is associated with well-known adverse effects that can range from relatively mild allergic reactions, acidosis, citrate toxicity and hypocalcaemia to severe anaphylactic reactions, transfusion associated lung injury, infectious disease transmission, circulatory overload and immunosuppression [7,8] . In addition, administering large amount of replacement fluids in the form of red blood cell, crystalloids or colloids are found to dilute the coagulation factors thereby resulting in disorder of coagulation and further increasing the surgical bleeding [9] .

To overcome these problems associated with massive blood loss requiring transfusions, several strategies have been devised and investigated to reduce blood loss and thus the transfusion requirements. These strategies include developing preoperative erythrocyte mass using erythropoietin [10,11], perioperative blood salvage in the form of preoperative autologous blood donation or intraoperative blood salvage using the cell saver, [12,13] normovolemic hemodilution [14] and controlled hypotension [15] . However none of these techniques are without complications [16]. Complications associated with these techniques and considering the availability and cost-effectiveness, has led to the investigation of alternative hemostatic agents that include aminocaproic acid, tranexamic acid (TXA), desmopressin, aprotinin, and conjugated estrogens [15].

In patients subjected to neurosurgery, the inflammation is parenchymal and the cellular response is dominated by macrophages and T-lymphocytes. Furthermore, neuroinflammatory mechanisms tightly interact with the coagulation system in both directions (inflammation influences coagulation and *vice versa*). Brain tissue is very rich in tissue factor (TF), and injury leads to formation of TF-FVIIa complexes and subsequently elicits a proinflammatory response. It has been shown that TF-FVIIa can induce synthesis of fibrinogen and increase its plasma levels [16].

The incidence of coagulation abnormalities in neurosurgery is 15−70%, depending on the definition and patient selection. In a recent meta-analysis a pooled incidence of acute traumatic coagulopathy was about 35%.

Tranexamic acid [TXA], a tissue plasminogen and plasmin inhibitor, is most commonly used, with evidence for benefit in cardiac, orthopaedic, urological, gynaecological, and obstetric surgery. In US, ὲ-aminocaproic acid, which also inhibits plasmin, is commonly used. TXA a protease inhibitor is used as a haemostatic agent, as it inhibits fibrinolysis. It is important to administer TXA early, within three hours of surgery [17]. Administration of TXA resulted in survival benefits even in a Traumatic Brain Injury [TBI] population, as shown in two recent meta-analyses [18,19]

In neurosurgical interventions TXA (1g immediately after diagnosis of an aneurysmal subarachnoid hemorrhage [aSAH], followed by 1g every 6 h up to the time the aneurysm has been clipped) reduced the mortality risk due to early rebleeding by 80% [20]. Data from randomized controlled studies on the efficacy and safety of antifibrinolytics in brain surgery are rare. A Cochrane review published in 2013 included all randomized controlled studies published between 1973 and 2002 [21]. The authors came to the conclusion that the short-term data were promising but felt that the studies were too heterogeneous to justify a general recommendation to use antifibrinolytics in the treatment of aSAH. Similarly, the European Stroke Organization is not ready to make such a recommendation on the basis of the data so far available [22].

## Ⅱ. AIMS AND OBJECTIVES
- To study the average blood loss during brain tumor surgery.
- To study the effect of tranexamic acid on blood loss in brain tumor resection surgery

## Ⅲ. MATERIAL AND METHODS
This study was conducted at Sher-i-Kashmir Institute of Medical Sciences, Soura, J&K, India for a period of two years (August 2015 to June 2017). Approval by our institutional ethical committee was taken prior to the start of the study. A proper informed consent was obtained from all patients included in the study. The study included 60 patients aged 18-65 years of both genders, planned for brain tumour resection surgeries (meningiomas, astrocytomas, gliomas and other vascular tumors) under general anesthesia.

## EXCLUSION CRITERIA
- Patients with known allergy to tranexamic acid.
- Patients with abnormal liver function.
- Patients with known contraindications to fibrinolytic agents.
- Patients with known renal dysfunction (creatinine>1.5mg/dl).
- Patients with coagulopathy on anticoagulation therapy (abnormal PT/PTT).
- Patients with thromboembolic events.
- ASA IV patients.

