THE EFFECTS OF TWO DOSAGE REGIMENS OF TRANEXAMIC ACID ON THE INCIDENCE OF BLOOD TRANSFUSION REQUIREMENTS IN HEMI-MANDIBULECTOMY

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ABSTRACT

Intra-operative bleeding during hemi-mandibulectomy can be significant and can lead to severe consequences if uncontrolled. Concerns about morbidities associated with significant blood loss, blood safety, continual blood shortage and the rising cost of transfusion services during major surgeries have generated interest in the reduction of transfusion requirements during and after surgery. Tranexamic acid (TXA), a haemostatic agent; is an antifibrinolytic agent that competitively inhibit the activation of plasminogen to plasmin, thus inhibits the dissolution and degradation of fibrin, stabilizes formed clot and reduces active bleeding. It has been used successfully in many surgical specialties to reduce perioperative bleeding. The objective of this study was to compare the effectiveness of 20 mg/kg and 10 mg/kg body weight of a single preoperative intravenous dose of tranexamic acid and 0.9% normal saline (control) on the incidence of blood transfusion in hemi-mandibulectomy. Forty-five (45) participants, who underwent elective hemi-mandibulectomy were included in this randomised, double blind clinical trial. A computer-based randomization method was used in the allotment of the participants into three groups and each group with 15 participants to receive 20 mg/kg or 10 mg/kg body weight of single preoperative intravenous dose of tranexamic acid and 0.9% normal saline. The study parameters were the demographics, the participants preoperative characteristics, units of blood transfused, which were recorded and analysed. Data obtained were analysed using SPSS version 23.0 to compare the study groups in terms of baseline preoperative information and intraoperative findings. The data were summarised in tables, charts and texts. The results were expressed in percentages, mean, standard deviations, median, and interquartile range. Changes in the quantitative variables were analysed using the one-way analysis of variance (ANOVA). The results of the statistical tests were considered significant at p-value of < 0.05. Blood transfusion requirement was 2 units (3.6%) in the 20 mg/kg TXA group, 17 (30.9%) units in the 10 mg/kg TXA group when compared with 36 (65.4%) units in the control group. This study demonstrated that preoperative intravenous administration of 20 mg/kg TXA produced a more profound clinical effect and is more effective than 10 mg/kg TXA in reducing intraoperative need for blood transfusion during hemi-mandibulectomy.

Keywords: Blood transfusion, Hemi-mandibulectomy, Tranexamic acid.
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INTRODUCTION

Intraoperative bleeding during hemi-mandibulectomy can be significant due to numerous microvasculature of the orofacial region, extensive dissections; increase fibrinolysis during surgery as well as inability to cauterize bleeding bone surfaces [1]. Intraoperative blood loss poses a great threat to the patient and can lead to severe consequences if uncontrolled. Despite all of the advancement in the science of blood loss control strategies, the need for blood transfusion during hemi-mandibulectomy and its attendant risks remains of immense concern [2, 3]. Concerns about morbidities associated with significant blood loss, blood safety, continual blood shortage and the rising cost of transfusion services have generated interest in the reduction of transfusion requirements during and after surgery [4, 5]. Current medical standard of care advocates a conservative and limited use of blood products, [3, 5] which further emphasizes the need for better control of bleeding. Several measures have been used to minimize intraoperative bleeding and reduce the need for blood transfusions [6, 7]. Techniques like preoperative infiltration of the surgical field with adrenaline, use of diathermy, use of biological materials like cellulose, bone wax, fibrin spray or glue were incorporated into surgery to aid in controlling bleeding intra-operatively which were hitherto difficult to manage [1, 8].

Towards the end of the last century, there was a growing recognition and respect of the wishes of patients; for example, the Jehovah's Witnesses denomination do not accept blood transfusion [9]. This has led to series of debates and has also brought the concept of "bloodless surgery" where blood conservation strategies are emphasized [9]. Practices employed in this regard include the use of cell salvage methods, [10] hypotensive anaesthesia, [11, 12]

tranexamic acid, [11-15] desmopressin, [16] and aprotinin [17, 18].

One target of modern-day blood conservation strategy is the fibrinolytic system.[8] Fibrinolysis is a physiological surface bound process where activated plasminogen degrades excess plasmin deposition at the site of vascular injury which improves fibrin clot localization and wound healing. Therapeutic inhibition of fibrinolysis has been shown to reduce blood loss in several clinical conditions [11, 15].

Tranexamic acid (TXA), a surface acting, antifibrinolytic agent that act by competitively inhibiting the activation of plasminogen to fibrin, stabilises formed clot and reduces active bleeding. It has been used successfully in many surgical specialties to reduce perioperative bleeding and the need for blood transfusion.

