

A Comparison Between Intravenous And Local Tranexamic Acid In Controlling Blood Loss in Patients Undergoing Hemireplacement Arthroplasty With Bipolar Prosthesis-A Randomised Controlled Trial

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Abstract

Introduction: Major orthopaedic surgeries are commonly associated with marked blood loss, and a subsequent need for blood transfusion is often encountered. The causes of bleeding are multifactorial, increased fibrinolytic activity being one of them. Administration of antifibrinolytic agents such as tranexamic acid (TA) perioperatively to stabilize the multiple microclots that form within the surgical wound. We wish to compare the effects of tranexamic acid in a preoperative dose of 15 mg/kg and effect of local tranexamic acid.

Methodology: A randomised controlled study in a single blind fashion was carried out in the Department of Orthopaedics, Gauhati Medical College and Hospital, Guwahati (Assam), from August 2015 to July 2017. The study was conducted on a total of 135 patients with patients undergoing hemireplacement arthroplasty surgery with bipolar prosthesis to evaluate the role of tranexamic acid in reducing blood loss.

Results: In our study, In IV group intra op blood loss was 104.50 ± 21.82 ml while post op blood loss was 64.50 ± 17.98 ml. so the total blood loss was 168.50 ± 30.09 ml. In local group intra op blood loss was 99.00 ± 27.03 ml while post op blood loss was 58.75 ± 13.75 ml. so the total blood loss was 157.25 ± 36.36 ml. In control group intra op blood loss was 148.00 ± 16.09 ml while post op blood loss was 117.25 ± 25.21 ml. so the total blood loss was 265.25 ± 34.89 ml.

Conclusion: After evaluating the effects of intravenous and local routes of administration of Tranexamic acid on intraoperative blood losses, blood transfusion requirements, and postoperative incidence of deep venous thrombosis in patients undergoing hemireplacement arthroplasty surgery with bipolar prosthesis we came to the conclusion that there is no difference among the routes of administration of TA given intravenous preoperatively and local intraperatively in controlling intraoperative and post operative blood loss but tranexamic acid reduces the blood loss intraoperatively and 24 hrs postoperatively by a highly significant degree, as well it causes a significant reduction in postoperative anemia and need for transfusion among these patients.

Keywords: hemireplacement arthroplasty, tranexamic acid.

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I. Introduction

Major orthopaedic surgeries are commonly associated with marked blood loss, and a subsequent need for blood transfusion is often encountered. The causes of bleeding are multifactorial, increased fibrinolytic activity being one of them. Although bleeding from these surgical sites is usually controllable, there may be significant blood loss. Several approaches have been used to reduce intraoperative blood loss, including hypotensive anaesthesia which has its own detrimental consequences. The use of allogeneic blood products increases the rate of transmission of infectious diseases, modulates the immune response, and increases the risk of postoperative infection. The alternate approaches are administration of antifibrinolytic agents such as tranexamic acid (TA) perioperatively to stabilize the multiple microclots that form within the surgical wound¹. Tranexamic acid is a synthetic amino acid. It is the trans stereoisomer of 4-aminoethylcyclohexane carboxylic acid and has a half life of 80 minutes. It is 3% protein bound, and is 95% excreted unchanged in the kidneys². Tranexamic acid competitively blocks the lysine binding sites of plasminogen, plasmin, and tissue plasminogen activator, thereby retarding fibrinolysis and blood clot degradation³. It is relatively inexpensive and does not appear to cause any significant untoward side effects^{3,4,5}. TA has been used in neuro, cardiac, spine and maxillofacial surgeries and has reduced the amount of blood loss and subsequent need for blood transfusion. Tranexamic acid, has been also been found to reduce blood loss and transfusion requirements in Orthopaedic surgery^{6,7,8,9,10}. However, its role with regard to its effects according to the type of surgery, dosage,

and timing of administration has not been well established .