Patients with intraoperative bleeding due to vessel injury.

Patients of either sex, aged 18-65 years were randomly allocated to either group - the study group and the control group (30 patients in each group) using computer generated random numbers in sealed envelopes. The investigator was present during the procedure for data collection purpose only and was not involved in the conduct of anesthesia. Preoperative Hemogram was obtained. All patients were given standard general anesthesia consisting of propofol, an opioid (fentanyl and morphine), muscle relaxant (atracurium or vecuronium) and a volatile anesthetic (isoflurane or sevoflurane) with oxygen in nitrous oxide. Minute ventilation was titrated to maintain EtCO2 of 28 to 32 mmHg. Esophageal temperature was maintained at ≥36ºC.

Anesthesia was maintained with propofol/ dexmedetomidine infusion, isoflurane (MAC 1.0±0.2), oxygen in nitrous oxide and opioid (fentanyl 1-2mcg/kg/hr). Standard as well as invasive monitoring including arterial catheter for invasive blood pressure, central venous catheter and urinary output catheter was used. Neurosurgeons with more than 10 years of experience operated upon the patients to avoid technical bias. Patients in the study group received tranexamic acid intravenously @10 mg/kg body weight over 10 minutes after induction and then maintenance of continuous infusion @ 1mg/kg/hr intraoperatively till skin closure. Patients in the control group received the same volume of saline per kg body weight as the volume of tranexamic acid in study group. Anesthesia technologist, not involved with the study, prepared the treatment medication and placebo in identical 50 ml syringes for

infusion pumps. Anesthesiologists and surgeons were blinded to randomisation and solution administered.

Fluid therapy was managed by administration of crystalloid solution and colloid. Adequate replacement and maintenance of intravascular volume was guided by monitoring arterial blood pressure, urine output ($\geq$1 mL/kg/hr), and central venous pressure. The amount of crystalloids and colloid given were recorded. A uniform policy for transfusion of blood was followed and blood transfusions were given if Hct fell below 25% by monitoring hourly hematocrit. Blood was started in accordance with the ASA Task Force practice guidelines for blood component therapy. Amount of blood transfused in each patient was recorded.

During surgery the blood loss was determined hourly by ABG samples for hematocrit and surgical suction bottles' blood volume. Blood loss on surgical gowns and drapes were included. Postoperative blood loss was measured from surgical drain for 24 hours.

Blood loss calculations was done by:
(i)     Surgical suction bottles/ gauze count
(ii)    Hematocrit estimation
(ii)    Hb loss = (Hb pre-Hbe) $\times$ BV + Hbt
Expected Blood Loss = 1000$\times$ Hb loss/ Hb pre
Where, Hb pre = initial preoperative Hb conc.
Hbe = Hb conc on 1st postoperative day.
Hbt = total amount of allogenic blood transfused

Tranexamic acid infusion was stopped at the end of the surgery and patient was extubated when standard criteria for weaning and extubation were met.

## STATISTICAL ANALYSIS

Statistical analysis was performed by the institutional biostatistician. The recorded data was compiled and entered in a spread-sheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Statistical software SPSS (version 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. Continuous variables were summarized as Mean±SD and categorical variables were summarized as percentages. Student's independent t-test was employed for comparison of continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables. Graphically the data was presented by bar diagrams. A P-value of less than 0.05 was considered statistically significant.

## IV. RESULTS

Preoperative haemoglobin value in the tranexamic acid group was 12.86 g/dL as compared to 13.45 g/dL in the placebo group and the difference was not statistically significant. (p=0.26).

The intraoperative blood loss in the tranexamic acid group was 332 ml as compared to 576 ml in the placebo group and this difference was statistically significant (p=0.01). The post operative blood loss in the tranexamic acid group was 81.3 ml as compared to 152 ml in the placebo group and this difference was also statistically significant (p=0.025). The total blood loss in the tranexamic acid group was 413.7 ml as compared to 729 ml in the placebo group and this difference was also statistically significant (p=0.006).

