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Effects of tranexamic acid on reducing blood loss in pelvic trauma: A randomised double-blind placebo controlled study

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ABSTRACT

Background: Management of pelvic trauma is complicated with patients' instability and remains high in skeletal injuries. The patients usually are young and in middle age and the management of bleeding is more important. The aim of this study is to assess the effects of Tranexamic Acid in Reducing Blood Loss in pelvic trauma: A Randomised Double-Blind Placebo Controlled Study.
Method and materials: In this randomized clinical trial study 106 patients with Pelvic Trauma (PT) were randomly divided into two groups. The case group received 1 g Intravenous TXA for loading dose and 3 dose per 8 h for the maintenance and control group received only serum 0.9% N.S (Normal Saline) or placebo. The Hemoglobin (Hb), Hematocrit (HCT), Pulse Rate (PR) and Blood Pressure (BP) was checked at admission, 24 h, 48 h and 72 h after admission.
Results: From 106 patients 61(%57.54) male and 45 (%42.46) female patients enrolled to the study. The mean age was 48.14 ± 13.54 and the range was 18–60 years old. There was no difference between two groups based on Blood Pressure at admission, 24 h, 48 h and 72 h after admission. There was a significant difference between two groups in 24 h, 48 h and 72 h after admission based on Hb and HCT amount.
Conclusion: based on our findings it appears that TXA can reduce bleeding amount in the first, second and third 24 h after surgery based on Hb and HCT without any effect on systolic and diastolic BP and PR. In other hand no side effect reported by any patients.

1. Introduction

Pelvic Trauma (PT) mortality is an unsolved problem in worldwide with a high prevalence estimated 37% in Singapore between 2001 to 2004.[1] Management of trauma is complicated with patients' instability specially in pelvic trauma and skeletal injuries. The patients usually are young and in middle age and the management of bleeding is more important.[2]

However, the bleeding of pelvic trauma is high but it is predictable and we can reduce mortality with control of bleeding and coagulopathy.[3] Coagulopathy is the result of trauma and massive bleeding because of consumption of platelet and clot factors and increase in plasmin and thrombin activation which is leading to activate fibrinolysis pathway.[4] It has been proved that antifibinolytis could reduce bleeding in orthopedics and cardiac surgery.[5,6]

Tranexamic Acid (trans-4-aminomethyl-cyclohexane-1-carboxylic acid,TXA) is a high potency synthetic antifibrinolytic drug competitive blockade reversible lysine-binding site of plasmin, plasminogen and tissue plasminogen activator which is inhibits plasmin and this blockade pathway concluded increase in clot factors and control pf massive bleeding.[4]

In many previous studies it has been proved that TXA can reduce bleeding during surgery in variable surgeries and also to reduce mortality up to one third.[7,8] Shakur et al. used 1 g IV TXA for loading dose and then 1 g over 8 h for the maintenance in 20,211 patients with trauma. They showed that TXA can reduce mortality, significant bleeding and also need to blood transfusion. They did not report any side effects during the study. They suggested 15 mg/kg as a minimum safe dose of TXA used for bleeding in patients with trauma but the best minimum dos is yet unclear.[9]

The aim of this study is to investigate the Effects of Tranexamic Acid on Reducing Blood Loss and also side effects in patients with pelvic trauma.

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2. Materials and method

2.1. Study design

106 patients with PT were randomly divided into two groups. The case group received 1 g Intravenous TXA for loading dose and 3 dose per 8 h for the maintenance and control group received only serum 0.9% N.S (Normal Saline) or placebo. The Hemoglobin (Hb), Hematocrit (HCT), Pulse Rate (PR) and Blood Pressure (BP) was checked at admission, 24 h, 48 h and 72 h after admission.

The two groups were compared based on age, sex, Mechanisms of trauma (Trauma, falling down, Fall from height), GCS (Glasgow coma state), Hb at admission, 24 h, 48 h and 72 h after admission, Hct Hb at admission, 24 h, 48 h and 72 h after admission, PR Hb at admission, 24 h, 48 h and 72 h after admission and BP 24 h, 48 h and 72 h after admission. The Hb was checked after admission and patients with Hb less than 7 received the packed cell. All procedures were performed by the same team and the same method of surgery.

This randomised double-blind clinical trial study was performed in the Department of Emergency Medicine of Poursina Hospital of Guilan University of Medical Sciences from January to June 2018 after being approved by the Ethics Committee of Guilan University of Medical Sciences. This clinical trial was registered in Iranian Registration of Clinical Trial Center (IRCT): IRCT20130710013947N7. Written informed consents were obtained from patients' accompanying family member/guardian prior to the enrollment.

