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Original Research Article

Comparative Study of the Amount of Blood Loss with the Use of Hemocoagulase and Tranexamic Acid in Intraoperative and Postoperative Period during Mitral Valve Replacement on Cardiopulmonary Bypass Surgery

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Abstract:

Objective: To compare the amount of bleeding with the use of Hemocoagulase and Tranexamic acid in intraoperative period.

Methodology: A Prospective, randomized study was conducted in the Department of Anesthesiology, Gandhi Medical College, and associated Hamidia hospital, Bhopal Madhya Pradesh among 60 Patients of 20-60 years old age group selective for MVR, and not on Anticoagulant therapy. After explaining the protocol to all patients, a written and informed consent was taken from all patients. A detailed history, complete physical examination and routine investigations were done for all patients with those who having ASA Grade II and III and NYHA Class II and III were randomly allocated into two groups; Group 1 given i.v Injection Hemocoagulase in the dose 1.0 NIH unit as intravenous infusion over 30 minutes prior to surgery then same dose i.v once a day for 3 days postoperatively. Group 2 given Tranexamic acid in standard dose 1 gm as i.v infusion over 30 min prior to surgery and same dose repeated once a day for 3 days postoperatively.

Results: The Mean Blood Loss intraoperatively of Group 1 was 453.33ml and in Group 2 was 747.5ml. The difference of blood loss among two groups was statistically significant (p value 0.00001) while Postoperatively, Mean Blood Loss of Group 1 was 400 ml and in Group 2 was 581.6 ml. The difference of blood loss among two groups was statistically significant (p value 0.0004).It shows that intraoperatively 35.79% reduction in blood loss in Group 1 comparison to Group 2 on other side Postoperatively 31.22 % reduction in blood loss in Group 1 in comparison to Group 2.

Conclusion: Bleeding reduces in Intraoperative and Postoperative period with the use of Hemocoagulase and Tranexamic acid in Intraoperative and Postoperative Period during Mitral Valve Replacement on Cardiopulmonary by Pass. Our study conclude that, Hemocoagulase is more effective than tranexamic acid to control the amount of blood loss and need of blood transfusion (both intra and postoperatively) in adult patients of ASA grade II and III during Cardiac Surgery under Cardiopulmonary bypass.

Keywords: Hemocoagulase, Tranexamic, Blood loss, ASA, MVR, Cardiopulmonary bypass.

Introduction

Haemorrhage necessitating blood transfusion is frequently observed after cardiac surgeries, particularly those that include the use of cardiopulmonary bypass (CPB). Cardiac surgeries utilise around 10% to 15% of the country's blood supply, and there is evidence indicating that this proportion is growing. This is mostly due to the increasing intricacy of cardiac surgical procedures. Most patients undergoing cardiac operations with CPB experience adequate wound clotting with heparin reversal and do not need blood transfusion. However, CPB results in a higher requirement for blood transfusion in comparison to other cardiac treatments. [1] Empirical evidence derived from a substantial cohort of patients enrolled in The Society of Thoracic Surgeons Adult Cardiac Surgery Database indicates that 50% of patients who have cardiac surgeries are administered blood transfusions. [2] Mounting data indicates that blood transfusion during cardiac operations is associated with worse short and long-term results. [3,4] Perioperative haemorrhage continues to be a significant complication both during and after surgical procedures, leading to higher rates of illness

and death. The main factors contributing to non-vascular sources of hemostatic perioperative bleeding are underlying undiagnosed bleeding disorders, the kind of surgical procedure, and acquired coagulation abnormalities resulting from bleeding, dilution of blood, or intake of hemostatic factors. For a patient experiencing bleeding, the usual treatment methods involve giving them blood products from a donor, using medications at the same time, and using more pure and artificially produced substances that help with blood clotting. Perioperatively, many hemostatic alterations take place following trauma and intricate surgical interventions, such as heart surgery and liver transplantation. Tranexamic acid, desmopressin, fibrinogen, and prothrombin complex concentrates are innovative approaches used for preventing and treating bleeding during surgery. The use of thrombo elastography, rotational thrombo elastometry, and platelet function tests in point-of-care patient testing has enabled a more comprehensive evaluation of precise targeted treatment for hemostasis.