**Table 1: Comparison based on preoperative Hb (g/dL) between two groups**

| Hb (g/dL) | Mean | SD | Min | Max | P-value |
|---|---|---|---|---|---|
| TXA Group | 12.86 | 1.589 | 10.1 | 16.5 | 0.265 |
| Saline Group | 13.45 | 2.411 | 9.8 | 18.1 | |

**Comparison based on preoperative Hb (g/dL) between two groups**
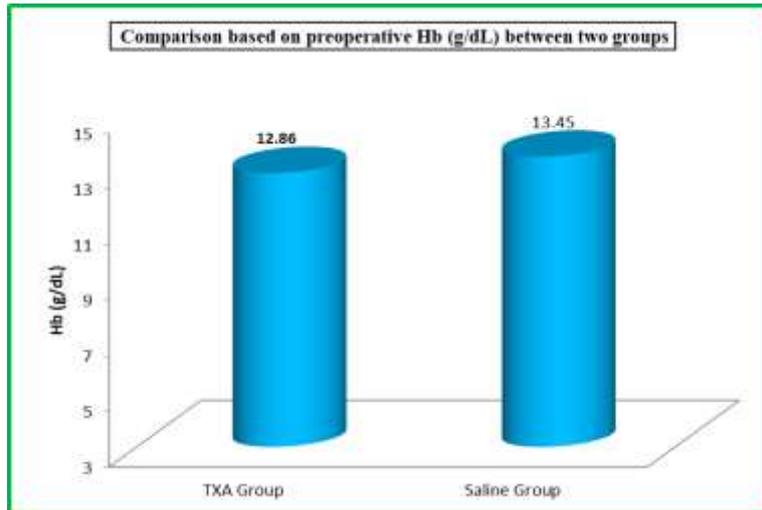
| Table 2: Comparison of perioperative blood loss (ml) between the two groups | | | | | |
|---|---|---|---|---|---|
| **Parameter** | **TXA Group** | | **Saline Group** | | **p-value** |
| | **Mean** | **SD** | **Mean** | **SD** | |
| Intraop Blood Loss (ml) | 332.3 | 413.20 | 576.7 | 289.99 | 0.011* |
| Postop Blood Loss (ml) | 81.3 | 144.14 | 152.3 | 87.56 | 0.025* |
| Total Blood Loss (ml) | 413.7 | 518.92 | 729.0 | 302.93 | 0.006* |



**Comparison of perioperative blood loss (ml) in two groups**
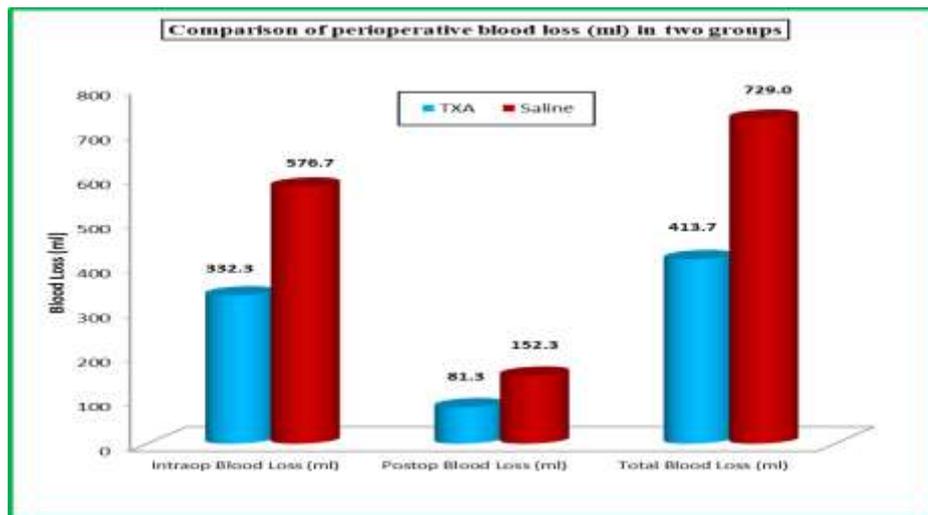
| Table 3: Comparison of blood transfusions in two groups | | | | | |
|---|---|---|---|---|---|
| **No. of Blood Transfusions** | | **TXA Group** | | **Saline Group** | | **P-value** |
| | | **No.** | **%age** | **No.** | **%age** | |
| Intraop | 0 | 20 | 66.7 | 15 | 50.0 | 0.101 |
| | 1 | 4 | 13.3 | 5 | 16.7 | |
| | 2 | 3 | 10.0 | 6 | 20.0 | |
| | ≥ 3 | 3 | 10.0 | 4 | 13.3 | |
| | Mean±SD | 0.7±1.36 | | 1.1±1.21 | | |
| Postop | 0 | 22 | 73.3 | 19 | 63.3 | 0.389 |
| | 1 | 4 | 13.3 | 5 | 16.7 | |
| | 2 | 3 | 10.0 | 4 | 13.3 | |
| | ≥ 3 | 1 | 3.3 | 2 | 6.7 | |
| | Mean±SD | 0.43±0.817 | | 0.63±0.964 | | |
| Total | 0 | 20 | 66.7 | 14 | 46.7 | 0.184 |
| | 1 | 1 | 3.3 | 3 | 10.0 | |
| | 2 | 2 | 6.7 | 4 | 13.3 | |
| | ≥ 3 | 6 | 20.0 | 9 | 30.0 | |
| | Mean±SD | 1.1±1.69 | | 1.7±1.76 | | |