Tranexamic acid is a synthetic analogue of the amino acid lysine (trans-4-aminomethylcyclohexane-1-carboxylic acid) [19, 20] and has a molecular weight of 157. It has been shown to decrease bleeding and the need for blood transfusion in trauma and major surgeries such as total hip and knee arthroplasty, [20-23] spine surgeries, [24, 25] and cardiac surgeries, [26] with documented evidence over the years [11-16]. The efficacy of tranexamic acid has been widely studied and proven in the Caucasians but studies on African climes are scanty.

The objective of this study was to compare the effectiveness of 20 mg/kg and 10 mg/kg body weight of a single preoperative intravenous dose of tranexamic acid and 0.9% normal saline (control) on the incidence of blood transfusion in hemi-mandibulectomy. The outcome of this study will add to the local experience, establish the effectiveness in blood transfusion reduction and perhaps establish a protocol for its use in hemi-mandibulectomy.

METHODOLOGY

This randomized, double blind, controlled clinical trial aimed at comparing the effectiveness of 20 mg/kg and 10 mg/kg body weight of a single preoperative intravenous dose of tranexamic acid and 0.9% normal saline (control) on incidence of blood transfusion in hemi-mandibulectomy was conducted on all patients who had hemi-mandibulectomy in our Centre. Informed consent and ethical clearance were obtained from the institution's Ethics and Research Committee (ADM/E22/A/VII/14733) respectively. Clinical trial registration was done at the Pan-African clinical trial registry (pactr.org), South African Medical research Council [PACTR202110492542152].

Participants aged 18-64 years, healthy and physical status I and II according to the American Society of Anaesthesiologists (ASA) physical status classification were included in the study. Participants who were excluded from the study were those less than 18 years and those older than 64years, those with known allergy to tranexamic acid, those with history or risk of thromboembolism (including patients on oral contraceptive pills, and anticoagulants); those with uncontrolled hypertension, renal or hepatic dysfunction and coagulopathy. Others were those with haematological diseases or any form of bleeding diathesis following a review of the clotting profile including platelet count less than 150,000/m^3 as well as those with history of convulsion. Patients with likelihood of difficult intubation (Mallampati III and IV) were also excluded from the study

The participants were assigned randomly into one of the three groups by a computer-generated random number into group A, B and group C. Those assigned to group A received a single intravenous dose of tranexamic acid of 10mg/kg body weight in 100 mL of 0.9% saline; assigned to group B received 20 mg/kg body weight in 100 mL of 0.9% saline while participants in group C received 100 mL of 0.9% normal saline prior to induction of anaesthesia. The participants were prospectively assigned in such a way that the anaesthetist who injected the study drug and recorded the parameters and the surgeons did not know the type of drug given. Sealed envelopes containing the information of the randomization allocation were prepared and kept with the clerical staff not involved in the study. The envelopes specified as groups A, B or C were transferred to a specific member of the surgical team not involved in the study just before the induction of anaesthesia. The brand of tranexamic acid used was Cyklokapron 500 mg/5 mL Ampoule, manufactured by Pfizer Pharmaceuticals, United States of America. They were sourced from the Pharmacy department of UBTH. These were administered over a 30 minutes duration prior to induction of anaesthesia.

The surgical techniques followed standard protocol involving scrubbing and draping, marking of incision sites and infiltration of the incision sites with saline adrenaline (1:200,000). Diathermy was also used where necessary.

The study parameters were:

1. The primary outcome was the intraoperative blood loss, which was calculated as follows: total volume of blood fluid in the suction bottle minus the volume of irrigating fluid used plus the number of used blood soaked gauze pads calculated as abdominal packs (30 cm x30 cm)=100 mL and gauze pads (10cm x10cm)=10 mL.

2. The incidence of blood transfusion (measured in units) (patient was indicated for blood transfusion when the blood loss exceeded the allowable blood loss (ABL) or 25% of the estimated blood volume),

Allowable blood loss (ABL) =

The estimated volume of blood in adult =70 mL/kg (male), 65 mL/kg (female).

In the descriptive statistics, categorical data were presented in frequency and percentages while the continuous data were presented in mean, median, standard deviation and interquartile range. They were summarised in tables, charts and texts. In inferential statistics, the categorical variables were analysed using Fisher's exact test or Chi square test where necessary. The data distribution was tested for normality with Shapiro-Wilk and Kolgomorov-Smirnov tests. The Kruskall Wallis test was used for intergroup comparisons for non-normally distributed data, while the Analysis of Variance (ANOVA) for normally distributed data. Intragroup comparisons were conducted using paired sample t-test. The analyses were done on per-protocol. The results of the statistical test were considered to be significant when the P value is less than 0.05. All data were analysed using the IBM statistical package for social sciences, IBM SPSS; version 23.0 (IBM Corp. Armonk, NY, USA).