Effective multimodal management strategies are necessary to enhance administration practices, decrease the use of allogenic blood products, and mitigate the potential dangers associated with transfusion. Cardiac procedures still face the significant issue of excessive bleeding as a major consequence. Upon occurrence, it has the potential to elevate both morbidity and death rates. Additionally, each further medical intervention results in an escalation in treatment expenses. The utilisation of blood components and blood products is elevated, along with the duration of operation, hence extending the length of stay in postoperative units and in the hospital.

While the frequency and criteria for blood transfusions may vary across various cardiac surgery departments, it is estimated that around 60% to 75% of patients have blood transfusion. [3,4] The risk of reintervention owing to bleeding in such surgeries varies from 2% to 6%, with a mortality rate ranging from 10% to 22%. [5,6] Hemocoagulase is an enzyme that exhibits serine protease activity on its substrate, fibrinogen.

A serine protease hydrolyzes a protein at the serine residue, resulting in protein degradation. Hemocoagulase is similar to thrombin, since both are serine proteases that act on fibrinogen. Fibrinogen is a crucial protein in the process of hemostasis, since it has a vital function in both platelet aggregation and the creation of fibrin clots.

Typically, when someone is injured, thrombin breaks down fibrinogen, leading to the formation of blood clots. Consequently, these clots serve to 'seal' the wound, allowing for the regeneration of the skin's epithelial cells. This is the inherent mechanism essential for tissue regeneration. Hemocoagulase can initiate clot formation, regardless of the presence or absence of tissue injury. This is due to the fact that Batroxobin is not affected by certain co-factors, such as thrombin. These blood clots have the potential to obstruct a vein and impede the circulation of blood. Tranexamic acid is an artificial compound derived from the amino acid lysine. The antifibrinolytic activity of this substance is achieved by reversibly blocking the lysine binding sites on plasminogen molecules. It hinders the activation of plasminogen in endothelial cells, hence impeding fibrinolysis and the degradation of blood clots. Several reports suggest that Hemocoagulase can reduce bleeding in intraoperative and post-operative period. When compared with Tranexamic acid Hemocoagulase reduce bleeding more comprehensively. Patient scheduled for cardiac surgery need a multimodal approach especially for coagulation management. Our study was a comparative evaluation of intravenous Hemocoagulase and Tranexamic acid during mitral valve replacement on cardiopulmonary bypass.

Objectives:

To compare the amount of bleeding with the use of Hemocoagulase and Tranexamic acid in intraoperative period.

Material and Methods:

This study was a randomised, prospective trial conducted at the Department of Anaesthesiology, Gandhi Medical College, and associated Hamidia Hospital in Bhopal, Madhya Pradesh. It was approved by the institute's ethics committee. The objective was to compare the impact of intravenous Hemocoagulase and Tranexamic acid on intraoperative and postoperative bleeding in primary elective mitral valve replacement surgery with cardiopulmonary bypass.

Inclusion criteria:

- Case Age Group between 20 To 60 Years.
- Patient Schedule For Elective MVR.
- Patient Not On Anticoagulant Therapy.
- Patient of ASA grade II & III
- NYHA class II & III

Exclusion criteria:

- Known or suspected allergy to drugs
- Revision Surgery.
- Patients with Ef <40%.
- Patient with History Of CVA and previous seizure activity.
- Patient on Anticoagulant Therapy
- Pregnancy and lactating female.
- Severe hepatic and renal impairment.

Following the explanation of the procedure to all patients, a written and informed consent was

obtained from each patient. All patients had a comprehensive history-taking, thorough physical examination, and standard diagnostic tests. A total of sixty patients were chosen for the trial, and informed permission was acquired from each of them.

Patient Randomization:

The patients were randomly allocated into one of the two groups: 30 patients in each group-:

Group 1:- Given iv injection Hemocoagulase in the dose 1.0 NIH unit as intravenous infusion over 30 minutes prior to surgery then same dose intravenously once a day for 3 days postoperatively.