Previous studies established the therapeutic plasma concentrations of tranexamic acid at 10 mg ml⁻¹ and the need for an 80% reduction in the activity of plasminogen activator for suppression of fibrinolysis in tissues. An i.v. dose of tranexamic acid 10 mg kg⁻¹ maintains such plasma concentration for only 3 h. These data suggest that a dose of 10 mg/kg may not be sufficient to prevent postoperative bleeding and support the rationale for using higher doses. In addition, studies found no significant reduction in postoperative blood loss in total hip replacement patients when TA was given towards the end of surgery and 3 hours later. Tranexamic acid is not associated with an increase in venous thromboembolic events because the effect of tranexamic acid is more pronounced in operative wounds than in the peripheral blood¹¹. Tranexamic acid 15 mg/kg given as a single preoperative bolus dose reduces postoperative and total blood loss, and packed cell transfusion requirements in primary total hip replacement surgery¹³. Tranexamic acid is not associated with an increase in venous thromboembolic events because the effect of tranexamic acid is more pronounced in operative wounds than in the peripheral blood.¹²

We wish to compare the effects of tranexamic acid in a preoperative dose of 15 mg/kg and effect of local tranexamic acid. We shall evaluate the effect of such a single preoperative bolus dose and local dose of tranexamic acid on perioperative blood losses, blood transfusion requirements, and postoperative incidence of deep venous thrombosis in patients undergoing hemireplacement arthroplasty and total hip replacement.

II. Materials And Methods

Following Institutional Ethical Committee approval and written informed consent, a randomised controlled study in a single blind fashion was carried out in the Department of Orthopaedics, Gauhati Medical College and Hospital, Guwahati (Assam), from August 2015 to July 2017. The study was conducted on a total of 135 patients with patients undergoing hemireplacement arthroplasty surgery with bipolar prosthesis to evaluate the role of tranexamic acid in reducing blood loss. The patients admitted in the Department of Orthopaedics, Gauhati Medical College, Guwahati, Assam were included in the study with the following inclusion and exclusion criteria:

Inclusion criteria:

1. All patients undergoing hemireplacement arthroplasty surgery with bipolar prosthesis for traumatic fracture Neck of Femur after pre anaesthetic checkup for uniformity of data collection.
2. Age group included in this study was 50 years to 80 years irrespective of sex
3. Competent neurological and vascular status of the affected limb.
4. Only patients with a near normal daily activities of life.
5. Patients who meet the medical standards for routine elective surgery
6. Giving informed consent.

Exclusion Criteria:

1. Patients who do not give consent
2. Patients aged <50yrs and >80yrs
3. Allergy to Tranexamic acid
4. Acquired disturbances of colour vision
5. Pre operative anaemia <9gm/dl
6. Pre operative use of anti coagulant therapy ie oral anti coagulants , heparin within 5 days of surgery
7. fibrinolytic disorders requiring intraoperative anti fibrinolytic treatment
8. Coagulopathy ie pre operative platelets count <150,000mm³ and prolonged Prothrombin Time >16
9. Previous history of thromboembolic disease
10. Significant co morbities such as liver disorders
11. We have excluded other indications of hip arthroplasty surgery such as Avascular Necrosis of head of femur, rheumatoid arthritis, ankylosing spondylitis etc.

All the patients were examined in detail and worker up to obtain pre anaesthetic clearance with the following investigations as listed Hb%, TLC, DLC, Platelet count, RBS, Creatinine, Sodium, Potassium, PT with INR, TSH, Chest X ray PA view and ECG. Clinical and Radiological parameters were recorded. patients were divided into 3 groups based on randomisation in accordance with the plan generated in the site www.randomisation.com to one either of the groups

Group A: received Intravenous Tranexamic acid

Group B: received topical Tranexamic acid

Group C: control group

Patients underwent operation under any anaesthesia as deemed suitable by the anaesthetic team (spinal anaesthesia/epidural anaesthesia).

