Efficacy of Tranexamic Acid with Hypotensive Anesthesia versus Hypotensive Anesthesia Alone on Intraoperative Blood Loss in Orthognathic Surgeries - A Comparative Study

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Abstract

Aim: To evaluate the efficacy of tranexamic acid with and without hypotensive anaesthesia on intraoperative blood loss in orthognathic surgeries. **Objectives:**To assess the amount of blood loss and need for any blood transfusion, quality of surgical field, duration of surgery and Pre-operative and post-operative Hb (g/dl).**Methodology:** This study was carried out between November 2016 to October 2018 on patients reporting to Department of Oral and Maxillofacial Surgery and Department of Orthodontics and Dentofacial Orthopaedics, Faculty of Dental Sciences, Ramaiah University of Applied Sciences, Bengaluru, with skeletal malocclusion, requiring corrective surgeries like anterior maxillary osteotomy, LeFort 1 osteotomy, bilateral sagittal split osteotomy and genioplasty. Patients are divided into study and control group. Patients in Study group received tranexamic acid along with hypotensive anaesthesia and Patients in Control group received only hypotensive anaesthesia. **Results:** We found significant reduction in the amount of blood loss, clear and better surgical field visibility in the study group when compared to the control group. The reduction in Hb (g/dl) levels was statistically significant in both the groups, there was no necessity of blood transfusion in either groups and there was not much variation observed in the duration of surgery amongst both the groups. **Conclusion:** Tranexamic acid along with moderate hypotension is a safe, effective and economic protocol in reducing the blood loss and improving the quality of surgical field, thus allowing for easier, more deliberate and accurate dissection.

Keywords: *Tranexamic Acid, Hypotensive Anesthesia, Orthognathic Surgery*

1. INTRODUCTION

The beauty of the face depends on the balanced architectural relationship of facial features like teeth, jaws, lips, nose, eyes, cheeks and chin. Any discrepancies in these structures are corrected by performing orthognathic surgery. Orthognathic surgery is also performed to alter the shape of the jaws to improve dental occlusion, stability, temporomandibular joint function, open the oropharyngeal airway and improve the patient's facial profile. Various surgical techniques are performed for the correction of dentofacial deformities. The most common includes LeFort I osteotomy with its modifications, anterior maxillary osteotomy, bilateral sagittal split osteotomy and genioplasty[1]

The orofacial region is highly vascular and significant blood loss can occur during orthognathic surgeries. Patients undergoing bimaxillary osteotomy procedures require blood transfusion occasionally. Yu et al (2000) reported that 72.4% of orthognathic patients require double jaw surgeries and that blood loss during simple LeFort osteotomies is about half that of multiple segmentalized osteotomies. Of the 72.4% patients undergoing bimaxillary osteotomy procedures 27–30% requires a blood transfusion[2].

Significant amount of blood loss during the surgery can be safely replaced by crystalloids and

colloids. If the blood loss exceeds 20% to 25% of the patient's total blood volume, the loss should be replaced with blood. Blood transfusion can be a life-saving intervention, however, like all treatments, it may result in acute or delayed complications and carries the risk of transfusion transmissible infections, including human immunodeficiency virus, hepatitis viruses, syphilis, and malaria and Chagas disease[3]. In order to reduce blood loss and improve visibility in the operative field, hypotensive anaesthesia, acute normovolaemic haemodilution, preoperative autologous blood donation, and various pharmacological agents have been used during orthognathic surgery. Tranexamic acid, a synthetic amino acid of lysine inhibits fibrinolysis, has been shown to reduce blood loss and need for blood transfusion in cardiac surgery, knee arthroplasty surgery, spine surgery and orthopaedic surgery[4].

The aim of the study is to evaluate the efficacy of tranexamic acid with and without hypotensive anaesthesia on intraoperative blood loss in orthognathic surgeries.

