

Impact of Intravenous Tranexamic Acid on Intraoperative Bleeding during Endoscopic Sinus Surgery

Pawan Kumar Padhy,¹ Ramakrishnan Narayanaswamy²

ABSTRACT

Introduction

Bleeding during surgery is one of the most important concerns in endoscopic sinus surgery (ESS). The study conducted was aimed at assessing the efficacy of tranexamic acid on bleeding during endoscopic sinus surgeries.

Materials and Methods

A total of 30 patients were enrolled for the study. Lund and Mackay symptom score and radiological staging was used to compare clinical profile. The surgical field was assessed by the surgeon who was blinded, i.e., was not aware of which set of patients were receiving the drug. Boezaart and van de Merwe grading scale was used to assess the intraoperative surgical field. Both groups were selected so as to comprise of patients having similar clinical profile in terms of symptom score and radiological staging.

Results

In the arm receiving tranexamic acid, blood loss was found to be less and statistically significant ($p=0.0157$). The surgical field in endoscopic sinus surgery is more important factor in determining the completion and satisfactory outcomes of the surgery. Significantly high percentage (80%) of patients who were given the drug had a grade 2 scale when compared to (26.7%) in patients not receiving the drug. The difference in score in surgical field grading scale was also statistically significant ($p=0.0034$). The reported side effects of tranexamic acid mainly include nausea, vomiting, and possibly arterial or venous thrombosis, however none of the patients in our study had any side effects of the drug. Post-operative stay in the hospital was uneventful.

Conclusion

Intravenous Tranexamic acid reduced the intraoperative bleeding significantly and was useful in providing a better operative field.

Keywords

Endoscopic Sinus Surgery; Tranexamic Acid, Intravenous; Hemorrhage

Chronic rhinosinusitis (CRS) with polyps is a common disease. Sinus surgeries for chronic rhinosinusitis with polyps are commonly done by endoscopic techniques.^{1,2} One of the most important concerns in endoscopic sinus surgery (ESS) is bleeding during surgery. Bleeding during endoscopic surgeries is common and a major concern for both anaesthesiologists and otolaryngologists.³ The most important source of bleeding during ESS are the capillaries.⁴ Also, mean

arterial pressure (MAP) can influence the severity of bleeding.^{5,6}

Controlled hypotension is a way to decrease bleeding during surgery; this may be achieved by using drugs like nitroprusside sodium, nicardipine, nitro-glycerine, beta blockers and also a high dose of anaesthesia drugs like halothane, isoflurane and propofol. Nasal decongestants like oxymetazoline, cocaine and adrenaline^{1,7}, lidocaine combined with adrenaline⁸ and fibrin glue (that is composed of biologic coagulants like thrombin, fibrinogen and cryoprecipitate) can also be used for this purpose. Although the volume of bleeding during ESS is low, considering the limited access to surgery and limitation in visibility of surgical site by endoscope, even low amounts of bleeding can interfere

1 - Department of ENT, Military Hospital, Agra

2 - Department of ENT, Command Hospital(CC), Lucknow Cantt

Corresponding author:

Dr Ramakrishnan Narayanaswamy
email: drnramak5632@gmail.com

with surgeons' visibility.⁹ Then, the surgeon will have to use suction frequently and this will increase the risk of further manipulation of field and also more bleeding and longer duration of surgery.¹⁰ It can cause limitations in visualizing the surgical site and thus increase the risk of intracranial complications as well as possible injury to other adjacent organs, such as the vasculature of the eye.¹¹ One of the popular ways to prevent such problems is administering antifibrinolytic agents, such as tranexamic acid (TA). TA is a hydrophilic antifibrinolytic drug that can be administered orally or intravenously to decrease intra operative bleeding. This product prevents plasminogen linking with fibrin to make plasmin and stabilizes the formed clot.¹² TA has dose dependent complications, such as nausea, vomiting, headache, blurred vision and vertigo. Although, there are some reports of thrombosis on using this product but incidence of such complications is low¹³ and generally, this drug is safe.¹⁴ The aim of the study is to assess the effect of intravenous tranexamic acid on haemorrhage during Endoscopic Sinus Surgery.

Materials and Methods

The study was conducted at the Department of Otolaryngology-Head and Neck Surgery, Command Hospital (Eastern Command), Kolkata, a tertiary care centre. In this comparative interventional study, 30 patients were planned for Endoscopic Sinus Surgery from January 2017 – June 2018.

Subjects included in this study comprised of patients of CRS with polyposis with comparable clinical profile in terms of no. of polyps and sinuses involved. The age range was 12-60 yrs. The patients had to be ASA grade I/II, as all patients were administered controlled hypotensive anaesthesia.

The patients with co morbidities like hypertension, chronic kidney disease, chronic lung disease, malignancies, bleeding diatheses, patients having history of thromboembolic phenomena or those on anticoagulant therapy were excluded from the study.