For estimation of blood loss

- a. Intra operative blood loss: Dry gauze pieces and mops used during the operation were preoperatively weighed. Intraoperative blood loss were then be measured by carefully weighing the blood soaked gauge pieces and mops used during the operation and subtracting the previously measured weight. Weight(gram) of blood was then converted to volume(millilitres) of blood by dividing the weight in grams by specific gravity of blood at 37°C . Suction bottles in the suction machine were made empty and dry for each patients before the operation. Blood collected in the suction bottle were then calculated measuring the volumes in the suction bottles during surgery and subtracting the fluid (NaCl 0.9%) used for wash .
- b. For post operative blood loss: One low vacuum drain was used for postoperative wound drainage(submuscular).Postoperative blood loss in the vacuum collectors were noted at 24 hrs post operatively.Crystalloids ,colloids and blood transfusion were used to replace intraoperative blood loss.The operating time was noted down for each patient. Hb%, Platelet count, PT and APTT were done 24hrs post operatively.The number of units and the time of transfusion were recorded.

All patients were examined daily for clinical signs of DVT.History was taken regarding pain ,swelling and fever.Patients were examined for tenderness,change in colour and warmth.Two clinical tests were done to elicit DVT namely Homan’s sign and Moses’s sign. Results for continuous variables are represented as mean values \pm SD. Statistical analysis of continuous variables included unpaired (2 tailed) t-tests for independent samples. A p value of < 0.05 was considered statistically significant

III. Results And Observation

Following Institutional Ethical Committee approval and written informed consent, a randomised controlled study in a single blind fashion was carried out in the Department of Orthopaedics,Gauhati Medical College and Hospital, Guwahati,Assam from August 2015 to July 2017.The study was conducted on a total of 135 patients undergoing hemi replacement arthroplasty with bipolar prosthesis. All the pre operative investigations and clinical examination were done in this study and patients were then planned for surgery. The patients were randomly allocated into three groups in a single-blind fashion and received tranexamic acid intravenous (15 mg/kg) before surgery or 1gm tranexamic acid in 20ml NS before closure of surgical site or placebo.The results and observation between the three groups were as follows:

1.Intra And Postoperative Blood Loss

In IV group intra op blood loss was 104.50 ± 21.82 ml while post op blood loss was 64.50 ± 17.98 ml. so the total blood loss was 168.50 ± 30.09 ml.

In local group intra op blood loss was 99.00 ± 27.03 ml while post op blood loss was 58.75 ± 13.75 ml. so the total blood loss was 157.25 ± 36.36 ml

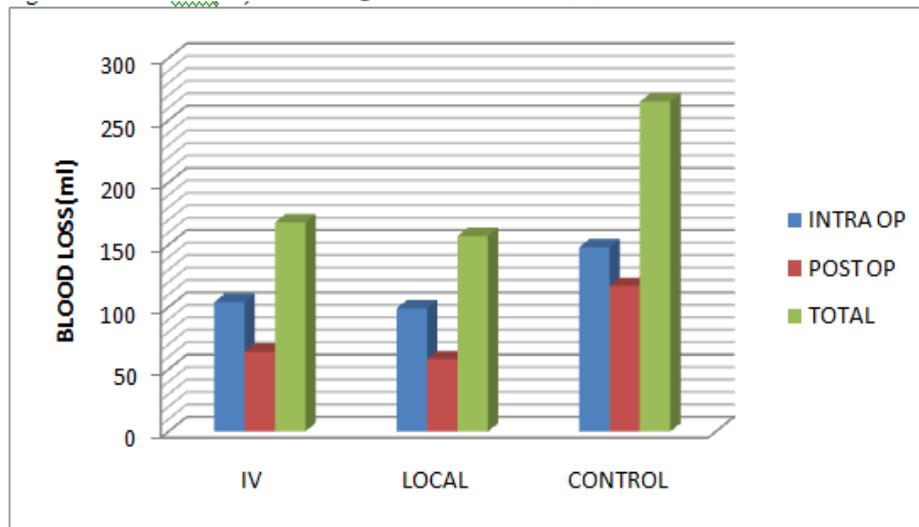
In control group intra op blood loss was 148.00 ± 16.09 mlwhile post op blood loss was 117.25 ± 25.21 ml. so the total blood loss was 265.25 ± 34.89 ml

