



COMPARATIVE EVALUATION OF TRANEXAMIC ACID AND HEMOCOAGULASE ON BLOOD LOSS IN ORTHOPEDIC HIP SURGERIES.

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ABSTRACT

Introduction: Major hip surgeries are often associated with significant blood loss. Aim of this clinical study, was to evaluate the efficacy of intravenous hemocoagulase, tranexamic acid in reducing perioperative blood loss and blood transfusion requirements in these surgeries.

Material and Method: With approval of institutional ethics committee and written informed consent, a prospective, randomised study is undertaken on 60 patients from 16 to 60 years of age belonging to ASA physical status I and II, posted for elective lower limb surgery. These patients were randomly divided into two study groups of 30 patients each using 'slip in the box' method for randomization. Group 1 (n=30) received 1gm IV tranexamic acid in normal saline to make a total volume of 500 ml, 10 minutes prior to incision. Group 2 (n=30) received 1 NIH of IV hemocoagulase in normal saline to make a total volume of 500 ml, 10 minutes prior to incision. The patients were intraoperatively monitored for hemodynamic parameters and blood loss and collection in the drain on postoperative day 1 was noted. The duration of surgery was noted. Postoperatively, Hb and Hct analysis and coagulation profile were done.

Side effects and complications of drugs were also recorded.

Results: Total perioperative blood loss in group 1 was 732.33 ± 82.39 ml and group 2 was 690.67 ± 70.86 ml which was not statistically significant. There was no statistically significant difference in percentage fall in Hb and hct between the two groups but statistically significant difference was noted within the groups between pre-op and values after 24 hrs.

Conclusion: Hemocoagulase and tranexamic acid can markedly reduce blood loss and transfusion requirements in major hip and surgeries. No apparent adverse events were observed.

KEYWORDS : Blood Loss, Tranexamic Acid, Hemocoagulase, Coagulation profile, Hip Surgeries.

Introduction

Major orthopedic hip surgeries are associated with excessive perioperative blood loss and necessitates blood transfusion in the absence of blood conservation strategies. Surgery affects the coagulation system and the fibrinolytic system shuts down due to increased release of plasminogen activator inhibitor inducing a state of hyperfibrinolysis accelerating clot degeneration and increasing surgical site bleeding(1). Blood loss and subsequent transfusions are associated with major morbidity and mortality. In order to reduce the amount of bleeding during hip surgery, the technical operative measures and antifibrinolytic agents are required to improve hemostasis (2). Blood conservation strategies commonly used in orthopedic surgeries are tourniquet application and use of various pharmacological procoagulants and antifibrinolytic agents. Orthopedic hip surgeries do not allow the use of tourniquet and hence this method is impractical. Hemostatic agents reduce blood loss and decrease the number of patients who require blood transfusion (3). Antifibrinolytic agents in current use include naturally occurring serine protease inhibitor, aprotinin, the synthetic protease inhibitor nafamostat and the synthetic lysine analogues epsilon aminocaproic acid and tranexamic acid(4). Lysine analogues reversibly bind to the lysine binding site on plasminogen, thereby inhibiting the conversion of plasminogen into plasmin. Tranexamic acid is a competitive inhibitor of plasminogen activator. The intravenous tranexamic acid has been shown to be very useful in reducing blood loss in major hip surgeries (5-9).

Procoagulants used to reduce blood loss are hemocoagulase and ethamsylate. Both are used perioperatively in orthopedic surgeries.

Hemocoagulase is a mixture of purified enzymes isolated from the venom of South American viper called *Bothrops atrox*, which is free from neurotoxin and other toxic substances. By combination of thrombin like activity and thromboplastin like activity, hemocoagulase accelerates initiation, formation and

stabilisation of clotting process (10).

Hemocoagulase shortens bleeding time and clotting time by promoting coagulation at bleeding site and hence reduces blood loss (11-12). In therapeutic doses, it does not cause intravascular coagulation, and only promotes the physiological process of coagulation.

