A Comparative Study to Assess Effectiveness of Hemocoagulase, Tranexamic Acid and a Combination of both in Reducing Perioperative Blood Loss and Transfusion Requirement in Patients Undergoing Major Hip and Femoral Surgeries

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ABSTRACT

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

Material and methods: 80 patients undergoing hip/femoral surgeries were randomly divided into four groups of 20 each, to receive 0.9% saline (C-control), hemocoagulase (H), tranexamic acid (T) and both agents in combination (B). The amount of perioperative blood loss, transfusion requirements and overall drainage was assessed. The hemoglobin concentration was recorded preoperatively and on postoperative day one.

Results: Total perioperative blood loss in group T and group H was less by 42.9% and 50.9% compared with group C, while in group B it was reduced by 68.6%, 44.9% and 36.1% compared to group C, T and H respectively. The amount of allogenic blood transfusion in group T and group H were reduced by 64.7% and 76.5% compared to group C, while group B decreased by 94.1%, 83.3% and 75% compared to group C, T and H.

Conclusion: Hemocoagulase and tranexamic acid can markedly reduce blood loss and transfusion requirements in major hip and femoral surgeries. The combination seems to achieve best results and was superior to either of the two drugs used alone. No apparent adverse events were observed.

Keywords: Blood Loss, Tranexamic Acid, Hemocoagulase, Transfusion, Hip and Femoral Surgeries.

INTRODUCTION

Major orthopaedic hip surgeries are commonly associated with marked blood loss, and a subsequent need for blood transfusion. Use of allogenic blood products, increases the risk of transmission of infectious diseases and risk of postoperative infection. Several methods[1] have been used to reduce and control perioperative blood loss, like hypotensive anaesthesia[2] and administration of drugs such as ethamsylate, aprotinin, tranexamic acid and hemocoagulase. Hypotensive anaesthesia may have detrimental consequences.[3,4]

The aim of this prospective randomized, double blinded clinical study, was to evaluate the efficacy of intravenous hemocoagulase, tranexamic acid and the combination of these two agents, in reducing perioperative blood loss and blood transfusion requirements in major orthopaedic hip surgeries.

Tranexamic acid is a synthetic derivative of amino acid lysine (4-aminoethyl cyclohexane carboxylic acid).[5] It has antifibrinolytic effect, through reversible blockade of lysine binding sites on plasminogen molecules. It acts by reducing the conversion of plasminogen to plasmin. It thus blocks dissolution of haemostatic fibrin, which stabilizes fibrin structure and thereby may decrease blood loss.[6,7]

Hemocoagulase is a procoagulant mixture of purified enzymes isolated from venom of South American Viper Bothrops atrox. It is free of neurotoxin and other toxins. It has thromboplastin and thrombin like enzyme activities, thereby accelerating the initiation, formation and stabilization of clotting process. In therapeutic doses, it does not cause intravascular coagulation, and only promotes physiological process of haemostasis.[8,9]

MATERIAL AND METHODS

After prior approval from the institutional ethics committee, a prospective randomized double blinded clinical study was designed. Eighty patients of ASA grade I/ II, between 30 and 65 years of age, weighing 40-80 kg, scheduled to undergo elective surgery for femoral fracture like open reduction and internal fixation, hemiarthroplasty, total hip replacement (THR), under regional anaesthesia were included in the study.

Patients having severe systemic disease like diabetes, hypertension, ischaemic heart disease, haemoglobin <10 g/dL, history of any previous thromboembolic episode or coagulation anomaly, haemorrhagic diathesis, DVT or history of anticoagulant therapy or those undergoing bilateral or revision surgeries were excluded from the study. Pregnant females and patients unwilling to participate were also not a part of the study. Patients subjected to surgeries

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extending beyond 180 minutes in duration were excluded from the study.