Group 2: Given Tranexamic acid in standard dose 1 gm as intravenous infusion over 30 minutes prior to surgery and same dose repeated once a day for 3 days postoperatively. Intraoperative and postoperative amount of blood loss was assessed by ABL Formula.

Surgical Procedure:

Every patient was premedicated with Glycopyrrolate (0.01 mg/kg), Midazolam (o.o5-0.1mg/kg), Fentanyl (1-2mcg/kg), Ondansetron (0.1mg/kg) intravenously about 30 minutes prior to induction of anaesthesia. Anaesthesia was induced with intravenous Thiopentone (3-4 mg/kg) or Fentanyl (4-5mcg/kg) and Vecuronium bromide (0.1-0.2 mg/kg) was used to facilitate endotracheal intubation with appropriately sized tube, (generally 8.5 mm for males and 7.5 mm for females).The lungs were mechanically ventilated with a mixture of oxygen (50%) and nitrous oxide (50%) to maintain normocapnia. Maintenance of anaesthesia was achieved with Isoflurane, Fentanyl, and Vecuronium. Fentanyl (1-5mcg/kg) was given before incision. Anticoagulation with Heparin (3mg/kg) through a central venous line was done 10 mins prior to initializing CPB to achieve a target ACT > 480 seconds. CPB was established via a standard median sternotomy, aortic root cannulation, and double atrial cannulation for venous return. Post CPB, anaesthesia was maintained with 50% O2 and 50% Air, isoflurane 0.5 to 1%, fentanyl (1-2mcg/kg), and vecuronium (1/4th of induction dose). Post CPB blood loss assessment was done by weighing of sponges and amount of blood in suction bottle. Blood loss after closure of sternum and post-operative period was assessed by amount of blood in chest drain.

Outcome Assessment:

Calculating blood loss in theatre; first, by weighing a dry swab. Secondly, Weigh blood soaked swabs as soon as they are discarded and subtract their dry weight (1ml of blood weighs approximately 1gm). Third, subtract the weight of empty suction bottles from the filled ones. Fourth, estimate blood loss into surgical drapes, together with the pooled blood beneath the patient and onto the floor. Fifth, note the volume of irrigation fluids; subtract this volume from the measured blood loss to estimate the final blood loss.

The Actual Blood Loss is a modification of the Gross formula: ABL= BV [Hct (i) - Hct (f)]/ Hct (m) Blood Volume=Body Wt in Kgs x 70 mlkg-1 Hct (i), Hct (f) and Hct (m): the initial, final and mean (of the initial and final) Hematocrits respectively. weight Adults: 70ml/ kg body weight.

Statistical Analysis:

Nominal categorical data between the groups were compared using Chi-square test or Fisher's exact test as appropriate. P <0.05 was taken to indicate a statistically significant difference. z score test also used for calculation of p value along with Chi-square test.

Observation and Results:

Table 1: Demographic variables

Variables	Groups		Total
	1	2	
Age			
20-30	10	10	20
31-40	15	10	25
41-50	04	09	13
51-60	01	01	02
Gender			
Male	13	10	23
Female	17	20	37
ASA Grade			
II	20	18	38
III	10	12	22
NYHA Grade			
II	18	18	36
III	12	12	24

The mean duration of surgery in group 1 was 4 hours 25 min and group 2 was 4 hours 40 min respectively. There was no significant difference between two groups (p = 0.43)

The Mean Duration of Bypass of group 1 was slightly longer than group 2, but this difference was statistically not significant [P=0.25], Thus both groups were comparable.

The Mean Blood Loss intraoperatively of group 1 was 453.33ml and in group 2 was 747.5ml. The difference of blood loss among two groups was statistically significant (p=0.00001).

The Mean Blood Loss postoperatively of group 1 was 400 ml and in group 2 was 581.6 ml. The difference of blood loss among two groups was statistically significant (p= 0.0004).

