HAEMOSTATIC ROLE OF TRANEXAMIC ACID IN ENDOSCOPIC SINUS SURGERY – AN INTERVENTIONAL STUDY

Farhan Halim, Zaheer Ul Hassan*, Tarique Ahmed Maka, Kinza Shakil, Adnan Halim***, Aliya Halim*****

Combined Military Hospital, Bannu Pakistan, *Combined Military Hospital, Peshawar Pakistan, **Combined Military Hospital, Risalpur Pakistan, ***Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To compare preoperative intravenous tranexamic acid with placebo in terms of operative estimated blood loss, in patients undergoing endoscopic sinus surgery.
Study Design: Quasi experimental study.
Place and Duration of Study: Department of ENT, CMH Peshawar, from Jan 2017 to Jun 2017.
Methodology: Patients were divided into 2 groups by lottery method. The case group received intravenous tranexamic acid 15mg/kg body weight in 100 ml of normal saline and the control group received 100 ml of normal saline only in identical syringes 15 minutes before start of surgery. At the end of surgery intraoperative hemorrhage was estimated by estimating for blood loss based on the contents of suction container after subtracting the irrigation fluid and the nasopharyngeal packing measurement via electronic scale (1ml of blood weighs 1 gram).
Results: In our study, 30 (46.15%) in case group and 37 (56.92%) in control group were between the age of 18-30 years whereas 35 (53.85%) in case group and 28 (43.08%) in control group were between the age of 31-50 years. Mean ± SD was calculated as 32.0 ± 6.29 in case group and 31.78 ± 6.59 years in control group, 34 (52.31%) in case group and 29 (44.62%) in control group were males while 31 (47.69%) in case group and 36 (55.38%) in control group were females. Evaluation of mean blood loss in both groups was done, it shows 104.15 ± 3.44 ml in case group and 184.32 ±10.14 ml in control group, *p*-value was 0.0001.
Conclusion: We concluded that preoperative intravenous tranexamic acid significantly reduces operative estimated blood volume loss when compared to placebo in patients undergoing endoscopic para nasal sinus surgical procedures.

Keywords: Endoscopic paranasal sinus surgery, preoperative intravenous tranexamic acid, estimated peri-operative blood volume loss.

INTRODUCTION

Endoscopic sinus surgery is one of the modern technique of removing pathological lesions of the nasal cavity and paranasal sinuses including nasal polyposis and sinusitis. The procedure is preferred over conventional nasal surgery due to its higher success rate and lesser chances of complications[1]. Bleeding during surgery is a common inevitable complication and a cause of major concern. Although, the amount of bleeding during surgeries is low, but taking into account the limited environment of surgery and limitation in visibility of surgery site by endoscope, a small amount of bleeding can interfere with visibility of surgeon, which will lead to frequent use of suction and will increase the risk of manipulation of field leading to more bleeding and subsequently prolong duration of surgery. Several methods have been utilized to prevent bleeding during endoscopic surgeries such as head elevation, bipolar diathermy, packing, vasoconstrictor drugs, controlled hypotensive anaesthesia and the use of intravenous anaesthesia techniques[2]. One of the popular methods to deal with hemorrhage is to administer antifibrinolytic agent such as tranexamic acid. Tranexamic acid is an anti-fibrin synthetic agent that binds to the lysine binding sites of plasminogen and plasmin. After saturation of binding sites the parting of plasminogen from

Correspondence: Dr Tarique Ahmed Maka, ENT Department, CMH Risalpur, Pakistan (*Email: tariqmaka@yahoo.com)*
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fibrous fibrillation takes place and thus prevent fibrinolysis. Any tissue injury can activate enzymes release such as tissue plasminogen activator that will convert plasminogen to plasmin and activate fibrinolysis process. Tranexamic acid can inhibit fibrin degradation by impeding the activity of this enzyme[3]. Tranexamic acid prevents plasminogen linking with fibrin to make plasmin and thus stabilizes the formed clot[4]. A study conducted in Tehran, Iran in 2015 showed that there was significantly lesser blood loss in tranexamic acid cases as compared to the placebo[5]. The rationale of study was to assess the haemostatic role of tranexamic acid versus placebo in endoscopic sinus surgery.