The patients were randomized. Computer based random number table was used to create two groups (A and B) to ensure an even distribution of treatment

allotment. Group A was given IV tranexamic acid (TA) and Group B was given normal saline (control). Outcome measures included the Boezaart and van de Merwe grading scale¹⁵ to assess the intraoperative surgical field and estimated blood loss based on suction container contents with irrigation fluid subtracted (Intraoperative blood loss was estimated by the attending anesthesiologist at the end of surgery). The surgeon was not aware of which patient is receiving the drug (TA), in order to create blinding and eliminate bias during scoring by surgeon in the Boezaart and van de Merwe grading scale. All injections of TA were given by the anaesthetist to provide blinding to the study.

It was a bolus dose of 10 mg/kg TA given immediately after induction of anaesthesia. All surgeries were performed by the same surgical team unaware of which patient received TA. Same concentration of topical vasoconstrictors (4% xylocaine with 1 in 2,00,000 adrenaline) in nasal packings were used and microdebrider was used during all the surgeries. There was no difference in preoperative oral steroid use between groups. As an institutional protocol, we administer oral steroids i.e. tab prednisolone 1mg/kg daily pre-operatively for five days in each case. Injection Amoxycillin-Clavulanic acid 1.2 gm intravenous 12 hourly was given in first 48 hrs in all patients, till the nasal packs were removed. Boezaart and van de Merwe grading scale as given below at Table I, which was used in our study is a validated scale to evaluate surgical field quality and satisfaction of the surgical team. Recently, a multi-centre standardized reliability analysis verified the inter-observer and intra-observer reliability of the Boezaart scale.

Statistical analysis was done by populating data into a Microsoft excel spreadsheet and then analysing by SPSS 24.0. and Graph Pad Prism version 5. The Independent Samples t-test compares the means of two independent groups in order to determine whether there is statistical evidence that the associated population means are significantly different. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. p-value ≤ 0.05 was considered as statistically significant.

Table I: Boezaart and van de Merwe grading scale.¹⁵

GRADING	OPERATIVE FIELD
0	No bleeding (cadaveric conditions).
1	Slight bleeding: no suctioning required.
2	Slight bleeding: occasional suctioning required
3	Slight bleeding: frequent suctioning required. Bleeding threatens surgical field a few seconds after suction is removed
4	Moderate bleeding: frequent suctioning required and bleeding threatens surgical field directly after suction is removed
5	Severe bleeding: constant suctioning required; bleeding appears faster than can be removed by suction; surgical field severely threatened and surgery usually not possible

Results

The study comprised of 30 patients enrolled between Jan 2017 and Jun 2018. The patients were randomised into two groups of 15 each. The study employed strict inclusion and exclusion criteria as described above, to ensure a homogeneous population who had bilateral disease with comparable clinical profile and radiologic staging. The average radiological staging score was around 17 in both groups.

We found that in Group B (control), the mean blood loss (mean \pm SD) of patients was 438.3333 ± 40.3408 ml with range 370.0000 - 500.0000 ml and the median was 430.0000 ml and in Group A (TA), the mean of blood loss (mean \pm SD) of patients was 404.6667 ± 30.6749 ml with range 340.0000 - 450.0000 ml and the median was 420.0000 ml. Difference between blood loss in two groups was statistically significant ($p=0.0157$).

It was found that in Group B (control), 4(26.7%) patients had Boezaart and van de Merwe scale grade II and 11(73.3%) patients had Boezaart and van de Merwe scale grade III. Whereas in Group A (TA), 12(80.0%) patients had grade II and 3(20.0%) patients had grade III operative field. Difference between Boezaart and van de Merwe grading of the two groups was statistically significant ($p=0.0034$).

Discussion

Endoscopic Sinus Surgery is done for the treatment of patients with chronic sinonasal disease who do not respond to the conventional medical management. The main issue in sinus surgery is blood loss due to the vastly vascular nature of the mucosa. Poor visualization during surgery can lead to difficulty in identification of structures and result in complications or inadequate surgery. Systemic infusion of antifibrinolytic drugs efficiently decreases bleeding during and after surgery.

Our study aimed at studying the impact of bolus dose of tranexamic acid given immediately after induction of anaesthesia on intraoperative bleeding or visualization. Boezaart and van de Merwe grading scale was used to assess the intraoperative surgical field and estimated blood loss was based on suction container contents with irrigation fluid subtracted.

In our study a strict inclusion and exclusion criteria resulted in a small sample size with 15 patients in each group. In our study difference between blood loss in two groups was statistically significant ($p=0.0157$) suggesting a significant reduction in blood loss, which is in accordance to previous studies.

Assessment of difference between intraoperative surgical field using Boezaart and van de Merwe grading scale was statistically significant ($p=0.0034$). In comparison to 12 (80%) patients of TA group only 4

(26.6%) patients of no drug group had a better surgical field (Grade II) as per Boezaart and van de Merwe grading scale. Only 3 out of 15 (i.e. 20%) patients of TA group had a Grade III score compared to 11 out of 15 (i.e. 73.3 %) patients in the control group. In all cases the grading was either Grade II or Grade III. This better surgical field (Grade II) was very convenient and had a positive impact on the surgery.