The difference between blood loss was not significant in IV and LOCAL groups but difference in the blood loss was significant in the CONTROL group compared with the other two groups

Table 1: Blood loss (ml)

Blood Loss	IV Group	Local Group	Control Group	Total	P value
Intra op	104.50 ± 21.82	99.00 ± 27.03	148.00 ± 16.09	115.50 ± 32.06	< 0.05
Post op	64.50 ± 17.98	58.75 ± 13.75	117.25 ± 25.21	76.83 ± 35.25	< 0.05
Total	168.50 ± 30.09	157.25 ± 36.36	265.25 ± 34.89	192.00 ± 62.88	< 0.05

Figure 1: Blood loss(ml)



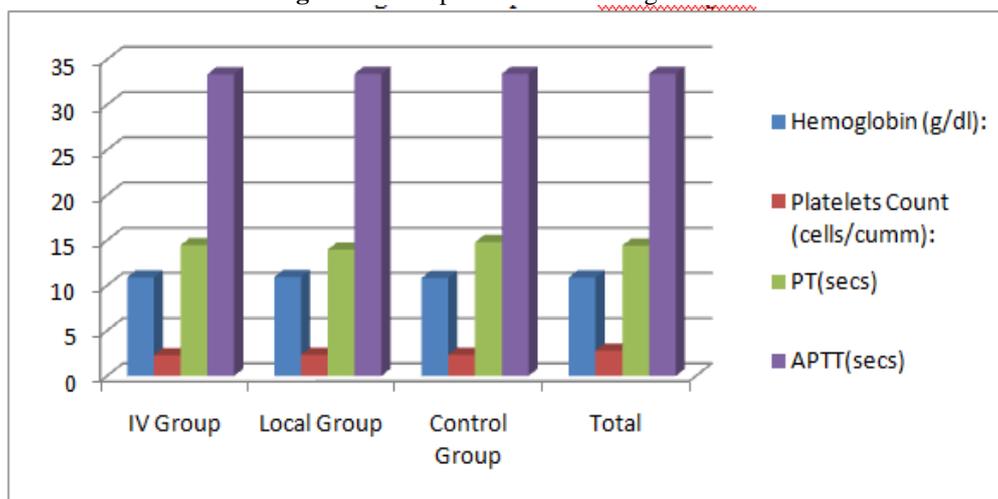
2.Preoperative Haematological Data

There were no significant difference between the three groups with respect to Preoperative haematological data such as Haemoglobin(g/dl), Prothrombin time(secs), Platelet count(lacs/cumm), and Activated Partial Thromboplastin Time (secs)

Table 2: Pre operative haematological data

	IV Group	Local Group	Control Group	Total	P value
Hemoglobin (g/dl):	10.89±1.09	10.94±1.41	10.83±1.00	10.88±1.16	0.957
Platelets Count (cells/cumm):	2.30±0.49	2.35±0.56	2.33±0.53	2.79±0.54	0.119
PT(secs)	14.47±1.00	13.98±1.09	14.80±1.17	14.42±1.13	0.066
APTT(secs)	33.38±0.90	33.46±0.84	33.48±0.78	33.44±0.83	0.918