METHODOLOGY

It was quasi experiment study conducted at department of ENT and Head & Neck Surgery, Combined Military Hospital Peshawar, from January 2017 to December 2017, with prior permission from hospital ethical review committee. The sample size was calculated using WHO sample size calculator. By keeping significance level 0.05, power of test 80%, unexposed population proportion 35% and anticipated population proportion 14%, a sample size of n=130 (65 in each group) was calculated[5]. Non-probability, consecutive sampling was applied for selection of all the patients. Cases of both gender, ranging between the ages 18-50 years suffering from bilateral ethmoidal paranasal polyps, chronic rhinosinusitis who were unsuccessful from medical treatment and having no previous history of sinonasal surgery that complied were included in the research.

Patients having anemia, bleeding diathesis, ongoing anticoagulant therapy, thrombotic events history, myocardial ischemia, cerebrovascular thrombosis, diabetic and hypertensive, or unfit for general anesthesia were excluded from our research.

Sample population was recruited from ENT department, Combined Military Hospital Peshawar. After taking informed consent, detailed ENT examination was carried out to select the sample. All patients being worked up for Functional Endoscopic Sinus Surgery underwent full examination before surgery, details of fibreoptic nasal examination were recorded and imaging involving computed tomography of paranasal sinuses preoperatively was reported by a radiologist. Patients were divided into 2 groups by lottery method. In case group tranexamic acid 15mg/ kg body weight in 100 ml of normal saline and in the control group 100 ml of normal saline only in identical syringes were used 15 minutes before start of surgery. At the end of surgery intraoperative hemorrhage was estimated by estimating for blood volume loss based on the contents of suction container after subtracting the irrigation fluid and the nasopharyngeal packing measurement via electronic scale (1ml of blood weighs 1 gram).

The SPSS version 17 was used for analyzing data. Descriptive statistics were calculated for all variables. Quantitative variables were analyzed as mean ± standard deviation. Qualitative variables were summarized as percentages and frequencies. Effect modifiers like age & gender were addressed through stratification. Post stratification Independent t-test was applied to link the variance between the two groups. A p-value ≤0.05 was considered statistically significant.

RESULTS

The mean age in case group was 32.0 ± 6.29 years whereas 31.78 ± 6.59 in the control group. The difference was insignificant (p=0.197) between both groups. Age distribution of the cases displayed that 30 (46.15%) in case group and 37 (56.92%) in control group were between 18-30 years of age whereas 35 (53.85%) in case group and 28 (43.08%) in control group were between 31-50 years of age (table-I).

Gender distribution showed 34 (52.31%) in case group and 29 (44.62%) in control group were male while 31 (47.69%) in case group and 36 (55.38%) in control group were females (table-I).

The mean blood loss in case group was 104.15 ± 3.44 ml whereas in control group it was 184.32 ± 10.14 ml. The mean blood loss was

significantly lower (p<0.001) in case group as compared to the control (table-II).

The effect modifiers like age & gender were addressed through stratification. Post stratification t-test was applied (table-III & IV).

Table-I: Age and gender distribution (n=130).

Parameter		Case group (n=65)		Control group (n=65)	
		Cases	Percentage	Cases	Percentage
Age (years)	18-30	30	46.15	37	56.92
	31-50	35	53.85	28	43.08
	Total	65	100	65	100
	Mean ± SD	32.0 ± 6.29		31.78 ± 6.59	
Gender	Male	34	52.31	29	44.62
	Female	31	47.69	36	55.38
	Total	65	100	65	100

Table-II: Blood volume loss comparison (n=130).

Blood Volume loss (ml)	Case group (n=65)	Control group (n=65)	*p*-value
	Mean ± SD	Mean ± SD	
	104.15 ± 3.44	184.32 ± 10.14	0.001

Table-III: Stratification for blood loss with regards to age.

	Age Group (years)	Case group (n=65)	Control group (n=65)	*p*-value
		Mean ± SD	Mean ± SD	
Blood loss (ml)	18-30	104.23 ± 3.35	184.35 ± 10.38	<0.001
	31-50	104.09 ± 3.56	184.29 ± 10.01	

Table-IV: Stratification for blood loss with regards to gender.

	Gender	Case group (n=65)	Control group (n=65)	*p*-value
		Mean ± SD	Mean ± SD	
Blood loss (ml)	Male	103.65 ± 3.26	183.79 ± 10.48	<0.001
	Female	104.71 ± 3.60	184.75 ± 9.99	

DISCUSSION

Endoscopic sinus surgery (ESS) is regularly performed technique by ENT specialists due to the high success rate, low complication and improvements in imaging devices, and computer assisted surgical intervention[5]. However, bleeding during and after ESS is a problem that concerns surgeons and reducing bleeding is a significant challenge. Previous studies established the satisfactory results of tranexamic acid, on hemorrhage propensity in patients go through surgery[6,7,8].