RESULTS

Forty-eight (48) consecutive patients were screened and included in the study. However, three (3) of the participants were dropped while forty-five (45) who underwent hemi-mandibulectomy completed the study as shown in the Figure 1(Consort Flow Chart).

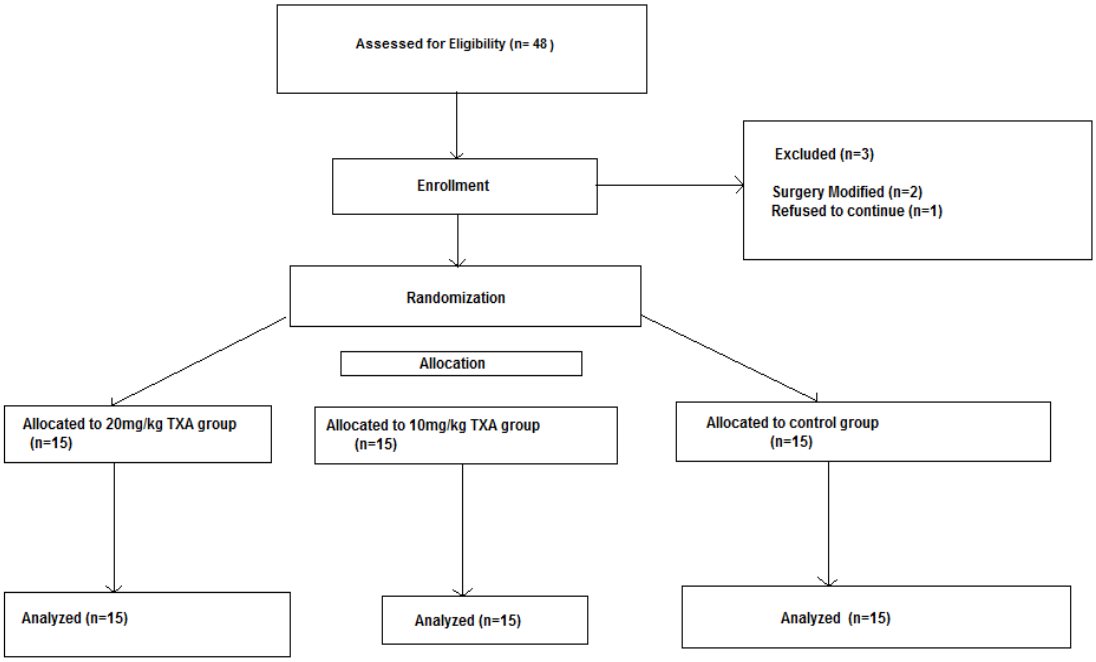

Figure 1: Participant's enrolment allocation is summarized in the CONSORT flow chart

There were 23 (51.1%) males and 22(48.9%) females as the study participants, representing a male to female ratio as 1:1. The median age of the patients was 30 years with an interquartile range of 25-45 years. There was no statistically significant difference in the distribution of demographic characteristics among the study groups (P>005). Table 1 shows the demographic characteristics of the study groups' participants while Table 2 shows the clinical characteristics.

Table 1: Demographic characteristics of the groups (participants)

Study groups	**(A) n (%)**		**(B)**	**(C)**	**Overall n**	**Test statistic**	**P value**
Sex							
Male	9	8 (53.3)	6(40.0)				
Female	6	7 (46.7)	9 (60.0)				0.537
Total		15 (100.0)	15 (100.0)				
Age							
≤20 yrs	0 (0.0)	1(6.7)	5 (11.1)		Fisher		
21-30 yrs	5(33.3)	7(46.7)	7 (46.7)			=9.580	0.476
31-40 years	3(20.0)	1(6.7)	1 (6.7)				
41-50 years	4(26.7)	2(13.3)	3 (20.0)				
51-60 years	1(6.7)	0(0.0)	0 (0.0)				
≥ 60 years	2(13.3)	1(6.7)	3 (20.0)				
Total	15(100.0)	15(100.0)	15				
*Median age	32(28-49) yrs	30(20-33)	29 (24-				
							0.099†

*the Age data was not normally distributed; the result was presented using median and interquartile range. †The Kruskall Wallis Test was used; (A)=20mg/kg TXA, (B)=10mg/kgTXA, (C)=0.9% saline

Table 2: Clinical characteristics of the groups (participants)