Figure 2: Pre operative haematological data



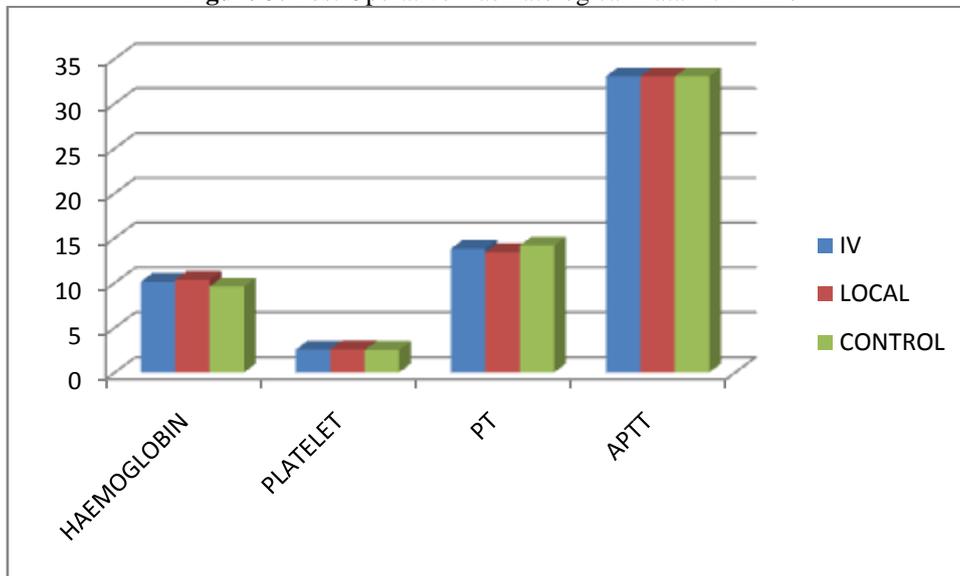
3.post operative haematological data at 24 hrs

There were no significant difference between the three groups with respect to Postoperative haematological data such as Haemoglobin(g/dl), Prothrombin time(secs), Platelet count(lacs/cumm), and Activated Partial Thromboplastin Time (secs)

Table 3: Post Operative Haematological Data At 24 Hrs

	IV Group	Local Group	Control Group	Total	P value
Hemoglobin (g/dl):	10.11±1.05	10.33±1.16	9.58±1.02	9.40±1.09	0.251
Platelets Count (cells/cumm):	2.55±0.36	2.59±0.49	2.52±0.50	2.45±0.47	0.059
PT(secs)	13.80±1.10	13.41±1.23	14.16±0.92	13.79±1.12	0.103
APTT(secs)	33.04±0.83	33.04±0.94	33.03±0.53	33.03±0.77	0.998