2. OBJECTIVES ARE TO ASSESS

1. The amount of blood loss and need for any blood transfusion
2. The quality of surgical field
3. The duration of surgery
4. Pre-operative and post-operative Hb(g/dl)

3. METHODS AND METHODOLOGY

This comparative study was done on patients reporting to Department of Oral and Maxillofacial Surgery and Department of Orthodontics and Dentofacial Orthopaedics, Faculty of Dental Sciences, Ramaiah University of Applied Sciences, with skeletal malocclusion, requiring corrective surgeries like anterior maxillary osteotomy, LeFort 1 osteotomy, bilateral sagittal split osteotomy and genioplasty, between November 2016 to October 2018.

INCLUSION CRITERIA

All ASA-1 patients with age ranging between 17 to 30 years having skeletal malocclusion requiring orthognathic surgical procedures like-LeFort 1 osteotomy, anterior maxillary osteotomy (AMO), bilateral sagittal split osteotomy (BSSO) and genioplasty (GP).

EXCLUSION CRITERIA

- Patients with cardiovascular, respiratory, renal and hepatic diseases which would alter the blood loss and hemodynamic status of the patients.
- Patients allergic to tranexamic acid.
- Patients suffering from bleeding disorders.
- Patients who are on medications like fibrinogen, tretinoin, oestradiol valerate which would cause interaction with tranexamic acid.
- Pregnant and lactating mothers.
- Patients who are on birth control pills or oral contraceptive pills.
- Patients associated with cleft lip and palate

After obtaining written informed consent 12 patients requiring 16 surgical procedures who fulfilled the inclusion criteria were included in the study, they were further divided into study group and control group as follows:

1) Study group -patients receiving tranexamic acid along with hypotensive anaesthesia
2) Control group - patients receiving hypotensive anaesthesia alone.

The study group and control groups were further divided into 3 subgroups based on the types of surgical procedures planned which included anterior maxillary osteotomy (AMO), bilateral sagittal split osteotomy (BSSO) and genioplasty (GP).

PRE-OPERATIVE INVESTIGATIONS

1. OPG
2. Lateral cephalogram
3. Chest X ray
4. OT panel
    - Complete blood count
    - Serum electrolyrtes
    - Urine routine examination
    - Liver function test
    - Random blood sugar
    - HIV
    - HBSAg

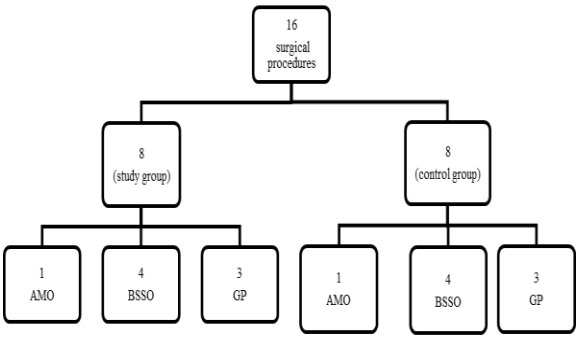

Fig. 1 Pre-Operative investigations

3. METHODOLOGY

Anaesthesia was induced by intravenous Thiopentone sodium and Succinyl choline. Patients were intubated by nasoendotracheal intubation. Anaesthesia was maintained with 2-2.5 minimum alveolar concentration (MAC) of sevoflurane and with incremental doses of Midazolam, Vecuronium bromide, Fentanyl. All patients in both the groups were given hypotensive anaesthesia, mean blood pressure, around 70-75 mm Hg was maintained till osteotomy fragments were fixed.

In study group tranexamic acid was administered intravenously as an initial bolus dosage of 10 mg/kg body weight before starting the skin incision over a period of 20 minutes and then followed by 1mg/kg was administered everyone hour till the end of the surgery. Inj CTRI 1gm, Inj Metrogyl 100ml(500mg), Inj Dexona 8mg were given intraoperatively every 8hours. Surgical techniques used were Dal Pont's Bilateral Sagittal Split Osteotomy with Hunsuck modification, the Tenon technique of Genioplasty and Cupar's approach for Anterior Maxillary Osteotomy. Intraoperative monitoring comprised electrocardiography, blood pressure, O2 saturation and heart rate. Blood pressure was monitored by non-invasive method (Oscillometry). Systolic, diastolic & mean arterial blood pressure, oxygen saturation and heart rate were recorded every 5 minutes. Duration of anesthesia was calculated from induction to extubation and duration of surgery was calculated from start of incision to placement of last suture. Pre-operatively Hb(g/dl) was assessed one day prior to the surgery and post-operatively Hb(g/dl) was assessed on post-operative day one. Blood loss was measured by reducing the amount of saline used, from the volume of fluid in suction unit, and weight of the dry gauze including throat pack was deducted from the weight of blood-soaked gauze and throat pack. 1 gm of weight was considered 1 ml of blood. The need for transfusion of blood perioperatively was decided by anesthesiologist.