Variables	**Study groups**			**Overall**	**Test statistic**	**P value**
	(A) (n=15)	(B) (n=15)	(C) (n=15)			
Weight (kg)	66.13±7.22	59.6±9.04	65.73±7.26	63.82±8.49		0.060
PCV (%)	38.12±3.33	36.83±3.2	34.17±1.12	35.37±7.45		0.061
Preop Hb	12.54±0.89	12.29±1.02	11.75±1.29	12.19±1.11		0.134
Heart rate	78.67±8.54	84±13.52	83.6±7.54	82.09±10.27		0.291
Systolic	123.47±8.26	118.73±8.93	119.33±5.92	120.51±7.92		0.208
BP (mmHg)						
Diastolic BP	67.67±19.91	71.87±6.15	72.6±7.09	70.71±12.61		0.523
24hrPostop Hb (g/dl)	11.19±0.80	10.82±0.73	10.74±0.58	10.92±0.72		0.188
	n (%)	n (%)	n (%)	n (%)		
ASA status						
I	9(60.0)	11(73.3)	9(60.0)	29(64.4)	X^2=1.245 ===0.776	0.791
II	6(40.0)	4(26.7)	6(40.0)	16(35.6)		
Site distr.						
Right	10(66.7)	7(46.7)	9(60.0)	26(57.8)	χ^2=1.2755	0.649

Left)	5(33.3)	8(53.3)	6(40.0)	19(42.2)		
Difficult intubation						
I	6(40.0)	6(40.0)	4(26.7)	16(35.6)	X^2=1.245 1.=0.776	0.791
II	9(60.0)	9(60.0)	11(73.3)	29(64.4)		
Total	15(100.0)	15(100.0)	15(100.0)	45(100.0)		

ANOVA Test (A)=20mg/kg TXA, (B)=10mg/kg TXA, (C)=0.9% saline

Table 3: The effect of two dosage regimen of TXA on blood loss of the study groups

Variable	**Study groups**			**Overall**	**P-value**
	A Mean±SD	**B** Mean±SD	**C** Mean±SD	Mean±SD	
Blood loss(mls)	824.67±370.11	1431.33±334.04	2596.67±878.2	1617.56±536.71	20mg/kgvs10mg/kgvs Control = <0.001 10mg/kgvs Control= <0.0001 20mg/kgvs10mg/kg= <0.0001 20mg/kgvs control =<0.001

A total of 31(69%) participants whose estimated blood loss exceeded the allowable blood loss required blood transfusion; of these, 2 (4.4%) patients in the 20mg/kg group required 1 unit of blood each. In the 10 mg/kg group, 11(24.4%) patients required 1 unit each, while 3 (6.7%) received 2 units each. In the 0.9% saline (control) group, 1(2.2%) received 1 unit, 8 patients received 2 units each, 5 patients received 3 units each, while 1(2.2%) patient received 4 pints. Also, 14 patients did not receive any unit of blood, 13 (28.9%) patients of which are of the 20 mg/kg TXA group while 1(2.2%) was of the 10 mg/kg TXA group. All the participants in the 0.9% saline group had transfusion. There was a significant difference among the groups in terms of number of units transfused, with 20 mg/kg TXA showing statistically significant reduction in the amount of blood transfused compared with the 10mg/kg TXA and the control groups. Table 3 shows the effect of the two dosage regimens of TXA and 0.9% normal saline on blood transfusion requirement while Figure 2 shows the comparison of blood transfusion requirements among the groups/participants.

Table 3: Blood transfusion requirements among the study groups

Transfusion requirement	**A** **n (%)**	**B** **n (%)**	**C** **n (%)**	**Total** **n (%)**	**Test Statistics**	**P-value**
0 unit	13(28.9)	1(2.2)	0(0.0)	14(31.1)	Fishers	<0.0001
1 unit	2(4.4)	11(24.4)	1(2.2)	14(31.1)	Test=48.893	
2 unit	0(0.0)	3(6.7)	8(17.8)	11(24.4)		
3 unit	0(0.0)	0(0.0)	5(11.1)	5(11.1)		
4 unit	0(0.0)	0(0.0)	1(2.2)	1(2.2)		
Total	15(33.3)	15(33.3)	15(33.3)	45(100.0)		