Material and Methods

The present study was conducted after obtaining the clearance from institutional ethical committee and written informed consent on 60 patients of either sex belonging to ASA grade I or grade II in the age group of 30-65 years, undergoing major orthopaedic hip surgeries. Patients having respiratory, cardiac or systemic dysfunction, renal insufficiency, liver impairment, having DVT or coagulation disorders, on anticoagulant therapy, pregnant or lactating females, with known allergy to study medications were excluded from the study.

The 60 patients were randomly divided into two study groups of 30 patients each using 'slip in the box' method for randomization. Group 1 (n=30) received 1gm IV tranexamic acid in normal saline to make a total volume of 500 ml, 10 minutes prior to incision. Group 2 (n=30) received 1 NIH of IV hemocoagulase in normal saline to make a total volume of 500 ml, 10 minutes prior to incision.

After taking the patient inside the operation theatre, peripheral vein was cannulated using an 18 G intravenous cannula. Basic monitors to monitor SPO₂, NIBP, HR, and ECG electrodes were applied. Intraoperatively blood pressure was maintained between 90-110 mm Hg. The study drugs were given to respective group patients. The patients were intraoperatively monitored for hemodynamic parameters and blood loss.

Intraoperatively, the blood loss was measured by weighing swabs, sponges, operative drapes and by measuring the

volumes in the suction bottles after surgery and postoperatively by measuring the amount of blood collected in the drain in post anaesthesia care unit.

The duration of surgery was noted. Postoperatively, hemoglobin (Hb) and hematocrit (Hct) analysis and coagulation profile were done and collection in the drain on postoperative day 1 was noted.

Side effects and complications of drugs were also recorded.

Statistical Analysis

Statistical analysis was done using Statistical Package of Social Science (SPSS Version 20; Chicago Inc., USA). Data comparison was done by applying specific statistical tests to find out the statistical significance of the comparisons. Quantitative variables were compared using mean values and qualitative variables using proportions. Significance level was fixed at P < 0.05. Statistical tests employed for the obtained data in our study were Chi-Square test, Student's t-test and ANOVA.

Results

There were no significant differences between the two groups regarding to age, gender, weight, ASA physical status and duration of surgery as shown in table 1.

Table 1: Patient characteristics in the two study groups.

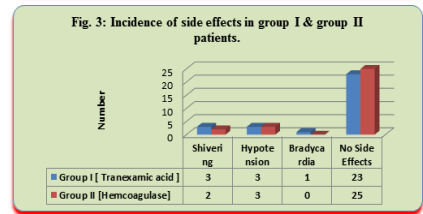
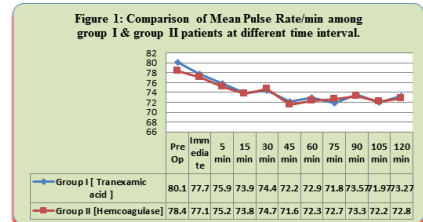
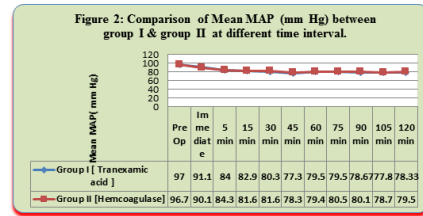
Characteristic	Group I	Group II	p-value
Age (Years)	53.37 (±8.19)	53.83 (±6.71)	0.810
Gender Ratio (Male: Female)	16:14	13:17	0.438
Weight (Kg)	68.93 (±12.33)	68.57 (±12.43)	0.909
ASA Grade (Grade I: Grade II)	14:16	15:15	0.796
Duration of surgery(min)	96.50 (±18.76)	99.87 (±20.47)	0.493

Table 2: Total blood loss & reduction in postop Hb and Hct in the two study groups.

Parameters on post-op day 1	Group I	Group II	
Total blood loss(ml)	732.33 (±82.39)	690.67 (±70.859)	0.040
Percentage fall in Hb	10.25(±2.33)	9.76(±2.06)	0.386
Percentage fall in Hct	9.35 (±1.34)	8.89(±1.05)	0.149

Table 2: Changes in coagulation profile in the two study groups.