The protocol for management of blood loss during surgery is as follows: Blood loss up to allowable blood loss is replaced with crystalloid solutions (1:3 ratios). When blood loss is more than the allowable blood loss, it is replaced by blood transfusion.

Estimation of Estimated Blood Volume (EBV) and Allowable Blood Loss (ABL)

Estimated Blood Volume (EBV):

Neonates: 85 –90 ml/kg body weight, Children: 80ml/kg body weight, Adult: 70ml/kg body weight.

ABL = EBV x (Preoperative Hb - Lowest acceptable Hb)

(Average of preoperative and lowest acceptable Hb)

Allowable Blood Loss:

Table 1a. Allowable blood losses

METHOD	HEALTHY	AVERAGE CLINICAL CONDITION	POOR CLINICAL CONDITION
Percentage method (acceptable loss of blood volume)	30%	20%	less than 10%
Hemodilution method (lowest acceptable hemoglobin or hct)	9g/dl (27%)	10g/dl (30%)	11g/dl (33%)

CLINICAL PARAMETERS

I. Blood loss: Normal saline was used for irrigation, gauze of standard size was used, volume of saline, weight of the gauze, throat pack and mop were determined prior to surgery

- The volume of saline used was recorded and volume of fluid (saline + blood) in suction was noted
- Weight of blood-soaked gauze, throat pack and mop were recorded

Blood loss = A + B

A = Volume of fluid in suction unit – Volume of saline used

B = Weight of blood-soaked gauze, throat pack and mop – Weight of dry gauze, throat pack and mop

II. Quality of surgical field by using fromme's ordinal scale (Duraiswamy et al 2012)

- 5-Massive bleeding; cannot carry out dissection.
- 4-Severe bleeding; significantly compromises dissection.
- 3-Moderate bleeding slightly compromises dissection.
- 2-Mild bleeding, a nuisance but does not compromises dissection.
- Minimal bleeding; not a surgical nuisance.
- 0-No bleeding; virtually bloodless field.

Surgical field was rated every 15 minutes by using fromme's ordinal scale.

III. Duration of surgery was measured in minutes
IV. Preoperative and postoperative haemoglobin was assessed
V. Blood transfusion if required was recorded

Comparison of Mean Blood Loss (Ml) In the Study and the Control Groups

Mean estimated blood loss in the study and the control groups were 109 ± 39.1 ml and 207.4 ± 75.13 ml respectively. The estimated blood loss in study group was significantly less when compared to control group and the value was statistically significant (p=0.005) (Table 1) (Figure 5).

Fig 2 Measurement of blood pressure heart rate and systolic, diastolic and mean arterial pressure

Fig 3 Weight of blood-soaked gauge measuring using weighing machine

Fig 4 Blood mixed with saline in the suction unit

Table 1b. Comparison of mean blood loss in the study and control groups

Group	N	Mean (in ml)	Sd	Mean difference	t-value	p-value
Study	8	109.0	39.1	98.13	3.27	0.005
Control	8	207.3	75.13			

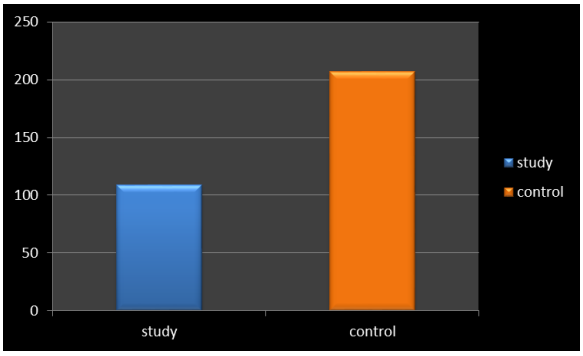

Fig 5 Comparison of Mean Blood Loss (ml) in the Study and the Control group

Distribution of Surgical Field Rating on the Study and Control Groups:

Over all surgical field rating was noted, in the study group 60% of the surgical field rating was under score 1 and 40% of surgical field rating was under score 2. Similarly in control group 85% surgical field rating was under score 2 and 15% surgical field rating was under score 3 . This data shows that the surgical field rating was clear in the study group when compared to the control group (Table 2)

Comparison of Mean Duration of Surgery between the Study and Control Groups

The mean duration of surgery in the GP study group was 87.33 + 20.03 minutes and, in the control, group was 103.3 + 15.28 minutes. The mean duration of surgery in the BSSO study group was 138.7 + 6.2 minutes and in the control, group was 155.0 + 13.50 minutes and in AMO group was 100min and in control group was 100min. There is no statistically significant difference between both the groups in GP, BSSO and AMO surgeries. (Table 3) (Fig. 6).

Table 2. Distribution of surgical field rating in the study and control group

Time	Group	Surgical field								Total
		Minimal		Mild		Moderate		Severe		
		n	%	n	%	n	%	n	%	
15	Study	0	0	4	66%	2	33%	0	0	6
	Control	0	0	5	62%	2	25%	1	12.5%	8
30	Study	3	50%	3	50%	0	0	0	0	6
	Control	0	0	1	12.5%	5	62.5%	2	25%	8
45	Study	3	50%	1	16%	2	33%	0	0	6
	Control	0	0	4	50%	3	37%	1	12.5%	8
60	Study	2	33%	4	66%	0	0	0	0	6
	Control	1	12.5%	6	75%	1	12.5%	0	0	8

75	Study	1	20%	4	80%	0	0	0	0	5
	Control	4	50%	3	37.5%	1	12.5%	0	0	8
90	Study	2	40%	2	40%	1	20%	0	0	5
	Control	3	37.5%	4	50%	1	12.5%	0	0	8
105	Study	2	40%	3	60%	0	0	0	0	5
	Control	2	28.5%	3	42%	2	28%	0	0	7
120	Study	1	25%	3	75%	0	0	0	0	4
	Control	2	40%	2	40%	1	20%	0	0	5
135	Study	2	33.3%	4	66.6%	0	0	0	0	6
	Control	4	80%	1	20%	0	0	0	0	5
150	Study	1	100%	0	0	0	0	0	0	1
	Control	3	100%	0	0	0	0	0	0	3
165	Study	0	0	0	0	0	0	0	0	0
	Control	1	100%	0	0	0	0	0	0	1

Table 3. Comparison of mean duration of surgery between the study and control groups of surgeries

	Group		**Mean**	**Sd**	**Mean difference**	**t- value**	**p- value**
GP	Study	3	87.33 min	20.03	-16.0	1.100	0.33
	Control	3	103.3 min	15.28			
BSSO	Study	4	138.7 min	6.2	-16.5	-2.18	0.70
	Control	4	155.0 min	13.5			
AMO	Study	1	100 min	-	0	-	-
	Control	1	100 min	-			

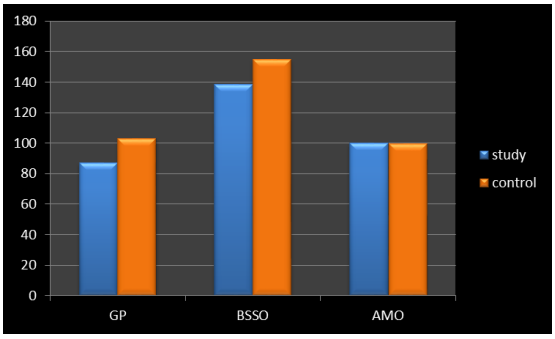

Fig 6 Comparison of mean duration of surgery between the study and control groups of surgeries

Comparison of Difference between the Mean of Pre-Op and Post-Op Hb (G/Dl) In the Study and Control Groups

The mean pre-op Hb (g/dl) in control group and study group were 14.10±1.71 g/dl and 4.36±1.25 g/dl respectively. Similarly, the mean post-op Hb (g/dl) in control group and study group were 12.07±1.46 g/dl and 12.95±1.58 g/dl respectively. By analyzing the data, it was noted that the reduction in the post-op Hb (g/dl) was statically significant in both the groups. (Table 4,5) (Figure 7, 8).