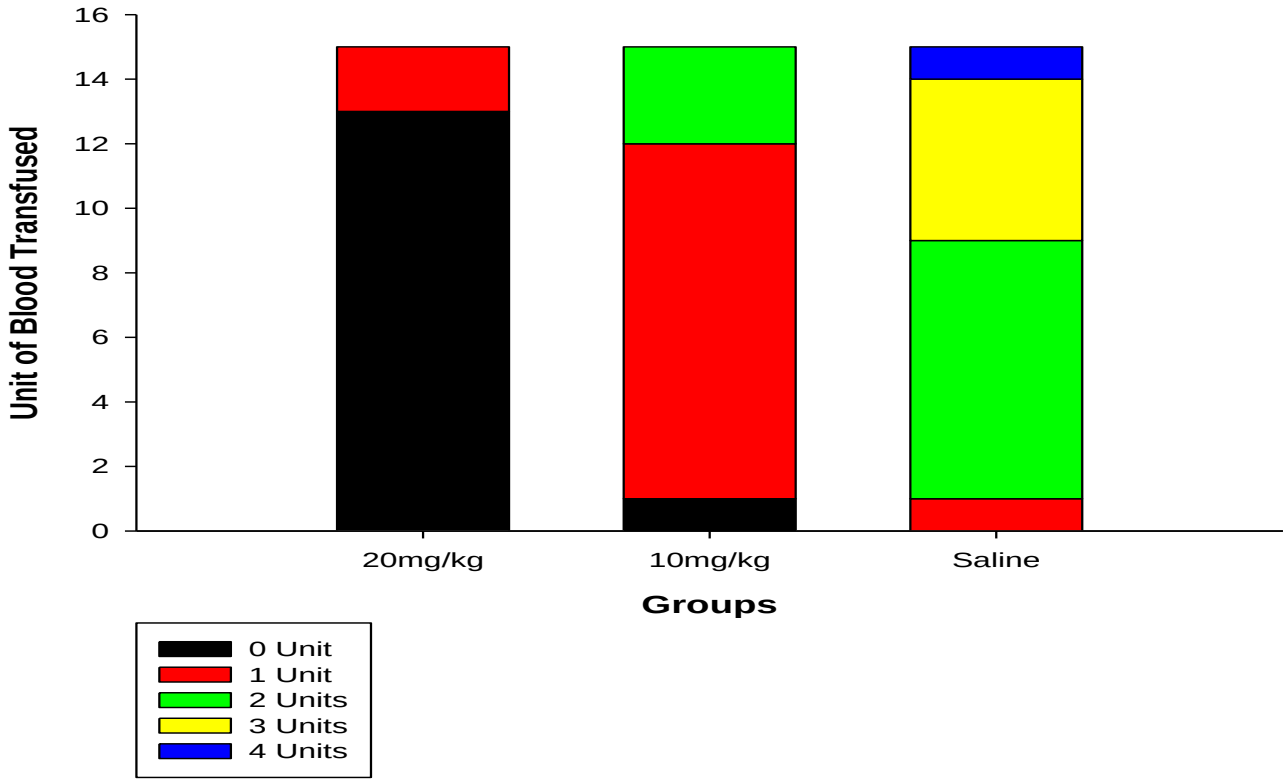

Figure 2: Comparison of blood transfusion requirements among the groups/participants

DISCUSSION

Tranexamic acid has proven to be a vital tool in the physicians' armamentarium to reduce blood loss and decrease transfusion requirements in major surgeries [22, 27-35]. It was hypothesized that no statistically significant difference would be found in the incidence of blood transfusion among the groups/participants. However, this study showed that tranexamic acid significantly reduced the amount of intraoperative blood transfusion requirements. It also showed that 20 mg/kg body weight TXA has a more profound clinical effect than the 10 mg/kg body weight of tranexamic acid.

The use of tranexamic acid was associated with significant reduction in intraoperative bleeding in the study groups, 824.67±370 mL in the 20 mg/kg TXA group and 1431.33±334.0 mL in the 10 mg/kg TXA group when compared with the control group (2596.67±878.2 mL), resulting in significant reduction in the incidence of blood transfusion requirements in this study.

Thirty (31) patients in both the tranexamic acid groups and the control received allogenic blood transfusion. The use of tranexamic acid was associated with significant reduction in the incidence of blood loss and blood transfusion requirements in this study. Though, this study did not show a statistically significant difference in the number of participants requiring transfusion between the tranexamic acid groups and the control group (16 vs 15), nevertheless, the amount of blood transfused was remarkably higher in the control group than the tranexamic acid groups (3.6% vs. 30.9% vs 64.5%) and blood transfusion requirement was generally reduced. The reduced transfusion rate may be related to the decreased blood loss, shorter duration of surgery, skill and experience of the surgeons as well as the site of the lesion being operated [9]. The reduced transfusion rate in this study is consistent with Apipan *et al.*, [36] who reported lower transfusion rate in their study.

The finding of reduced intraoperative blood transfusion requirements in this study is consistent and comparable with the results of previous randomized clinical trials [11, 12, 19, 20, 22, 36, 37] and meta-analyses [21, 23, 27] of individual studies of intravenous tranexamic acid administration in patients who had orthognathic, orthopedic, trauma, obstetric/gynecologic, cardiac, oral, urology and neurosurgical cases, which

demonstrated a reduction of blood loss and the incidence of blood transfusion.