Figure 3: Post Operative Haematological Data At 24 Hrs



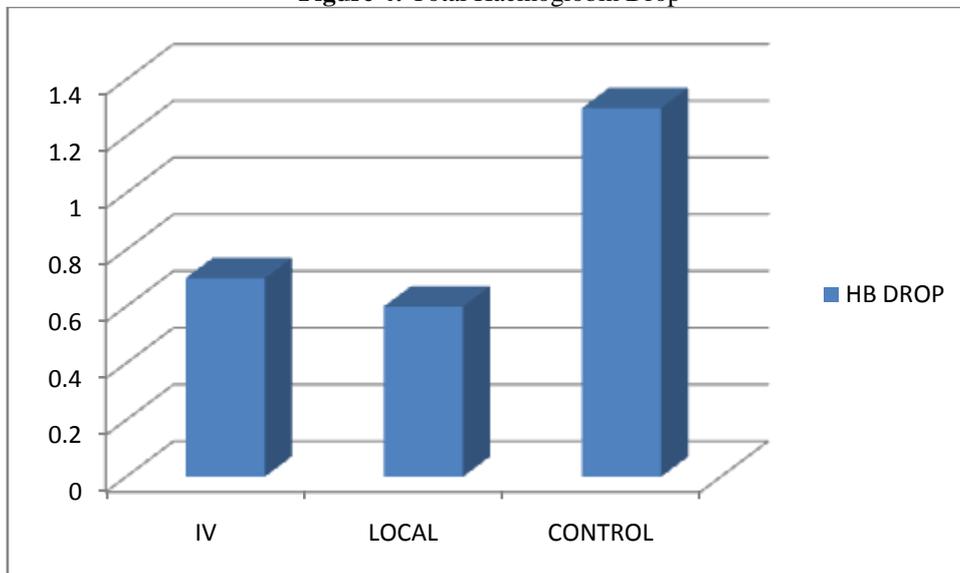
4.Total Haemoglobin Drop

Total Haemoglobin drop post operatively at 24 hrs in the IV group was 0.7 and in the LOCAL group was 0.6 and in the CONTROL group was 1.3. The difference in the IV and LOCAL group was not significant but the difference was significant between the CONTROL group and the other two groups.

table 4: total haemoglobin drop

	IV	LOCAL	CONTROL	P VALUE
HB DROP(gm/dl)	0.7	0.6	1.3	<0.05

Figure 4: Total Haemoglobin Drop



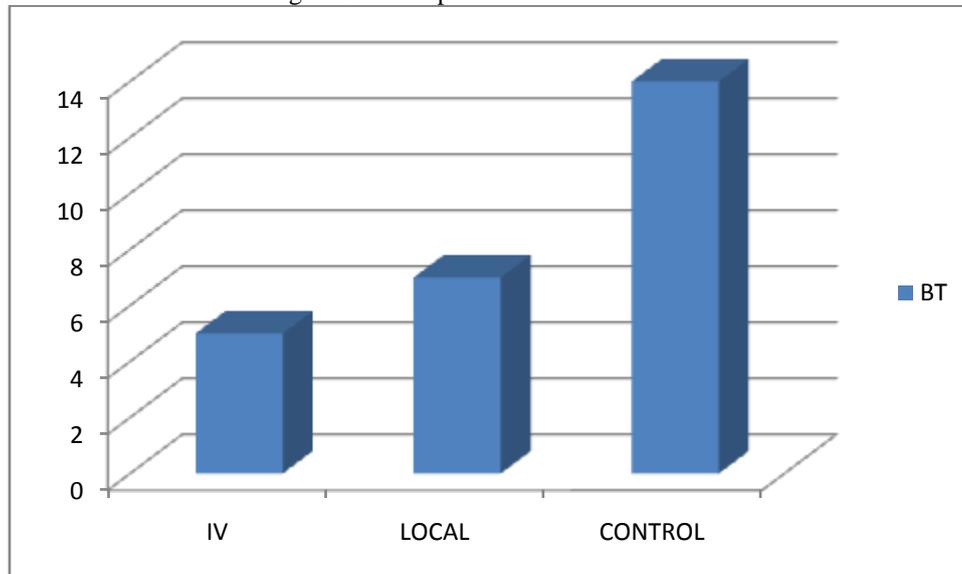
5.Post Operative Blood Transfusion

Number of patients receiving post operative blood transfusion in IV group was 5 while in LOCAL group was 7 and in CONTROL group was 14.

Table5: Post operative blood transfusion

	IV	LOCAL	CONTROL
BT	5	7	14

Figure 5: Post operative blood transfusion



IV. Discussion

A randomised controlled study in a single blind fashion was carried out in the Department of Orthopaedics, Gauhati Medical College and Hospital, Guwahati (Assam), from August 2015 to July 2017. The study was conducted on a total of 135 patients with patients undergoing hip arthroplasty surgery to evaluate the role of tranexamic acid in controlling intra operative blood loss.

In present study we studied the patients between 50yrs to 80 yrs of age group.