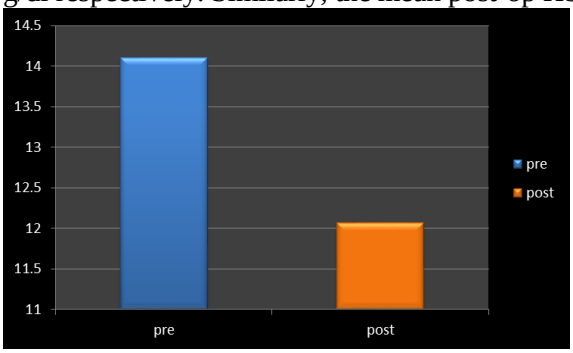

Fig 7. Comparison of pre-op Hb (g/dl) and post-op Hb (g/dl) in the control group

Table 4. Comparison of pre-op Hb g/dl and post-op Hb g/dl in the study group

Hb g/dl	Mean g/dl	Sd	Mean difference	t-value	p-value
Pre-op	14.36	1.25	1.413	1.97	0.06*
Post-op	12.95	1.58			

Table 5. Comparison of pre-op Hb g/dl and post-op Hb g/dl in the control group

Hb g/dl	Mean g/dl	Sd	Mean difference	t-value	p-value
Pre-op	14.10	1.71	2.02	2.02	0.02*
Post-op	12.07	1.46			

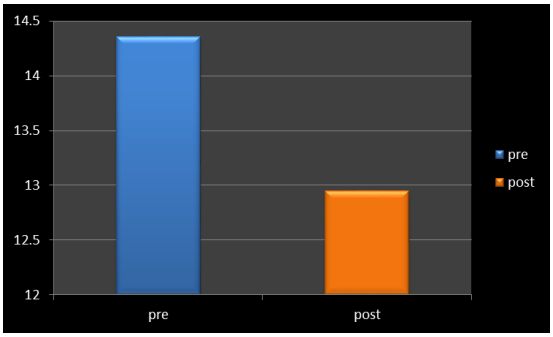

Fig 8. Comparison of pre-op Hb g/dl and post-op Hb g/dl in the study group

4. DISCUSSION

Maxillofacial orthognathic surgery is widely practiced globally and is well established because of its capacity to correct many dentofacial deformities. Although surgical precision is important, the clinician should also pay attention to other parameters such as the operating time and intra-operative blood loss (Yu CNF et al. 2000) [2].

Blood is a finite resource with a limited shelf life and is associated with considerable processing costs. Utilization of this resource needs critical review to reduce the risks to patients and the hospital costs. So various preoperative, and intraoperative protocols have been developed to conserve blood. This is especially relevant when

considering the elective nature of orthognathic surgery (Duraiswamy et al. 2012)[5].

Hypotensive anesthesia is a well-established, effective and safe technique which is particularly useful in Oral and Maxillofacial surgery. The use of drugs to reduce bleeding and autotransfusion has recently emerged as additional complementary approaches for the conservation of blood. The pharmacological approach to blood conservation is attractive because it aims to limit the primary loss of blood during the operation (Sabovic M et al. 2003; Eipe N et al. 2006).A number of drugs including aprotinin, tranexamic acid, epsilon amino caproic acid, desmopressin, prostacyclin, dipyridamole, recombinant factor VIIa and erythropoietin have been investigated for reducing intra-operative blood loss. Amongst all the pharmacological interventions currently available, the serine protease inhibitor aprotinin and lysine analogue tranexamic acid have shown the greatest evidence for efficacy in reducing perioperative blood loss (Eipe N et al. 2006)[6, 7].