The results of this study are also similar to the results of Choi *et al*. [38] in their randomized controlled study to evaluate the effect of tranexamic acid as intravenous bolus dose of 20 mg/kg on the volume of blood loss, and blood transfusion requirements in seventy-three patients scheduled for bimaxillary osteotomy and they found that tranexamic acid significantly decreased the volume of intra-operative blood loss by 30% and decrease the incidence of blood transfusion. This study is also in agreement with Christabel *et al.* [15]. In their triple blind randomized clinical trial on 49 patients scheduled for Le Fort osteotomy to evaluate the efficacy of tranexamic acid in conjunction with hypotensive anesthesia on volume of blood loss found that bolus dose of intravenous tranexamic acid 10 mg/kg in combination with hypotensive anesthesia could decrease volume of blood loss, decrease incidence of blood transfusion, and improved the quality of surgical field. Strong evidence that tranexamic acid reduces the need for transfusion in surgery has been available for many years [39, 40]. There are clear benefits both from the mortality-morbidity and economic-cost perspectives [39]. Some of these benefits include reduction of intraoperative blood transfusion and its associated morbidities, reduction in cost of transfusion and treatment [41, 42]. Similarly, the Cochrane review of the effect of antifibrinolytics on blood loss and transfusion requirement, [43] found that tranexamic acid significantly reduced blood transfusion by 39%, representing an absolute risk reduction of 18%.

CONCLUSION

This study revealed a significant reduction in the incidence of blood transfusion requirements between the patients who received preoperative intravenous tranexamic acid and those who received normal saline. In comparison, this study also demonstrated that 20 mg/kg TXA produced a more profound reduction than 10 mg/kg on incidence of blood transfusion requirements.

RECOMMENDATION

Tranexamic acid should be considered as an adjunct in potentially haemorrhagic cases in order to reduce the incidence of allogenic blood transfusion and associated morbidities in hemi-mandibulectomy.

REFERENCES

1. SHAH, A., PALMER, A.J.R. & KLEIN, A.A. (2020). Strategies to minimize intraoperative blood loss during major surgery. *Britain Journal of Surgery*, **107**(2): 26-38.
2. CARSON, J.L., CARLESS, P.A. & HERBERT, P.C. (2012). Transfusion thresholds and other strategies for guiding allogeneic red blood transfusion. *Cochrane Database System Review*, **4**: CD002042.
3. INNES, G. (1998). Guidelines for Red blood cell and plasma transfusion for adults and children: an emergency physician's overview of the 1997 Canadian blood transfusion guidelines part 1: Red blood cell transfusion. Canadian Medical Association Expert Working Group. *Journal of Emergence Medicine*, **16**(1): 129-131.
4. OMISAKIN, O.O., AJIKE, S.O., AMINU, S.M. & EGUMA, S.E. (2013). Blood ordering and transfusion practices in maxillofacial surgery in a Nigeria tertiary hospital. *International Research in Medical Sciences*, **1**(4): 40-45.
5. AGUILERA-ROIG, X., JORDAN-SALES, M., NAITERA-CISNEROS, L., MONILLAU-GUARCIA, J.C. & MARTINEZ-ZAPATA, M.J. (2014). Tranexamic acid in orthopaedic surgery (in Spanish). *Rev Esp Cir. Orthop. Traumatol*, **58**(1): 52-56
6. GOODNOUGH, L.T., BRECHER, M.E., KANTER, M.H. & AUBUCHON, J.P. (1999). Transfusion medicine. Second of two parts-Blood transfusion. *New England Journal of Medicines*, **340**(7): 525-533
7. INNES, G. (1998). Guidelines for Red blood cell and plasma transfusion for adults and children: an emergency physician's overview of the 1997 Canadian blood transfusion guidelines part 1: Red blood cell transfusion. *Canadian Medical Association Expert Working Group. Journal of Emergence Medicine*, **16**(1): 129-131.
8. SHAH, N., GUPTA, A. & PATEL, D. (2013). Strategies to Decrease Blood loss in Patients who undergo total knee replacement: A prospective study of one hundred and fifty cases. *JISRF Recon Rev*, **3**(4): 18-26.
9. HEMELEN, G.V., AVERY, C.M.E., VENN, P.J.H., CURRAN, J.E., BROWN, A.E. & LAVERY, K.M. (1999). Management of Jehovah's Witness patients undergoing major head and neck surgery. *Head Neck*, **21**(1): 80-84.
10. LOUBSER, P., STOLTZ, S.M., SCHMOKER, J.D. & BONIFACIO, F. (2003). Blood conservation techniques for Jehovah's Witness patients undergoing complex aortic surgery: A report of three cases. *Journal of*

Cardiothoracic Vascular Anaesthesia, **17**(4): 528-535.