Table 6: Intra operative blood loss(ml)

	IV(ml)	LOCAL(ml)	CONTROL(ml)
UENO et al	290.3 ± 124.1	278.7 ± 113.0	241.1 ± 97.0
Present study	104.50±21.82	99.00±27.03	148.00±16.09

Intra operative blood loss in the study of UENO et al in the IV group was 290.3 ± 124.1 while in the LOCAL group was 278.7 ± 113.0 and in CONTROL group was 241.1 ± 97.0¹¹¹ and in present study In the IV group it was 104.50±21.82 while in LOCAL group it was 99.00±27.03 and in CONTROL group it was 148.00±16.09. In our study there was no significant difference between the IV and LOCAL group in terms of intra operative blood loss and significant difference between the CONTROL group and the other two groups.

UENO et al quote that TXA binds reversibly to plasminogen and blocks the binding of plasminogen to fibrin, which activates and transforms plasminogen to plasmin; TXA requires the time for plasminogen to be activated. Dahl et al. reported that the fibrinolytic response occurs in the early phases of operative procedures¹¹⁰, and Imai et al. reported that TXA reduces intra-operative blood loss¹⁰⁹. However, because of the short operation times in the study of Ueno et al, pre-operative TXA administration could not reduce intra-operative blood loss. Therefore, if the operation times were long, intra-operative blood loss would be low with pre-operative TXA administration¹¹¹. In the present study, as the operative time was longer than the study of Ueno et al, intraoperative blood loss was more in control group than in the study of Ueno et al.

Table 7: Post operative blood loss(ml)

	IV(ml)	LOCAL(ml)	CONTROL(ml)
UENO et al	252.9 ± 127.8	240.7 ± 127.1	372.2 ± 172.7
Present study	64.50±17.98	58.75±13.75	117.25±25.21

Post operative blood loss at 24 hrs in the study of UENO et al in the IV group was 252.9 ± 127.8 while in the LOCAL group was 240.7 ± 127.1 and in CONTROL group was 372.2 ± 172.7¹¹¹ and in present study In

the IV group it was 64.50±17.98 while in LOCAL group it was 58.75±13.75 and in CONTROL group it was 117.25±25.21. In our study there was no significant difference between the IV and LOCAL group in terms of post operative blood loss and significant difference between the CONTROL group and the other two groups which was comparable to other study.

Table 8: Total blood loss(ml)

	IV(ml)	LOCAL(ml)	CONTROL(ml)
EMERA et al	640±25	625±35	1100±30
UENO et al	560.0 ± 194.7	519.4 ± 184.6	613.3 ± 199.5
Present study	168.50±30.09	157.25±36.36	265.25±34.89

Total blood loss(ml) in the study of EMERA et al in the IV group was 640±25 while in the LOCAL group was 625±35 and in the CONTROL group was 1100±30¹¹² and in the study of UENO et al in the IV group was 560.0 ± 194.7 while in the LOCAL group was 519.4 ± 184.6 and in the CONTROL group was 613.3 ± 199.5¹¹¹ and in the Present study in the IV group was 168.50±30.09 while in the LOCAL group was 157.25±36.36 and in the control group was 265.25±34.89. In Present study the difference in total blood loss between the IV and LOCAL groups was not significant but the difference between the CONTROL group and the other two groups was found to be significant and is comparable with the other studies

Table 9: Post operative Haemoglobin drop(gm/dl)

	IV(Gm/Dl)	LOCAL(Gm/Dl)	CONTROL(Gm/Dl)
EMERA Etal	1.8	2.1	4.2
UENO Etal	1.9	1.9	3.2
Present Study	0.7	0.6	1.3

Post operative Haemoglobin drop at 24 hrs in the study of EMERA et al in the IV group was 1.8 while in the LOCAL group was 2.1 and in the CONTROL group was 4.2¹¹² and in the study of UENO et al in the IV group was 1.9 while in the LOCAL group was 1.9 and in the CONTROL group was 1.3¹¹¹ and in the present study in the IV group was 0.7 while in the LOCAL group was 0.6 and in the CONTROL group was 1.3. The difference between the IV and LOCAL group was not significant but that of CONTROL group was found to be significant with the other two groups comparable with other studies.