We planned this study to estimate the result of tranexamic acid on amount of blood volume loss in patients during endoscopic sinus surgery.

We compared our data with a previous research conducted in Tehran, Iran in 2015 showed that there was considerably lesser blood volume in tranexamic acid group as compare to in the placebo group (107.7 ± 45.1 Vs 189.3 ± 51ml)[5]. Our results are comparable with the above study.

Eldaba *et al* evaluated the result of tranexamic acid on the hemorrhage during the endoscopic paranasal sinus surgical procedure but this study was conducted in children population[6]. They recorded that solo dose of tranexamic acid intra venous in children during the endoscopic sinus surgery much clears excellence of surgical field, lessens bleeding per operative, and extent of surgical procedure.

Das *et al* evaluated the efficacy of single preoperative bolus dose of tranexamic acid on blood volume loss deterrence, red blood cell transfusion in patients undergoing head and neck cancer surgery and concluded that tranexamic considerably lessens blood loss and chances of colloid,

blood, and crystalloid transfusion caused by head and neck cancer surgery[9].

Ker *et al* carried out a detailed analysis evaluating the result of tranexamic acid on transfusion of blood, events of thromboembo-lism, and mortality in post-operative patients[10]. They revealed that out of 129 trials, carried out between 1972 and 2011, total 10,488 patients were included. Probability of receiving transfusion of blood was reduced by using tranexamic acid (confidence of 95% with interval 0.58 to 0.65; $p<0.001$, risk ratio 0.62). This result persisted as the analysis was restricted to trials using satisfactory distribution concealment (0.68, 0.62 to 0.74; $p<0.001$). The result of tranexamic acid on stroke (1.14, 0.65 to 2.00; $p=0.65$), pulmonary embolism (0.61, 0.25 to 1.47; $p=0.27$), myocardial infarction (0.68, 0.43 to 1.09; $p=0.11$) and DVT (0.86, 0.53 to 1.39; $p=0.54$), were indeterminate. The group using the tranexamic acid (0.61, 0.38 to 0.98; $p=0.04$) showed fewer deaths. Even though the analysis was limited to trials using satisfactory concealment there was significant improbability (0.67, 0.33 to 1.34; $p=0.25$). Cumulative meta-analysis showing that reliable evidence that tranexamic acid reduces the need for transfusion, has been available for over 10 years. These findings support our results but no stroke, pulmonary embolism, myocardial infarction and deep vein thrombosis was recorded in our study and these findings were similar for any mortality.

Alimian *et al* evaluated the results of tranexamic acid on blood volume loss and improves quality of surgical field during endoscopic sinus surgical procedure, they recorded that blood volume loss in the tranexamic acid cases was 184 ± 64 mL as compare to the the placebo cases, 312 ± 75 mL on average (P b 0.01)[11]. The median hemorrhage score in the tranexamic acid cases was considerably lesser than the placebo cases [2 (1-3) vs 2.5 (2-4); P b 0.0001]. The surgeons feel pleased with the quality of surgical field in the tranexamic acid cases as compare to the placebo cases [median score: 4 (3-5) vs 3 (1-5), P b 0.001]. They concluded that tranexamic acid efficiently lessens hemorrhage and improves the quality of surgical field.

Some other former studies described that intra-venous injection of tranexamic acid to patients undergoing head & neck cancer surgery, oral surgery, liver transplantation, cardiac surgery and spine surgery reduced intra-operative and post-operative hemorrhage[12-18].

Finally, our data and other above mentioned studies justify the hypothesis that the "use of intravenous tranexamic acid helps in achieving hemostasis and improving the surgical field during endoscopic sinus surgery". However, some other multicenter trials are required to validate our findings.

CONCLUSION

Systemic administration of tranexamic acid could decrease blood loss and operative time intraoperatively, increasing the satisfaction of surgeons. It did not provoke intraoperative hemodynamic changes, postoperative vomiting or nausea and coagulation parameters abnormality. We concluded that preoperative intravenous tranexamic acid significantly reduces operative estimated blood volume loss when compared to placebo in patients undergoing endoscopic para nasal sinus surgical procedures.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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