The mean intraoperative transfusion requirement in the tranexamic acid group was 0.7 units as compared to 1.1 units in the placebo group and this difference was not statistically significant p=0.1. Also the postoperative transfusion requirement was less in the tranexamic acid group i.e. 0.43 units as compared to 0.63 units in the placebo group but the difference was not statistically significant p=0.38.
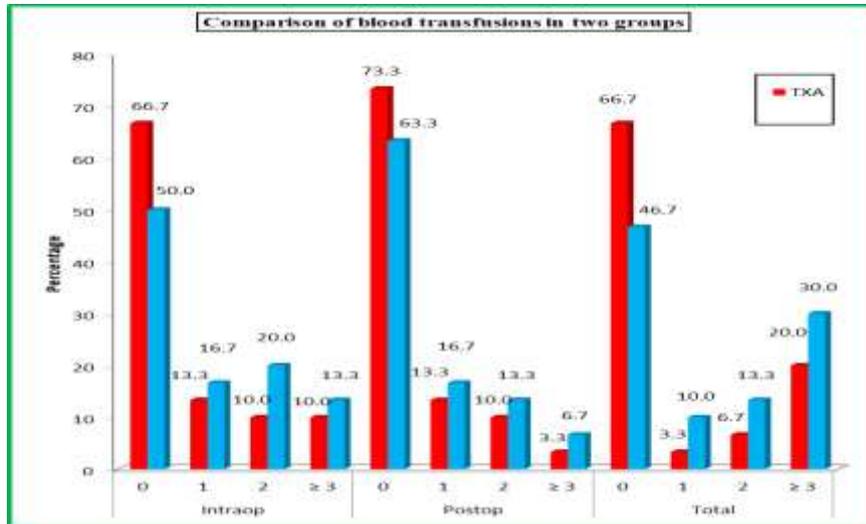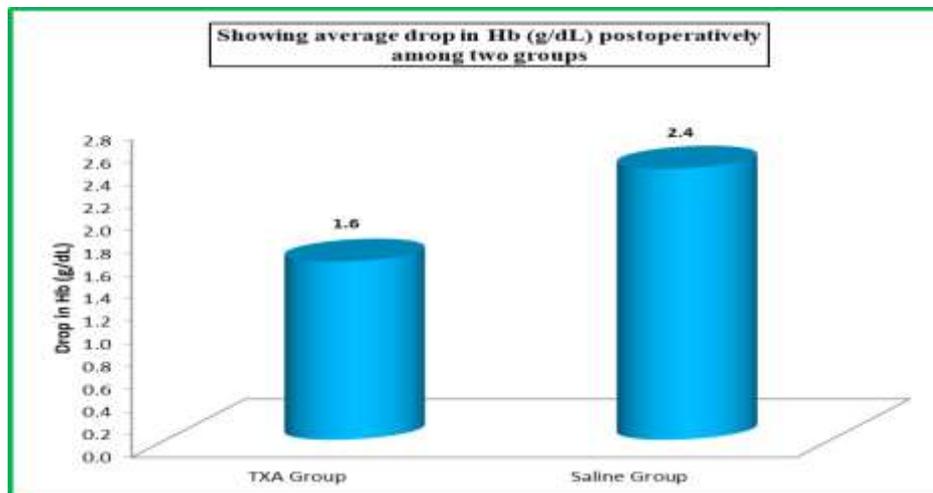