11. PRAVEEN, K., NARAYANAN, V., MUTHUSEKHAR, M.R. & BAIG, M.F. (2001). Hypotensive anaesthesia and blood loss in orthognathic surgery: a clinical study. *British Journal of Oral Maxillofacial Surgery,* **39**(2): 138-140.
12. LIN, S., MCKENNA, S.J., YAO, C.F., CHEN, Y.R. & CHEN, C. (2017). Effects of Hypotensive Anaesthesia on reducing intraoperative blood loss, duration of operation and quality of surgical field during orthognathic surgery: A systematic review and meta- analysis of randomized controlled trials. *Journal of Oral Maxillofacial Surgery,* **75**(1): 73-86.
13. SANKAR, D., KRISHNAN, R., VEERABAHU, M. & VIKRAMAN, B. (2012). Evaluation of the efficacy of tranexamic acid on blood loss in orthognathic surgery. A prospective, randomized clinical study. *International Journal of Oral Maxillofacial Surgery*, **41**(6): 713-717.
14. KARIMI, A., MOHAMMADI, S.S. & HASHEMINSAB, M. (2012). Efficacy of tranexamic acid on blood loss during bi-maxillary osteotomy: a randomized double-blind clinical trial. *Saudi Journal of Anaesthesia,* **6**(1): 41-45.
15. CHRISTABEL, A., MUTHUSCKLAR, M.R., NARAYANAN, V., ASHOK, Y., SOH, C.L., ILANGOVAN, M. & KRISHNAN, N. (2014). Effectiveness of tranexamic acid on intraoperative blood loss in isolated Le Fort I osteotomies: a prospective, triple blinded randomized clinical trial. *Journal of Craniomaxillofacial Surgery*, **42**(7): 1221-1224.
16. ZELLIN, G., RASMUSSON, L., PALSSON, J. & KAHNBERG, K.E. (2004). Evaluation of haemorrhage depressors on blood loss during orthognathic surgery: a retrospective study. *Journal of Oral Maxillofacial Surgery,* **62(**6): 662-666.
17. EFTEKHARIAN, H.R., VAHEDI, R., KARAGAH, A. & TABRIZI, R. (2014). Effect of tranexamic acid irrigation on perioperative blood loss during orthognathic surgery. A double-blind, randomized controlled clinical trial. *Journal of Oral Maxillofacial Surgery*, **73**(1): 129-133.
18. STEWART, A., NEWMAN, L., SNEDDON, K. & HARRIS, M. (2001). Aprotinin reduces blood loss and the need for transfusion in orthognathic surgery. *British Journal of Oral Maxillofacial Surgery,* **39**(5): 365-370.
19. MOHAMED, A.Z. & ABDELAZIZ, K.I. (2015). Effect of Intravenous tranexamic acid on Blood loss and quality of surgical field in orthognathic surgery. *Malaysian Journal of Medicinal Research*, **26**(1): 111-119.
20. HAYNES, M., CALDER, P. & SCOTT, G. (2003). The use of tranexamic acid to reduce blood loss during total knee arthroplasty. *The Knee*, **10**(4): 375-377.
21. HO, K.M. & ISMAIL, H. (2003). Use of intravenous tranexamic acid to reduce allogeneic blood transfusion in total hip and knee arthroplasty: A meta-analysis. *Anaesthesia Intensive Care*, **31**(5): 529-537.
22. POERAN, J., RASAL, R., SUZUKI, S., DANNINGER, T. & MAZUNDER, M., OPPERER, M., BOETNER, F. & MENTSOUDIS, S.G. (2014). Tranexamic acid use and postoperative outcomes in patients undergoing total hip or knee arthroplasty in the United States: Retrospective analysis of effectiveness and safety. *British Medical Journal,* **349**(8): 482-485.
23. YANG, B., LI, H., WANG, D., HE, X., ZHANG, C. & YANG, P. (2013). Systematic review and meta-analysis of perioperative intravenous tranexamic acid use in spinal surgery. *PLoS. One*, **8**(2): 55-56.
24. ELWATIDY, S., JAMJOOM, Z., ELGAMAL, E., ZAKARIA, A., TURKISTANI, A. & EL-DAWATLY, A. (2008). Efficacy and safety of prophylactic large dose of tranexamic acid in spine surgery. *Spine*, **33**(24): 2576-2579.
25. SIGAAT, S., TREMLEY, B., QUATARA, A., COUTURIER, R., TABERLET, C., GRASSIN-DELYLE, S., DRAYFUS, J.F., SCHLUMBERGER, S. & FISCHER, M. (2014). Comparison of two doses of tranexamic acid in adults undergoing cardiac surgery with cardiopulmonary by-pass. *Anaesthesia,* **120**(3): 590-600.
26. SENGHORE, N. & HARRIS, M. (1999). The effect of tranexamic acid on blood loss after third molar extraction under a day case general anaesthetic: a randomized controlled trial. *British Dental Journal*, **186**(12): 634-636.
27. KER, K., EDWARDS, P., PEREL, P., SHAKUR, H. & ROBERTS, I. (2012). Effects of tranexamic acid on surgical bleeding; systematic review and cumulative meta-analysis. *British Medical Journal,* **344**:e3054.
28. ZHANG, H., CHEN, J., CHEN, F. & QUE, W. (2012). The effect of tranexamic acid on blood loss and use of blood products in total