Patients were randomly allocated into four groups of 20 each (n=20). Written explained consent was obtained from each patient. Routine investigations and a detailed pre anaesthetic checkup was performed. Randomization was done by opaque sealed envelope technique.

The study drug was added to normal saline by an independent anaesthetist, to make a total volume of 500 mL of solution. Drug in each group was administered over 20 min and observations were made by another anaesthetist, who was unaware of the drug contained in 500 mL solution, to ensure double blinding. Haemodynamic parameters (heart rate, systolic, diastolic and mean arterial blood pressure, respiratory rate), haemoglobin concentration, platelet count, bleeding time, clotting times, coagulation profile were noted preoperatively. Patient in each group, received corresponding drug (over 20 min), 25 minutes prior to the incision. Patients in GROUP C (Control group) received 500 ml 0.9% normal saline. GROUP T patients received tranexamic acid 500 mg, GROUP H patients were given hemocoagulase 1 NIH and GROUP B patients received hemocoagulase 1 NIH and 500 mg tranexamic acid.

Systolic blood pressure was maintained between the range of 90-110 mm Hg throughout the surgery. Intraoperative blood loss was managed with the use of crystalloids. Total amount of perioperative blood loss was assessed as intraoperative loss and collection in the drain on day one postoperatively. Intraoperative loss was calculated collectively as amount of blood in suction jar, surgical site spillage and amount soaked in surgical sponges.

The amount of blood in the suction jar was calculated as the total amount collected minus the amount of normal saline used for irrigation. Surgical site spill was calculated approximately as, the area corresponding to a diameter of 50 cm = 250 mL, 75 cm = 500 mL, 100 cm = 1000 mL. The amount soaked in surgical sponge was assessed as a single 30 x 30 cm sponge as 150 mL when fully soaked.

Duration of surgery from time of incision upto skin closure was noted. Haemoglobin concentration and volume of blood in the drain on postoperative day one were measured. The number of units of packed red blood cells transfused during hospital stay was recorded, and complications were documented. Reduction in haemoglobin concentration, exceeding 25% of preoperative level was taken as a criterion for blood transfusion.

STATISTICAL ANALYSIS

Demographic characteristics, haemodynamic parameters, duration and type of surgery, preoperative platelet count and preoperative and postoperative mean haemoglobin concentrations, were compared between all groups and data was analyzed. Biostatistical analysis was done using Openepi, GraphPad and Minitab softwares. For quantitative variables, descriptive statistics (mean and standard deviations) were computed. Comparison of means in groups C, T, H and B was done using ANOVA. For categorical data chi-square test was applied. P value <0.05 was considered significant and <0.001 as highly significant.

RESULTS

All groups were comparable with respect to their demographic profile, baseline haemodynamic parameters, preoperative haemoglobin concentration and platelet count, duration and type of surgery as depicted in figure 1.

As shown in Table 1, intraoperative blood loss through suction, floor spill and swab was found to be 1065 ± 123.7 mL in group C, 567.5 ± 83.15 mL in group T, 525 ± 52.57 mL in group H and 315 ± 60.91 mL in group B. Collection in the drain on post-op day one was 192 ± 32.3 mL in group C, 150 ± 14.9 mL in group T, 92 ± 10.05 mL in group H and 78.5 ± 13.87 mL in group B. Total amount of blood loss (intraoperative + drain) was 1258 ± 136.48 mL in group C, 717.5 ± 78.33 mL in group T, 617 ± 52 mL in group H and 394.5 ± 62.95 mL in group B.

The amount of intraoperative bleeding in group T and group H decreased similarly (*P*=0.061) by 46.7% and 50.7% compared with group C, while group B was reduced by 70.4%, 44.5% and 40% compared to group s C, T and H respectively (*P* =0.00). Overall drainage of group T, H and B decreased by 21.9%, 52.1% and 59.1% compared with group C respectively, while group H was reduced by 38.7% compared with group T (*P*=0.00). Drainage in group B decreased by 47.67%, 47.77% and 59.1% as compared to groups T, H and C (*P*=0.00).