The Mean Blood Loss postoperatively of group 1 was 853.33ml and in group 2 was 1329.1ml. The difference of blood loss among two groups was statistically significant (p=0.000001) [Table 2]

Table 2: Duration of surgery and blood loss

Parameters	Group 1 (Mean±SD)	Group 2 (Mean± SD)
Duration of surgery	4 hours 25 min ± 0.86	4 hours 40 min ± 0.61
Duration of bypass	122.53 ± 20.411	116.80 ± 18.138
Intraoperative blood loss	453.33ml ± 134.50	747.50ml ± 234.74
Postoperative blood loss	400.00ml ± 135.17	581.60 ml ±233.29
Total blood loss	853.33ml ± 244.72	1329.10 ± 397.71

In group 1 , 4 patients were transfused with 1 unit PRBC and only 1 patient transfused with 2 units of PRBC whereas in group 2, 13 patients transfused with 1 unit of PRBC and 6 patients transfused with 2 units PRBC, this comparison is statistically significant (P=0.00022). In group 1 at 24 hours postoperatively 3 patients transfused with 1 unit PRBC whereas in group 2, 8 patients transfused with 1 unit of PRBC, this comparison is statistically not significant. In group 1 at 72 hours postoperatively; no patients transfused whereas in group 2, only 3 patients transfused with 1 unit of PRBC, this comparison is statistically not significant.

Table 3: Blood transfusion postoperatively

Blood transfusion postoperatively		Groups 1	Group 2
Just after CPB	1unit PRBC	04	13
	2 unit PRBC	01	06
At 24 hours	1unit PRBC	03	08
	2 unit PRBC	00	00
At 72 hours	1unit PRBC	00	03
	2 unit PRBC	00	00

In group 1, out total 30 patients; 5 patients transfused with 1 unit PRBC and 3 patients transfused with 2 units PRBC, none of the patients transfused with 3 units of PRBC therefore total 8 patients transfused. Whereas in group 2, out of 30 patients transfused with 1 unit PRBC, 9 patients transfused with 2 units PRBC and 4 patients transfused with 3 units of PRBC therefore total19 patients transfused out of 30 patients. This comparison is statistically significant (p=0.00438).

Table 4: Total blood transfusion (Intra and Postoperatively)

Transfusion	Groups	
	1	**2**
1unit PRBC	5	6
2 unit PRBC	3	9
3unit PRBC	0	4

Discussion:

In our study we used 1 unit of intravenous Hemocoagulase via infusion 30 minutes before surgery and same dose repeated at 24, 48 and 72 hours postoperatively. Our study was comparable with the work of Qian Yong-yue et al [7] who did the study in 48 patients by using one unit Hemocoagulase intravenously 30 min before operation after induction and same dose repeated 24, 48 and 72 hours after surgery.

Mean duration of surgery was 4 hours 25 minutes ± 0.86 and 4 hours 40 minutes ±0.61 in group 1 and group 2 respectively. The mean duration of surgery in group 2 was slightly longer than group 1 but this difference was statistically not significant (p=0.43). Thus both groups were comparable. Mean duration of bypass in group 1 was 122.53 ±20.411 minutes and in group 2 was 116.80 ± 18.138 minutes. The mean duration of bypass in group 1 was slightly longer than group 2 but this difference was statistically not significant (p=0.43). Thus both

groups were comparable. Mean blood loss intraoperatively in group 1 and group 2 was 453.33±134.5ml and 747.5±234.74ml respectively. There was 39.35% reduction in blood loss in group 1 in comparison to group 2. This difference of blood loss among two groups was statistically significant (p=0.00001). Mean blood loss postoperatively in group 1 and group 2 was 400±135.17ml and 581.6±233.29ml respectively. There was 31.22% reduction in blood loss in group 1 in comparison to group 2. This difference of blood loss among two groups was statistically significant (p=0.0004).