| Table 4: Average drop in Hb postoperatively between the groups | | | | | |
|---|---|---|---|---|---|
| Drop in Hb (g/dL) | Mean | SD | Min | Max | p-value |
| TXA Group | 1.6 | 0.947 | 0.1 | 3.3 | 0.001* |
| Saline Group | 2.4 | 0.735 | 1.3 | 3.7 | |



The average drop in the haemoglobin values postoperatively in the tranexamic acid group was 1.6 g/dL as compared to 2.4 g/dL in the saline group and this difference was statistically significant (p=0.001)

| Table 5: Comparison of average drop in HCT postoperatively between the two groups | | | | | |
|---|---|---|---|---|---|
| Drop in HCT | Mean | SD | Min | Max | p-value |
| TXA Group | 6.2 | 2.642 | 2.2 | 11.6 | 0.006* |
| Saline Group | 8.4 | 3.353 | 4.0 | 14.1 | |
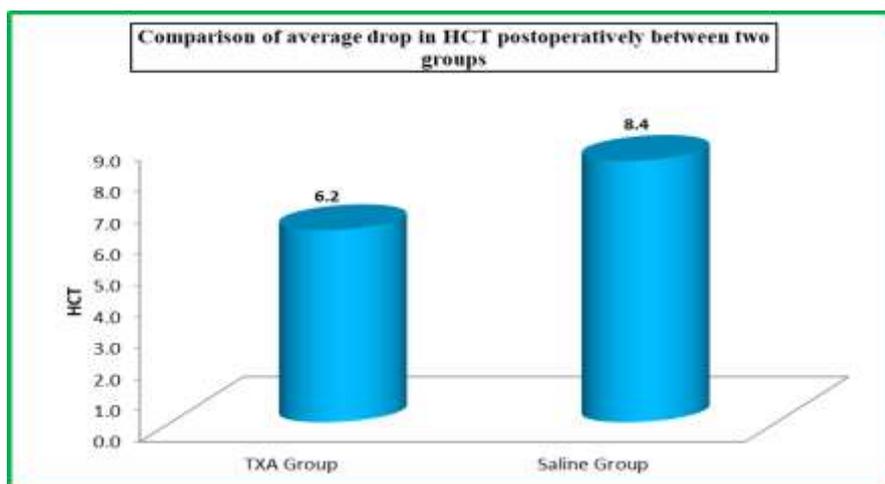
The average drop in the haematocrit values in the post operative period for the tranexamic acid group was 6.2% as compared to 8.4% in the placebo group and the difference was statistically significant (p=0.006)

## V. DISCUSSION

Tranexamic acid has been shown to be effective in reducing blood transfusion in a variety of settings, including spine [23], obstetric [24], urologic [25], major orthopedic [26], and trauma [27] patients. Tranexamic acid is an effective antifibrinolytic and acts as a plasmin inhibitor to prevent clot breakdown. Furthermore, others have speculated that the benefits of tranexamic acid may extend beyond clot stabilization through suppression of proinflammatory mediators [28].

Our study is novel, because there are very few studies in the literature regarding the use of tranexamic acid in elective neurosurgical procedures. In our study, we demonstrated that the administration of tranexamic acid was associated with decreased blood loss and a reduced frequency of transfusion of blood products at our institution.

Tranexamic acid reduced death due to bleeding in patients with trauma. The CRASH-2 trial, which recruited 20,211 adults with acute traumatic bleeding, showed that tranexamic acid reduced death due to bleeding, with no apparent increase

in vascular occlusive events. Planned analysis of the effect of tranexamic acid by the start of treatment showed that early treatment is essential [29].