Figure 2 shows that total blood loss of group T and group H decreased by 42.9% and 50.9% (slightly higher) compared with group C (*P*<0.001), while in group B it was reduced

Parameter	Group C	Group T	Group H	Group B	P value
Intraoperative loss (mL)	1065± 123.7	567.5± 83.15	525± 52.57	315± 60.91	0.00
Drain (mL) on day one postop	192± 34.3	150± 14.9	92± 10.05	78.5± 13.87	0.00
Total blood loss (mL)	1258± 136.5	717.5± 78.33	617± 52	394.5± 63	<0.001

Table-1: Comparison of perioperative blood loss in various groups

Parameter (on postop day one)	Group C	Group T	Group H	Group B	*P* value
Postoperative Hb (gm%)	7.59 ± 1.3	8.76 ± 1.09	8.62 ±0.96	9.61± 1.15	<0.05
Postoperative Hb fall (gm%)	3.72 ± 0.88	2.37 ± 0.35	2.12± 0.36	1.48± 0.42	0.00
% fall in Hb	33.09 ± 8.5	21.47± 3.96	19.9± 4.03	13.53±4.25	<0.05
Transfusion Requirement	17	6	4	1	<0.05

Table-2: Postoperative transfusion and reduction in postoperative haemoglobin

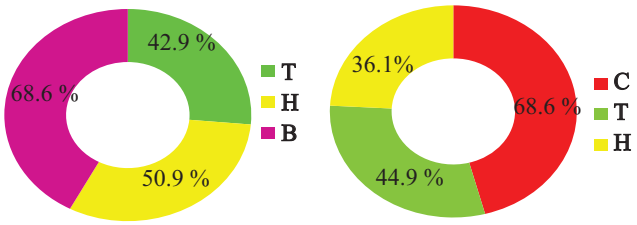

Figure-1: Reduction in total blood loss

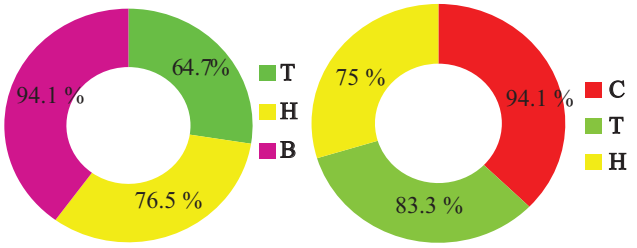

Figure-2: Allogenic blood transfusions

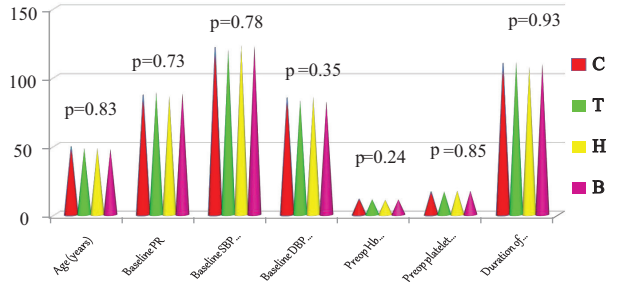

Figure-3: Comparison of demographic and baseline hemodynamic parameters

by 68.6%, 44.9% and 36.1% compared to group C, T and H respectively (P<0.001).

The amount of allogenic blood transfusion, as illustrated in figure 3, were reduced by 64.7% and 76.5% in group T and group H respectively as compared to group C, while group B decreased by 94.1%, 83.3% and 75% compared to group C, T and H (P<0.05).

Table 2 demonstrates that the amount of postoperative haemoglobin was highest group B (9.61± 1.15) and lowest in group C (7.59 ± 1.3), with group T (8.76 ± 1.09) and H (8.62 ±0.96) having similar values (P<0.05).