2.2. Inclusion criteria

one hundred and six patients with pelvic trauma who referred to hospital in first three hours after trauma with age ranging from 18 to 60 years old enrolled in this study.

2.3. Exclusion criteria

Patients who died during the study, with a history of anticoagulant drugs, oral contraceptive (OCP) use, abnormal INR (International Normalized Ratio), PT (Prothrombin Time) and PTT (Partial Thromboplastin Time) range, CVA (Cerebrovascular Accident), MI (Myocardial Infarction), Coagulopathy disorders, TBI (Traumatic Brain Injury), CPR (Cardiopulmonary resuscitation), Renal Failure, Smoking, Opioids, DM (Diabetes Mellitus), HTN (Hypertension), pregnancy and breastfeeding were excluded from the study. Patients' referred from other hospitals or more than 3 h after trauma.

2.4. Randomization

One hundreds and six simple syringes prepared by the emergency ward nurse and put in envelope from number one to one hundred and six. Fifty six of envelopes filled with 1 g TXA and others with serum 0.9% N.S. The nurse was responsible for safety of the drugs and check them every week. The syringes were delivered to one other nurse for injection. The syringes of TXA and N.S were blindly and intravenously injected to the patients by other nurse. The technician recorded the number of the syringeand informed the supervisor the name of the patients and number of syringe injected after admission.

2.5. Statistical analysis

Data have been presented as the mean ± standard deviation (SD). Fisher's exact testor X^2 (Categorical data) and independent samples *t*-test (numerical data) were used for comparisons. Statistical analyses were performed using SPSS software (SPSS, USA). *P* value ≤ 0.05 was regarded as statistically significant.

3. Results

One hundred and six patients with pelvic trauma who referred to hospital in first three hours after trauma including 61(%57.54) male and 45 (%42.46) female patients. The mean age was 48.14 ± 13.54 and the range was 18–60 years old.

Table 1 shows the distribution of sex and gender, mechanism of trauma and GCS score in two case and control groups. There was no difference between case and control groups based on sex, age, GCS at admission and Mechanism of trauma (Table 1). Comparisons between case and control groups' based on amount of Hb at admission, 24 h, 48 h and 72 h after admission showed in Table 2. There was no significant difference between 2 groups at admission but there was a significant difference between two groups is 24 h, 48 h and 72 h after admission based on Hb amount. Table 3 shows the amount HCT at admission, 24 h and 48 h after admission. Table 4 shows the PR of patients in case and control group at admission, 24 h, 48 h and 72 h after admission. Finally, Tables 5 and 6 show the Diastolic and Systolic pressure at admission, 24 h, 48 h and 72 h after admission.

There was no difference between two groups based on Blood Pressure at admission, 24 h, 48 h and 72 h after admission and this can prove the importance of using TXA in patients with pelvic trauma without any effect on vital signs. No side effect reported by both groups after discharged from hospital.

Table 1
Comparison of the studied variables between case and control groups in patients with pelvic trauma.

Variable	Case Group (n = 53)	Control Group (n = 53)	p-Value
Sex (%)			
Male	36 (67.92)	29 (54.71)	0.32
Female	17 (32.08)	24 (45.29)	
Age (range from 18 to 60)	15.47 ± 2.24	12.8 ± 0.24	0.75
GCS at admission (range)	11.1 ± 2.19 (10-15)	14.75 ± 1.02 (10-15)	0.68
Mechanism of Trauma:			
Accident	26	21	0.46
Fall from height	18	16	
Falling down	9	16	

GCS: Glasgow Coma Scale.
Data are presented as mean ± standard deviation or frequency (%).

Table 2
Comparison of the studied variables between case and control groups in patients with pelvic trauma.

Variable	Case Group (n = 53)	Control Group (n = 53)	p-Value
Amount of Hb at admission	12.32 ± 2.15	11.7 ± 1.2	0.09
Amount of Hb 24 h after admission	11.73 ± 1.05	12.8 ± 0.24	0.001
Amount of Hb 48 h after admission	11.58 ± 2.22	10.25 ± 0.14	0.0001
Amount of Hb 72 h after admission	11.45 ± 2.1	9.83 ± 1.26	0.0001

Data are presented as mean ± standard deviation or frequency (%).

Table 3
Comparison of the studied variables between case and control groups in patients with pelvic trauma.