Mean total blood loss in group 1 and group 2 was 853.33±244.72 ml and 1329.1±397.71ml respectively. There was 35.79% reduction in blood loss in group 1 in comparison to group 2.This difference of blood loss among two groups was statistically significant (p=0.000001). Tang Baiyun, Tong Cuiwen et al [8] noted significant reduction in bleeding volume on first, second, third day, even the total volume in Hemocoagulase group than that of the control group. Zhao Chuan long et al [9] noticed significant reduction in intraoperative blood loss and chest tube drainage volume at 12, 24 and 36 hours postoperatively.

On comparison of blood transfusion perioperatively, In group 1, 4 patients were transfused with 1 unit PRBC and only 1 patient transfused with 2 units of PRBC whereas in group 2, 13 patients transfused with 1 unit of PRBC and 6 patients transfused with 2 units PRBC, this comparison is statistically significant. P=0.00022 (Statistical method -z score test (z score = -3.6893). This comparison also shows that intraoperatively only 5 patients required blood transfusion out of 30 patients in group 1 whereas in group 2 total 19 patients require blood transfusion out of 30 patients.

On comparison of blood transfusion postoperatively after 24 hours In group 1 at 24 hours postoperatively 3 patients transfused with 1 unit PRBC whereas in group 2, 8 patients transfused with 1 unit of PRBC, this comparison is statistically not significant.(P = 0.09492).

On comparison of blood transfusion postoperatively after 72 hours in group 1 at 72 hours postoperatively in group 1, non of the patients required blood transfusion whereas in group 2, only 3 patients transfused with 1 unit of PRBC, this comparison is statistically not significant (p=0.07508).

On comparison of total blood transfusion intra and postoperatively, in group 1, out total 30 patients, 5 patients were transfused with 1 unit PRBC and 3 were patients transfused with 2 units PRBC therefore total 8 patients were transfused. Whereas in group 2, out of 30 patients 6 patients were transfused with 1 unit PRBC, 9 patients were transfused with 2 units PRBC and 4 patients were transfused with 3 units of PRBC, therefore 19 patients were transfused out of 30 patients. This comparison is statistically significant {(p=0.00438), statistical method- z score test, (z score = -2.8545)}. In 2004 Zhao Chuan long et al [10] also noticed that Hemocoagulase reduced the amount of intra and postoperative blood transfusion during cardiopulmonary operation. 2005 Liu Qi-Ning et al [11] observed that Hemocoagulase can reduce the transfusion volume at 24 hours after operation. In 2008 Yu Ben-tong [12] evaluated that blood transfusion volume and plasma transfusion volume with the use of Hemocoagulase at 24 hours after operation in patients with congenital heart disease scheduled for elective open-heart surgery. In 2015 He Keqiang Wang Ruiting et al [13] also noticed in their study that Hemocoagulase reduces intra and postoperative blood transfusion during heart valve replacement surgery under CPB.

In our study there were no complication observed in relation to Hemocoagulase and Tranexamic acid like drug adverse reaction. No hemodynamic changes in heart rate SBP, DBP and MAP. There were no renal, hepatic and neurological complications related to both the drugs. In 2001 Fan Qinming et al [14] did not find any adverse reaction in their study with the use of Hemocoagulase. In 2004 Qian Yong-yue et al [7] observed no adverse reaction with the use of Hemocoagulase during cardiac surgery. In 2008 Yu Ben-tong [15] also observed that there were no adverse drug reactions and complications in patients with congenital heart disease scheduled for elective open heart surgery with the use of Hemocoagulase.

Conclusion

Our study conclude that, Hemocoagulase is more effective than tranexamic acid to control the amount of blood loss and need of blood transfusion (both intra and postoperatively) in adult patients of ASA grade II and III during Cardiac Surgery under Cardiopulmonary bypass. Blood loss reduce in group 1 compared to group 2 intraoperatively and postoperatively. This shows, Hemocoagulase is more effective to reduce bleeding then Tranexamic acid in Intraoperative and Postoperative Period during Mitral Valve Replacement on Cardiopulmonary by Pass. Thus, in a tertiary care centre, use of Hemocoagulase in the peri and post-operative period is an effective measure to reduce morbidity and mortality in post valvular cardiac surgery patients.

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