Coagulation profile	Group I		Group II		P-value
	Pre-op	After 24 hrs	Pre op	After 24 hrs	
Prothrombin Time	12.41(±0.76)	12.67(±0.68)	12.43(±0.78)	12.46(±0.76)	0.001
Aptt	30.78(±3.42)	31.16(±3.26)	30.43(±3.10)	30.51(±3.12)	0.001
INR	1.08(±0.067)	1.13(±0.09)	1.10(±0.08)	1.12(±0.08)	0.001



Discussion

Major orthopaedic procedures including hip and knee replacement and spine surgery, are associated with severe bleeding because of extensive dissections through bony and fibrotic tissue and inability to cauterize bleeding bony surfaces.10,11 Tissue and vascular damage during surgery or trauma, stimulates cascade of coagulation leading to clot formation to prevent blood loss. However during surgery and trauma the fibrinolytic system is also activated which leads to premature breakdown of the clot and excessive blood loss.^{12,13}

Bhavani S. Vijay et al concluded that tranexamic acid significantly reduces postoperative blood loss and transfusion requirements during major hip and femoral surgeries. They observed that, the mean volume of blood in the drain was 39.33 ± 10.09 ml in tranexamic acid group, as compared to 91.11 ± 17.61 ml in placebo group showing a P<0.001. Mean percentage fall in haemoglobin at day 0 was 2.99 ± 3.45 in the study group as compared to 7.70 ± 6.05 in the placebo group (P<0.001).¹⁴

The total perioperative blood loss was approximately 31% lower in patients given hemocoagulase versus placebo (700.5 ± 45.81 vs 485.7 ± 30.01 ml, P=0.001), in the study performed by Hui-Min Hu et al15. The hemocoagulase group had significantly less intraoperative blood loss (326.1 ± 24.16 mL) compared to the placebo group (556.0 ± 43.58 mL), but there was no difference in the amount of blood/fluid transfused, postoperative haemoglobin There was statistically no significant difference between both the groups with respect to the percentage fall in haemoglobin & haematocrit.

S. Hiippala et al16 and Yamasaki et al17 in their study also found that there is no change in Hb & Hct values TA group on the first postoperative day. Roopa MN et al18 in his study on batroxobin & TXA and Hui-Min Hu et al15 in their study on botropase also did not found any statistically significant difference between parameters like Hb and Hct There was statistically no significant difference in the preoperative and after 24 hrs values of PT, aPTT & INR between the two groups. Similarly, Li Ping et al19 in his study on hemocoagulase with 40 patients undergoing orthopaedic surgeries also concluded that after 24hrs there was no significant change in coagulation state. Bhavani S. Vijay et al14 in their study on 45 patients undergoing hip & femoral surgeries with TXA found

no significant differences in coagulation parameters. Jansen et al.20 in his study on TXA conducted on 42 patients found that after 24 hrs PT & aPTT were unaffected, indicating that the observed blood loss was not caused by any major deficit in coagulation factors.

Both tranexamic acid and hemocoagulase have a role in controlling perioperative bleeding. Thorough literature search revealed paucity of studies directly comparing these two drugs for their efficacy and safety. Present study was designed to directly compare these two drugs and their combined use with regard to effectiveness in reducing blood loss and safety profile. Intraoperative blood loss, drainage, percentage fall in hemoglobin and hematocrit are reduced similarly with both the drugs. However, in view of absence of established data further investigations and studies are required to determine the effectiveness.

Conclusion

Preoperative administration of hemocoagulase 1 NIH significantly reduced the total blood loss after 24 hrs in comparison to the tranexamic acid given at the dose of 1000 mg bolus dose, 10 min prior to the incision in orthopaedic hip surgeries. There was no significant difference with respect to the hemodynamic parameters, percentage fall in Hb & Hct, platelet count and coagulation status due to either drug.