Variable	Case Group (n = 53)	Control Group (n = 53)	p-Value
Amount of HCT at admission	37.28 ± 6.28	36.94 ± 3.47	0.056
Amount of HCT 24 h after admission	35.3 ± 7.02	31.88 ± 3.54	0.002
Amount of HCT 48 h after admission	35.46 ± 6.65	32.95 ± 2.22	0.01
Amount of HCT 72 h after admission	35.1 ± 6.6	34.21 ± 3.44	0.36

Data are presented as mean ± standard deviation or frequency (%).

Table 4
Comparison of the studied variables between case and control groups in patients with pelvic trauma.

Variable	Case Group (n = 53)	Control Group (n = 53)	p-Value
Number of PR at admission	84.09 ± 7.41	82.7 ± 4.1	0.021
Number of PR 24 h after admission	83.87 ± 3.64	84.08 ± 3.64	0.83
Number of PR 48 h after admission	83.66 ± 6.72	83.81 ± 6.8	0.82
Number of PR 72 h after admission	83.81 ± 6.8	82.79 ± 3.64	0.34

Data are presented as mean ± standard deviation or frequency (%).

Table 5
Comparison of the studied variables between case and control groups in patients with pelvic trauma.

Variable	Case Group (n = 53)	Control Group (n = 53)	p-Value
Diastolic pressure at admission	75.38 ± 14.3	80.66 ± 4.8	0.01
Diastolic pressure 24 h after admission	76.26 ± 12.26	80.38 ± 7.89	0.06
Diastolic pressure 48 h after admission	76.72 ± 12.56	80.47 ± 7.35	0.07
Diastolic pressure hours after admission	78.4 ± 12.35	78.87 ± 4.96	0.78

Data are presented as mean ± standard deviation or frequency (%).

Table 6
Comparison of the studied variables between case and control groups in patients with pelvic trauma.

Variable	Case Group (n = 53)	Control Group (n = 53)	p-Value
Systolic pressure at admission	128.49 ± 27.29	133.77 ± 14.83	0. 21
Systolic pressure 24 h after admission	126.98 ± 24.89	132.26 ± 12.38	0.14
Systolic pressure 48 h after admission	124.89 ± 18.63	128.49 ± 15.73	0.27
Systolic pressure hours after admission	123.96 ± 21.46	125.09 ± 13.42	0.69

Data are presented as mean ± standard deviation or frequency (%).

4. Discussion

The aim of this study was to assess the efficacy and safety of Tranexamic Acid in reducing blood loss in patients with pelvis trauma. There was no statistically significant difference between the case and control groups based on age, sex, GCS at admission, mechanism of trauma, Hb, HCT, BP and PR of the enrolled patients. It has been showed in this study that TXA can reduce whole blood loss during hospitalization; however, did not effect on vital sings in the case group compared to the control group.

In a review study published by Roberts; he suggested that initiated administration of TXA before 3 h after trauma can reduce blood loss and massive bleeding. He showed that patients who received TXA after 3 h take less benefits and the important factor after trauma is early admission not TXA alone.[10]

Roberts also suggested using of TXA in emergency medicine or early given on arrival at hospital so this can confirm the purpose of this study to administer TXA in emergency medicine ward before operation.[10]

The minimum and also safe dose of TXA suggested in patients with trauma was 10 mg/kg for loading dose[9]; however, claeys et al

used 15 mg/kg for single dose perioperative and get extra benefits without side effect in patients underwent total hip replacement.[11]

In this study patients received 1 g TXA for loading dose and every 8 h for the maintenance for 3 dose in early admitted patients referred less than three hours after trauma. The results show the benefits of TXA received in case group compare with control group and in contrast with Roberts study and in compatible with shakur et al study.[10]

There was no difference between case and control groups based on sex, age, GCS at admission and Mechanism of trauma. There was no difference between two groups based on Blood Pressure and PR at admission, 24 h, 48 h and 72 h after admission however; There was a significant difference between two groups in 24 h, 48 h and 72 h after admission based on Hb and HCT amount. The results of this study was compatible with Guerriero et al.[12]

They also discussed about cost-benefits of TXA that can save money in various income countries in early administration so it can use in low or middle income countries.[12]

In conclusion, based on our findings it appears that TXA can reduce bleeding amount in the first, second and third 24 h after surgery based on Hb and HCT without any effect on systolic and diastolic BP and PR. In other hand no side effect reported by any patients.

Conflict of interests

None.

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