In all cases in both groups, ESS was completed and there was no restraint of surgical advancement by bleeding in any of the cases. There were no operative complications and all patients were discharged home after nasal pack removal on day 03 post op. There were no side effects noted in any of the 15 patients who received tranexamic acid.

A study was conducted by Chhapola and Matta at Mumbai Port Trust Hospital India.¹⁶ They did a comparative analysis of use of tranexamic acid in a total of 200 patients undergoing endoscopic nasal surgery and concluded that patients who received tranexamic acid showed decreased blood loss amounting to 72.48% ($p < 0.05$). Our study also had statistically significant reduction in blood loss ($p=0.0157$). The above study however included all endoscopic surgeries including septoplasty and did not use any scoring system to score the surgical field visualization.

Alimian and Mohseni from Department of Anaesthesiology, Tehran University of Medical Science, Iran also conducted an analogous study.¹⁷ A total of 84 patients (49 male and 35 female) with a median age of 35 years (range of 19-64 years) were registered for the study. Blood loss comparison showed 184 ± 64 mL in the TA group and 312 ± 75 mL in the placebo group, ($P < 0.01$). As per the surgeon's estimation, the median bleeding score in the TA group was significantly lower than that of placebo group [2 (1-3) vs 2.5 (2-4); $P < 0.0001$]. Like in our study, they also randomized patients to receive either IV tranexamic acid 10 mg/kg (TA group) or sterile water 0.1 mL/kg (placebo group) as a bolus dose immediately after induction of anaesthesia. This study used the same scale which we used in our study, to assess the surgical field. In the referenced study, however, they did not use any topical vasoconstrictors nor did they use a microdebrider, which were used in all cases of our study. The study population was similar

to our study in that patients were treated for chronic rhinosinusitis.

Sahar and Hasanein from Cairo University, Egypt did a triple arm study comparing effect of intravenous tranexamic acid and aminocaproic acid against placebo.¹⁸ A total of 90 patients, aged between 18 to 50 years were randomly allocated into 3 groups (tranexamic acid group/ aminocaproic acid group/normal saline i.e. control group). All patients were undergoing ESS for CRS. They concluded that both intravenous tranexamic acid and aminocaproic acid effectively reduce bleeding during ESS and improve surgical field visualisation and also reduce the duration of surgery. The referenced study compares tranexamic acid vs aminocaproic acid vs placebo (normal saline). They have also compared duration of surgery.

Langille et al stated that 28 patients (median age was 45 years; range was 23-80 years) were involved in the study.¹⁹ Final diagnoses comprised chronic rhinosinusitis with polyposis ($n = 23$) and chronic rhinosinusitis without polyposis ($n = 5$). It was determined that adjunctive intravenous tranexamic acid does not seem to result in a clinically meaningful decrease in blood loss (201 vs 231 mL; $p=0.60$) or improve visualization of the surgical field during ESS – Wormald grading scale (5.84 vs 5.80; $p=0.93$). This study is contradictory to previous studies. In this study, 05 patients had CRS without polyposis. This study has used Wormald grading scale for assessing the surgical field.

Three studies, mentioned below have reported the efficacy of topical and oral forms of tranexamic acid in achieving hemostasis and improving the surgical field in nasal surgeries, including ESS.

In a 2007 study by Athanasiadis et al, 20 patients who underwent ESS were randomized to be getting either 2.5 g of EACA solution, a second group getting 100 mg of TA solution and a third group getting 1 g of TA solution, while the opposite nasal cavity received only saline. TA was observed by the blinded surgeon as more effective than only saline (as placebo) in 80% of cases.²⁰

Another study included 60 patients with CRS.²¹ Thirty patients of the intervention group were given three pledgets soaked in 5% TA and 0.5% phenylephrine for 10 minutes in both nostrils before surgery. In the control

group 30 patients were given only 0.5% phenylephrine by similar technique. The volume of bleed and the clarity of surgical field were evaluated at 15, 30, and 45 minutes subsequently using Boezaart and van de Merwe grading scale. The quality of the surgical field in the intervention group was significantly better only in the first ($P=0.002$) and second ($P=0.003$) quarter but not in the third quarter ($P=0.163$). Moreover, bleeding was considerably less throughout all periods in the intervention group than in the control group ($P=0.001$).

In a study with 400 patients between 18-60 years, who underwent functional endoscopic sinus surgery with septoplasty and conchoplasty, 200 patients did not receive any hemostatic agent (control group) and the other 200 were administered 1 g of oral TA. Dose given was 1 g TA three times daily starting 2 hours before surgery, for 5 days. Bleeding was scrutinized throughout surgery and postop for 2 weeks. Patients who were administered oral TA had significantly lesser amount of operative and postoperative bleeding compared to controls.¹⁰

Conclusion

With the review of literature and results of our study, we can conclude that Inj. Tranexamic acid is a very safe drug and is very effective in reducing blood loss and improving the endoscopic surgical field and any medication or protocol that decreases bleeding may help to increase intraoperative visualization and help with surgical progress and allow for a more complete surgical procedure. Thus, we recommend the use of tranexamic acid in regular ESS for CRS with polyposis unless contraindicated.

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