References

- Murphy WG, Davies MJ, Eduardo A. The haemostatic response to surgery and trauma. *Br. J Anaesth.* 1993;70:205-13. [Pubmed]
- Amar D, Grant FM, Zhang H, Boland PJ, Leung DH, Healey JA.
- Antifibrinolytic therapy and perioperative blood loss in cancer patients undergoing major orthopedic surgery. *Anesthesiology.* 2003;98:337-42. [PubMed]
- The society of Thoracic Surgeons Blood Conservation Guideline Task Force:2011 Update to The Society of Thoracic Surgeon & The Society of Cardiovascular Anesthesiologists Blood Conservation Clinical Practice Guideline. *Ann Thorac Surg.* 2011;91:944-82.
- Verstraete M. Clinical application of inhibitors of fibrinolysis. *Drugs.* 1985;29:236.
- Wells PJ Safety and efficacy of methods for reducing perioperative allogenic transfusion: A critical review of the literature. *Am J Ther.* 2002;9:377-88.
- Mongan PD, Brown RS, Thwaites BG. Tranexamic acid and aprotinin reduce postoperative bleeding transfusions during primary coronary revascularization. *Anesth Analg.* 1998;87:258-65.
- Wu CC, Ho WN, Cheng SB, Yeh DC, Wen Mc, Liu TJ, et al. Perioperative parenteral tranexamic acid in liver tumor resection. *Ann Surg.* 2006;243:173-80.
- Makwana J, Paranjape S, Goswami J. Antifibrinolytic in liver surgery. *Indian J Anaesth.* 2010;54:489-95.
- Dalmau A, Sabate A, Acosta F, Garcia-Huete L, Koo M, Sansano T, et al. Tranexamic acid reduces red cells transfusion better than aminocaproic acid or placebo in liver transplantation. *Anesth Analg.* 2000;91:29-34.
- Samudralas s. Topical Hemostatic Agents in Surgery: A Surgeons Prespective. *ARON J* 2008 September; 88(3):S1-S11.
- Xiao-ming L, Ji-chun L, Bentong Y, Qi-cai W. Hemostatic effect of hemocoagulase on postoperative bleeding after pneumonectomy. *Chinese Journal of New Drugs and Clinical Remedies* 2009-12.
- Benoni G and Fredin H. Fibrinolytic inhibition with tranexamic acid reduces blood loss and blood transfusion after knee arthroplasty. A prospective, randomised, double-blind study of 86 patients. *J Bone Joint Surg [Br]* 1996; 78-B:434-440.
- Vijay BS, Bedi V, Mitra S, Das B. Role of tranexamic acid in reducing postoperative blood loss and transfusion requirement in patients undergoing hip and femoral surgeries. *Saudi Journal of Anaesthesia.* 2013;7:29-32
- Hui-Min Hu, Li Chen, Charles Edward Frary, Chi-Chih Chang, Hua Hui, Hai-Ping Zhang et al. The beneficial effect of Batroxobin on blood loss reduction in spinal fusion surgery: a prospective, randomized, double-blind, placebo-controlled study. *Archives of Orthopaedic and Trauma Surgery* 2015;135:491–497.
- Hiippala ST, Strid LJ, Wennerstrand MI, Arvela JV, Niemela HM, Mantyla SK, Kuisma RP, Ylinen JE. Tranexamic acid radically decreases blood loss and transfusions associated with total knee arthroplasty. *Anesthesia & Analgesia.* 1997 Apr 1;84(4):839-44.
- Yamasaki S, Masuhara K, Fuji T. Tranexamic Acid Reduces Postoperative Blood Loss in Cementless Total Hip Arthroplasty. *J Bone Joint Surg Am.* 2005; 87: 766-770.
- Effectiveness and Safety of Batroxobin, Tranexamic acid and a Combination in reduction of blood loss in Lumbar Spinal Fusion Surgery. MN, Roopa DA; Shetty, Ajay Prasad MS; Dumpa, Srikanth Reddy MS; Subarmaniam, Balavenkat MD; Kanna, Rishi Mugesh MS; Shanmuganathan, Rajasekeran PhD. *Spine: Post Acceptance: July 3, 2017 doi: 10.1097/BRS.0000000000002315*
- Li ping, Sun xue fang, Hao Jian Hua et al. Department of anaesthesiology, the 304th Hospital of PLA, Beijing 100037, China. Hemostatic effect of hemocoagulase in orthopaedic surgeries. *The journal of cervicodynia and lumbodynia;*2004-04.
- Jansen AJ, Andreica S, Claeys M, D'haese J, Camu F, Jochmans K. Use of tranexamic acid for an effective blood conservation strategy after total knee arthroplasty. *British journal of anaesthesia.* 1999 Oct 1;83(4):596-601.