knee arthroplasty: a meta-analysis. *Knee Surgery Sport Traumatol Arthrose*, **20**(9): 1742-1752.
29. ZHAO-YU, C., YAN, G., WEI, C., YUEJV, L. & YING-ZE, Z. (2014). Reduced blood loss after intra-articular artroplasty: a meta-analysis of the literature. *Knee Surgery Sports Traumatol Arthrose*, **22**(12): 3181-3I90
30. LI, Z.J., FU, X., XING, D., SHANG, H.F., ZANG, J.C. & MA, X.L. (2013). Is tranexamic acid effective and safe in spinal surgery? A meta-analysis of randomized controlled trials. *European Spine Journal*, **22**(9): 1950-1957.
31. HANG, F., WU, D., MA, G., YIN, Z. & WANG, Q. (2014). The use of tranexamic acid to reduce blood loss and transfusion in major orthopaedic surgery: a meta-analysis. *Journal of Surgery Research*, **186**(1): 318-327.
32. KAGOMA, Y.K., CROWTHER, M.A., DOUKETIS, J., BHANDARI, M., EIKELBOOM, J. & LIM, W. (2009). Use of antifibrinolytic therapy to reduce blood transfusion in patients undergoing orthopaedic surgery: a systematic review of randomized trials. *Thrombotic Research*, **123**(5): 687-696.
33. TSUTSUMIMTO, T., SHIMOGATA, M., OHTA, H., YUI, M., YODA, I. & MISAWA, H. (2011). Tranexamic acid reduces perioperative blood loss in cervical laminoplasty: a prospective randomized, controlled trial. *Spine*, **36**(3): 1913-I918.
34. SUKEIK, M., ALSHRYDA, S., HADDAD, F.S. & MASON, J.M. (2011). Systematic review and meta-analysis of the use of tranexamic acid in total hip replacement. *Journal of Bone and Joint Surgery British volume*, **93**(1): 39-46.
35. ALSHRYDA, S., SARDAR, P., SUKEIK, M., NARGOL, A., BLENKINSOPP, J. & MASON, J.M. (2011). Tranexamic acid in total knee replacement: a systematic review and meta-analysis. *Journal of Bone Joint Surgery British volume*, **93**(12): 1577–1585.
36. APIPAN, B., RUMMASAK, D. & NARAINTHONSAENEE, T. (2017). The effect of different dosage regimen of tranexamic acid on blood loss on bimaxillary osteotomy: a randomized, double-blind, placebo-controlled study. *International Journal of Oral Maxillofacial Surgery*, **47**(5): 608 -612.
37. PINEIRO-AGUILAR, A., SOMOZA-MARTIN, M., GANDARA-REY, J.M. & GARCIA-GARCIA, A. (2011). Blood loss in orthognathic surgery: a systematic review. *Journal of Oral Maxillofacial Surgery*, **69**(3): 885-892.
38. CHOI, W.S., IRWIN, M.G. & SAMMAN, N. (2009). The effect of tranexamic acid on blood loss during orthognathic surgery: a randomized controlled trial. *Journal of Oral Maxillofacial Surgery*, **67**(1): 125-133.
39. DUCLOY-BOUTHORS, A.S., JUDE, B., DUHAMEL, A., BROISIN, F., HUISSOUD, C., KEITER-MEYER, H., MANDELBROT, L., TILLOUCHE, N., FORTAINE, S., GOUCHEFF, L.E. DEPRET-MOSSER, S., VALLET, B., EXADELLI STUDY GROUP, SUSAN, S. (2011). High-dose tranexamic acid reduces blood loss in postpartum haemorrhage. *Critical Care*, **15**(2): R117.
40. NG, W., JERATH, A. & WASOWICZ, M. (2015). Tranexamic acid: a clinical review. *Anaesthesia Intensive Therapy*, **47**(4): 339-350
41. ABBASI, H., BEHDAD, S., AYATOLLAHI, V., NAZEMIAN, N. & MIRSHAMSI, P. (2012). Comparison of two doses of tranexamic acid on bleeding and surgery site quality during sinus endoscopy surgery. *Advanced Clinical Experimental Medicine*, **21**(6): 773-780.
42. TURTLE, J.R., RITTERMAN, S.A., CASSIDY, D.B., ANAZONWU, W.A., FROEHLICH, J.A. & RUBIN, L.E. (2014). Cost benefit analysis of topical tranexamic acid in primary total hip and knee arthroplasty. *Journal of Arthroplasty*, **29**(8): 1512-1515.
43. HENRY, D.A., CARLESS, P.A., MOXEY, A.J., O'CONNEL, D., STOKES, B.J., McCLELLAND, B., LEUPACIS, A. & FEGUSSON, D. (2007). Anti-fibrinolytic use for minimizing perioperative allogeneic blood transfusion. *Cochrane Database System Review*, **17**(4): CD001886.

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