No major difference was found between the groups regarding average haemodynamic parameters. No significant complication or thromboembolic episode was encountered.

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]

The Cochrane review on "antifibrinolytic use for minimizing perioperative blood transfusion" included 21 trials of tranexamic acid vs. control (hip and knee replacement), and reviewed 993 patients in orthopaedic surgery. It showed that tranexamic acid, significantly reduced allogenic blood transfusion (56%) and the total amount of blood lost during perioperative period (avg. 440 ml) in orthopaedic surgery.[14]

Bhavani S. Vijay, Vikram Bedi,[1] Subhro Mitra, and Bikramjit Das, 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). The number of patients required blood transfusions were lower in the study group than in the placebo group (P=0.01).[15]

Husted H[1], Blønd L, Sonne-Holm S, Holm G, Jacobsen TW, Gebuhr P, performed a prospective, randomized, double-blind study on 40 patients scheduled for primary total hip arthroplasty to determine the effect of tranexamic acid on perioperative blood losses and on the number of blood transfusions needed. Patients receiving tranexamic acid had a mean perioperative blood loss of 480 mL versus 622 mL in patients receiving placebo (P=0.3), a postoperative blood loss of 334 mL versus 609 mL (P=0.001), a total blood loss of 814 mL versus 1231 mL (P=0.001) and a total need for 4 blood transfusions versus 25 (P=0.04). No patient in either group had symptoms of deep venous thrombosis, pulmonary embolism or prolonged wound drainage.[16]

Yamasaki S[1], Masuhara K, Fuji T, in their study, reported that the total intraoperative blood loss in the tranexamic acid group (607 ± 298 mL) was similar to that in the control group (633 ± 220 mL), (P<0.001) and concluded that in patients undergoing total hip arthroplasty without cement, preoperative administration of tranexamic acid is associated with decreased postoperative blood loss during the first twenty-four hours, especially during the first four hours after surgery.[17]

Wang Dan, LI Yan-hui, MA Hai-chun, with the objective to investigate the effects of hemocoagulase on perioperative blood loss and coagulation in patients with low molecular heparin anticoagulation, undergoing total hip replacement found that intraoperative and postoperative 24 h bleeding volume were 629 ± 97 mL and 273 ± 87 mL in control group, and they were 312 ± 79 mL and 213 ± 74 mL with 2 IU of intravenous hemocoagulase (P<0.05). The rate of deep venous thrombosis were 13% and 7% in two groups, and there was no difference (P>0.05).[18]

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, Li Chen, Charles Edward Frary et al. 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

or RBC between the two groups.[19]

Xu Chengshi[1], Wu Anshi, Yue Yun in their study on patients undergoing surgery for adolescent idiopathic scoliosis, reported observations which were in agreement to this study. Blood loss in hemocoagulase group and tranexamic acid group, decreased by 35.3 and 42.8% (P=0.212) compared with control group, while in combination group was reduced by 64.5, 45.1 and 37.8% compared to control, hemocoagulase and tranexamic acid groups, respectively. The amount of allogenic blood transfusion in hemocoagulase group and tranexamic acid group was reduced by 57.6 and 72.4% compared to control group (P= 0.069), while in combination group decreased by 94.7, 87.5 and 80.9% compared to other three groups.[20]

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. The combination appears to achieve best results and seems to be superior than either of the two drugs used alone. Intraoperative blood loss, drainage, percentage fall in hemoglobin and allogenic blood transfusions are reduced similarly with the individual use of either of the drugs and markedly with the combination.

However, in view of absence of established data further investigations and studies are required to determine the effectiveness.

CONCLUSION

Hemocoagulase and tranexamic acid administered preoperatively, can markedly reduce blood loss and transfusion requirements in major hip and femoral surgeries. The combination of both the drugs is synergistic and is superior in efficacy with no major adverse effects. This would help to reduce allogenic blood transfusions and thus avoid transfusion related complications.

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