In our study the average drop in haemoglobin and HCT was significantly lower in TXA group. Accordingly, amount of blood loss was less in TXA group compared to saline group. (332ml vs 576 ml; $p = 0.011$). The transfusion requirement intraoperatively was less in TXA group with only 10 patients requiring blood transfusion compared to 15 patients requiring blood transfusion in saline group. Postoperatively only 8 patients needed blood transfusion in tranexamic acid group compared to 11 patients requiring blood transfusion in saline group. Our findings were similar to Ramya Vel et al [30].

Wong et al [31] also had similar findings in patients undergoing spinal fusion surgery.

In the immediate postoperative period, patients in the TXA group had higher postoperative Hb and Hct levels than the saline group. This could be due to the reduction in blood loss by TXA and thus better hemodynamics.

## VI. CONCLUSION

From our study, it is concluded that the administration of TXA resulted in a significant reduction in blood loss. Tranexamic Acid has been demonstrated to be a cost effective method of preventing hemorrhage in brain tumor surgery patients

when administered after induction of anesthesia and at the start of surgery.

**REFERENCES**
1. Birkmeyer J, Siewers AE, Finlayson EVA, et al. Hospital Volume and Surgical Mortality in the United States. *New England Journal of Medicine*. 2002; 346:1128-37.
2. Palmer JD, Sparrow OC, Iannotti F. Postoperative hematoma. A 5-year survey and identification of avoidable risk factors. Neurosurgery 1994; 35:1061–1065.
3. Deogaonkar A, De Georgia M, Mascha E, Todd M, Schubert A, IHAST Investigators. Intraoperative blood loss is associated with worse outcome after aneurysmal subarachnoid hemorrhage.J Neurosurg Anesthesiol 2006; 18: 302-3.
4. Palmer JD, Francis DA, Roath OS, Francis JL, Iannotti F. Hyperfibrinolysis during intracranial surgery. Effect of high dose aprotinin. J Neurol Neurosurg Psychiatry 1995; 58:104–106.
5. Olson JD, Kaufman HH, Moake J, O'Gorman TW, Hoots K, Wagner K, et al. The incidence and significance of hemostatic abnormalities in patients with head injuries. Neurosurgery 1989; 24: 825–832.
6. Singh VP, Jain D, Mohan R, Bhatia R, Bhargava M. Hemostatic abnormalities in brain tumors. Acta Neurochir (Wien) 1990; 102: 103–107.
7. Marcucci C, Madjdpour C, Spahn DR. Allogeneic blood transfusions: Benefit, risks and clinical indications in countries with a low or high human development index. Br Med Bull 2004; 70:15-28.
8. Soldan K, Barbara J. The risks of infection transmission by blood transfusion in England. J Clin Pathol 1999; 52: 405-8.
9. Murray DJ, Pennell BJ, Weinstein SL, Olson JD. Packed red cells in acute blood loss: Dilutional coagulopathy as a cause of surgical bleeding. Anesth Analg 1995; 80: 336-42.
10. Fearon JA, Weinthal J. The use of recombinant erythropoietin in the reduction of blood transfusion rates in craniosynostosis repair in infants and children. Plast Reconstr Surg 2002; 109: 2190-6.
11. Meneghini L, Zadra N, Aneloni V, Metrangolo S, Faggin R, Giusti F. Erythropoietin therapy and acute preoperative normovolaemic haemodilution in infants undergoing craniosynostosis surgery. Paediatr Anesth 2003; 13: 392-6.
12. Dahmani S, Orliaguet GA, Meyer PG, Blanot S, Renier D, Carli PA. Perioperative blood salvage during surgical correction of craniosynostosis in infants. Br J Anesth 2000; 85: 550-5.
13. Deva AK, Hopper RA, Landecker A, Flores R, Weiner H, McCarthy JG. The use of intraoperative autotransfusion during cranial vault remodeling for craniosynostosis. Plast Reconstr Surg 2002; 109: 58-63.
14. Hans P, Collin V, Bonhomme V, Damas F, Born JD, Lamy M. Evaluation of acute normovolemic hemodilution for surgical repair of craniosynostosis. J Neurosurg Anesthesiol 2000;12: 33-6.
15. Rosenblatt MA. Strategies for minimizing the use of allogeneic blood during orthopedic surgery. Mt Sinai J Med 2002; 69: 83-7.
16. Yao J, Harvath L, Gilbert DL, Colton CA. Chemotaxis by a CNS macrophage, the microglia. J Neurosci Res, 1990. 27(1): p. 36-42
17. CRASH-2 collaborators, Roberts I, Shakur H, Afolabi A, Brohi K, Coats T, Dewan Y et al. The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. Lancet, 2011; 377(9771): 1096-101.
18. Zehtabchi S, Abdel Baki SG, Falzon L, Nishijima DK. Tranexamic acid for traumatic brain injury: a systematic review and meta-analysis. Am J Emerg Med, 2014; 32(12): p. 1503-9.
19. Ker K, Roberts I, Shakur H, Coats TJ. Antifibrinolytic drugs for acute traumatic injury. Cochrane Database Syst Rev, 2015. 5: p. CD004896
20. Hillman J, Fridriksson S, Nilsson O, Yu Z, Saveland H, Jakobsson KE. Immediate administration of tranexamic acid and reduced incidence of early rebleeding after