In the present study, tranexamic acid was used as a haemostatic agent along with hypotensive anaesthesia. Tranexamic acid was administered intravenously in the dose regimen of 10mg/kg/hr as initial bolus followed by 1mg/kg/hr intra operatively.

One might question the efficacy of this dose regimen as various drug regimens are being used in other studies ranging from 10mg/kg to 100 mg/kg. Bridget K. Fiechtner observed that tranexamic acid in the dose regimen of 10mg/kg/hr, as initial bolus followed by 1mg/kg/hr intra operatively resulted in an adequate plasma concentration (>10 microgram/ml), to prevent fibrinolysis with relatively stable drug levels throughout the procedure. Larger doses do not provide additional haemostatic benefit (Krohn CD et al. 1993; Eftekharian H et al. 2014)[8,9].

We found that the mean estimated blood loss in the study and the control group was 109 + 39.1 ml and 207.4 + 75.13 ml respectively, the results obtained were in accordance with many studies (Song G et al. 2013; Zellin G et al. 2004; Eftekharian H et al. 2014; Duraiswamy et al. 2012). Application of tranexamic acid has reduced the amount of blood loss during surgeries that have been conducted in other fields like orthopaedic, cardiac, and neurosurgery [5,8,10,11].

We noted a significant reduction in the Hb (g/dl) levels in both the groups, furthermore reduction was seen in the control group when compared to study group. The results obtained were in accordance with many studies (Choi WS et al. 2009; Karimi A et al. 2012)[12, 13].

In our study, we noted that the overall surgical field rating was better in the study group as compared to the control group. The clear surgical field aided the surgeon in proper trimming and precise positioning of the osteotomy segments intraoperatively rather than struggling to achieve hemostasis. The results obtained were in accordance with many studies (Dolman et al.2000 and Duraiswamy Sankar et al, 2012)[5,14].

In our study, there was not much variation in the duration of surgery in both the groups. Comparison of the duration of surgery was done between the AMO groups, BSSO groups and GP groups, and no significant difference was noted between these groups. The results obtained were in accordance with many studies (Dolman et al, 2000 and Duraiswamy Sankar et al, 2012)[5, 14].

Several reports have shown that bimaxillary osteotomies are often associated with severe blood loss and require blood transfusion. In our study, the necessity of blood transfusion was assessed by the anesthesiologist based on the amount of blood loss, Hb (g/dl) concentration and duration of surgery. None of the patients in either group received blood transfusion. This was in accordance with studies done by Duraiswamy Sankar et al (2012) and Wing Shan Choi et al (2009)[5, 13].

In a study conducted by Ben J steel et al (2012) the most common complications which were encountered during the orthognathic surgeries were described. These include nerve exposure, soft tissue damage, tooth damage, fracture of the segment, excessive bleeding and bad split. Anesthesia complications included respiratory difficulty, malignant hyperpyrexia and sectioning

of endotracheal tube. Post-operative complications were infection, malocclusion, paresthesia, TMJ dysfunction, condylar resorption, post-operative bleeding, nausea and vomiting[15].

In our study, no such severe complications were noted. Mild discrepancy in the post op occlusion was taken care by using elastics in one patient in the study group. None of the patients in either group received blood transfusion.

Dunn j et al (1999) reviewed the uses of tranexamic acid in surgery and other indications and complications. They noted that the most common complications with the use of tranexamic acid were blurred vision, hypotension associated with rapid intravenous administration, diarrhea and nausea and vomiting. Thromboembolism was rarely noted in these studies. In our study with the use of tranexamic acid, we did not encounter any major complications which was in accordance with the study done by Duraiswamy Sankar et al (2012)[5, 16].

5. CONCLUSIONS

In the present study we found significant reduction in the amount of blood loss, clear and better surgical field visibility in the study group when compared to the control group. The reduction in Hb (g/dl) levels was statistically significant in both study group and control group, there was no necessity of blood transfusion in either of the groups and there was not much variation observed in the duration of surgery amongst both the groups.

Based on our study, we conclude tranexamic acid along with hypotensive anesthesia is a safe, effective and economic protocol in reducing the blood loss and improving the quality of surgical field, thus allowing for easier, more deliberate and accurate dissection.

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