Study Title:

Efficacy of Tranexamic Acid in reducing requirement of blood transfusion in Lower Limb Trauma Surgery: A prospective randomized controlled study

Date: 05th July, 2021

Study Protocol

This study was a single-centre, randomized controlled parallel group study with 1:1 allocation. After obtaining ethical approval from IEC (**Ref No. PHMA/GSMCH-17/IEC-29A**), 116 patients of lower limb trauma presenting to Emergency Department of Civil Hospital, Rajpura between April 2017 to August 2018 were taken up for the study. Written informed consent was obtained from all the participating patients.

Patient selection

The patients, aged 18-60 years, suffering from lower limb trauma were taken up for the purpose of the study. The presence of old implant or infection at the fracture site, or any blood coagulation disorder were the exclusion criteria for the study. The patients undergoing percutaneous wire placement procedures for fracture fixation were also excluded from the study. The other exclusion criteria were polytrauma, non-consenting patients, psychiatric patient. 16 patients were excluded due to old fracture, percutaneous wire fixation or non-consenting patient. A total of 100 patients met the inclusion criteria and were enrolled.

Pre-operative evaluation

The enrolled patients were assessed preoperatively and all relevant investigations done. The patients were taken up for surgery after stabilization of the general condition. Pre-operative blood transfusion was done as required to have Hb level of at least 9.5mg/dl.

Surgical intervention

The patients were administered spinal anaesthesia or general anaesthesia, depending on the anaesthetist's discretion. The patients were treated by internal fixation of fracture by means of plates or interlocking nails. They were given antibiotic prophylaxis at the beginning of surgery. Intra-operatively, all the patients were given Ringer Lactate and intravenous colloid solution (Haemaccel) for volume replacement.

The patients enrolled were randomly divided into 2 groups. The random allocation of the patients to either group was done by one of the authors using a random number table. Group Tranexamic Acid (Group A) had 50 patients who were given 1 gram of TXA intravenously pre-operatively. IV TXA was administered, at the time of start of surgical incision, by mixing 1 g of TXA in 100 ml of normal saline. Control group (Group B) had 50 patients which were kept as a control group and were not given TXA.

Post-operative evaluation

The requirement of number of units of blood transfusion post- operatively was recorded as a primary outcome measure. The post-operative blood transfusion was done if the patients' Hb level fell below 9.5 mg/dl. The secondary outcome measures included change in Haemoglobin level, total length of hospital stay and the evidence of deep vein thrombosis by Wells score. Patients of both groups were monitored by checking Haemoglobin (Hb) level as required. The Hb readings were expressed as mean ± Standard Deviation and range.

Other complications were monitored daily by looking for leg swelling for DVT, breathlessness and fall in saturation for pulmonary embolism, or a cardiac event

like angina or myocardial infarction, deterioration of mental status for stroke event. In case the patient would have any of these complaints, a medical opinion was sought and managed accordingly.

The probability of venous thromboembolism was suspected by use of Wells et al Clinical model to assess pre-test probability of DVT. Patients with a high probability were to be administered D-Dimer test and other relevant tests as needed to confirm thromboembolism.

No prophylactic treatment for DVT was planned. All the patients were monitored for development of DVT and treatment to be given for symptomatic cases only.

Renal function tests (RFTs) were done post surgery and at discharge. If the level of serum creatinine was elevated to above 1.4 mg/dl or the level of Blood Urea Nitrogen was higher than 25 mg/dl, then elevated RFT level was diagnosed and medical consultation was ordered.

Sample size calculation

Sample size was calculated based on a clinically significant effect with atleast 25% reduction in need of blood transfusion in the post-operative period. Assuming requirement of blood transfusion in control and intervention group to be 15% and 40% respectively, with a two-sided significance of 0.05 and a power of 80%, a total of 49 patients in each group would be required.

Statistical analysis

Statistical analysis was performed using Microsoft Excel 2016. Quantitative data comparison between groups was analyzed using two-sample student t-test. The level of significance was set at $p<0.05$.

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CONSORT 2010 Flow Diagram