aneurysmal subarachnoid hemorrhage: a prospective randomized study. J Neurosurg. 2002; 97: 771–8.

21. Baharoglu MI, Germans MR, Rinkel GJ, Algra A, Vermeulen M, van Gijn J, et al. Antifibrinolytic therapy for aneurysmal subarachnoid haemorrhage. Cochrane Database Syst Rev. 2013; doi:10.1002/14651858.cd001245.pub2.

22. Steiner T, Juvela S, Unterberg A, Jung C, Forsting M, Rinkel G. European Stroke Organization, European Stroke Organization guidelines for the management of intracranial aneurysms and subarachnoid haemorrhage. Cerebrovasc Dis. 2013; 35: 93–112.

23. Neilipovitz DT, Murto K, Hall L, Barrowman NJ, Splinter WM. A randomized trial of tranexamic acid to reduce blood transfusion for scoliosis surgery. Anesth Analg 2001; 93: 82-7.

24. Ducloy-Bouthors AS, Jude B, Duhamel A, Broisin F, Huissoud C, Keita-Meyer H, Mandelbrot L, Tillouche N, Fontaine S, Le Goueff F, Depret-Mosser S, Vallet B, Susen SEXADELI Study Group. High-dose tranexamic acid reduces blood loss in postpartum haemorrhage. Crit Care. 2011; 15: R117.

25. Rannikko A, Pétas A, Taari K. Tranexamic acid in control of primary hemorrhage during transurethral prostatectomy. Urology. 2004; 64: 955–8.

26. Zufferey PJ, Miquet M, Quenet S, Martin P, Adam P, Albaladejo P et al. Tranexamic Acid in Hip-Fracture Surgery (THIF) Study. Tranexamic acid in hip fracture surgery: a randomized controlled trial. Br J Anaesth. 2010; 104: 23–30.

27. Shakur H, Roberts I, Bautista R, Caballero J, Coats T, Dewan Y et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet. 2010; 376: 23–32.

28. Levy JH. Antifibrinolytic therapy: new data and new concepts. Lancet. 2010; 376: 3–4.

29. CRASH-2 collaborators, Roberts I, Shakur H, Afolabi A, Brohi K, Coats T, Dewan Y et al. The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. Lancet, 2011; 377(9771): 1096-101.

30. Ramya Vel, Bidkar Prasanna Udupi, Munaganuri Venkata Siva, Satya Prakash, Sethuramachandran, Adinarayanan, Sandeep Mishra et al. Effect of low dose tranexamic acid on intraoperative blood loss in neurosurgical patients. Saudi J Anesthesia 2015; 9(1): 42-48.

31. Jean Wong, Hossan El-Beheiry, Yoga Raja Rampersaud, Stephen Lewis, Henry Ahn, Yoshani De Silva et al. Tranexamic acid reduces perioperative blood loss in adult patients having spinal fusion surgery. Anesthesia Anglesia 2008 Nov; 107(5): 1479-86.

\*\*\*\*\*\*