Summary And Conclusion

A randomised controlled study in a single blind fashion was carried out in the Department of Orthopaedics, Gauhati Medical College and Hospital, Guwahati (Assam), from August 2015 to July 2017. The study was conducted on a total of 135 patients with patients undergoing hemireplacement arthroplasty surgery with bipolar prosthesis to evaluate the role of tranexamic acid in controlling intra operative blood loss to compare the effects of Intravenous and Local tranexamic acid. We divided the 135 patients into a group of patients receiving Intravenous and Local tranexamic acid while a third group received placebo with 45 patients in each group. We calculated the intra operative blood loss, post operative blood loss at 24 hrs and added to find out the total blood loss. We also calculated the amount of blood transfusion required by the patients post operatively.

Through this study carried over for 2 years the total blood loss in INTRAVENOUS group was 168.50±30.09 ml while in LOCAL group was 157.25±36.36ml and in CONTROL group was 265.25±34.89ml. Through various tests of statistics we found out that there was no significant difference in controlling blood loss between INTRAVENOUS and LOCAL routes of administration of tranexamic acid but there is significant difference between patients receiving Tranexamic acid and those not receiving tranexamic acid as the patients not receiving tranexamic acid have more blood loss. We came to the conclusion that there is no difference among the routes of administration of TA given intravenous preoperatively and local intraperatively in controlling intraoperative and post operative blood loss but tranexamic acid reduces the blood loss intraoperatively and 24 hrs postoperatively by a highly significant degree, as well it causes a significant reduction in postoperative anemia and need for transfusion among these patients. This would in turn, help avoid complications related with transfusion of blood and blood products. Nevertheless, no clinically relevant thromboembolic events were encountered in our study. We thus believe that the protocol adopted by us, using minimally effective dosage, was safe as far as thromboembolic complications are concerned. However, further investigation is necessary to determine the effectiveness.

Photographs



Figure1: Weight of dry pads on an electronic weighing machine



Figure2: Weight of blood soaked pads

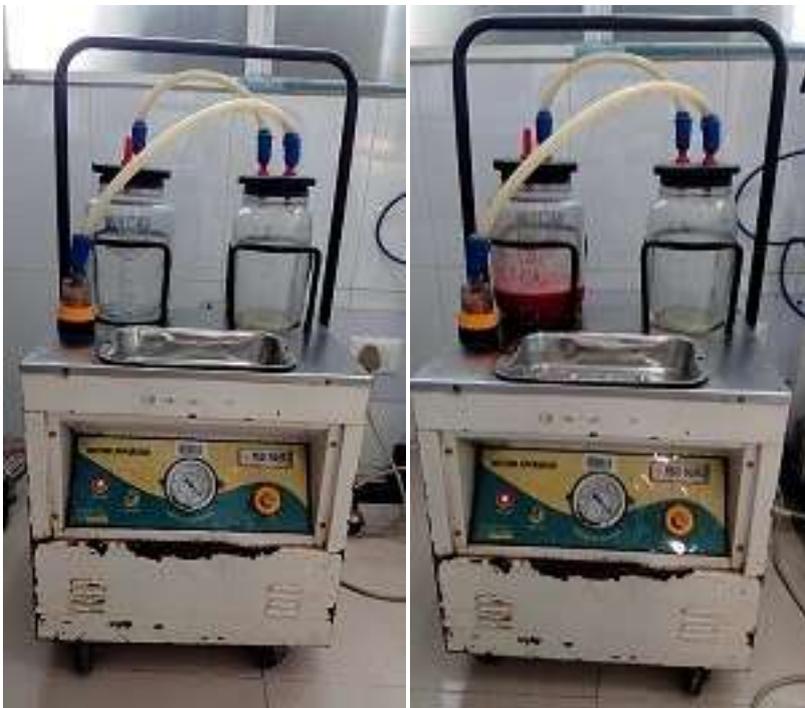


Figure3: Suction Machine



Figure4: Low vacuum drain

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