

A Comparative Study between Prophylactic High Dose of Tranexamic Acid and Low Doses Tranexamic Acid in Reducing Perioperative Blood Loss in Spine Surgery

This article was published in the following Scient Open Access Journal:

Journal of Clinical Anesthesia and Pain Medicine

Received January 09, 2017; Accepted February 14, 2017; Published February 21, 2017

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Abstract

Background and aim: The study aim was to compare whether high dose or low dose tranexamic acid have an effect in decreasing perioperative blood loss in spine surgery case and determine whether the expected reduction in the bleeding was capable of reducing the need for blood transfusion.

Patients and methods: This study was prospective, double blind, RCT study in which sixty patients were scheduled for posterior arthrodesis of spinal cord with fusion of one or two levels under general anesthesia. The patients were randomly allocated into three equal groups. Group C (control) received normal saline, group HD (high doses) received 50 mg/kg of tranexamic acid administered over 30 min before skin incision and continued at the rate of 20 mg/kg/h until the end of the procedure and group LD (low doses) received 10 mg/kg of tranexamic acid over 30 min before skin incision and continued at the rate of 1 mg/kg/h until the end of the procedure. The total amount of blood loss intraoperative and in the first 24 hours postoperative and hemoglobin concentration (preoperative and one day postoperative) were recorded.

Results: HD group and LD group showed a highly significant decrease in blood loss in comparison with the control group ($p < 0.001$). Blood loss in HD group was significantly less than in LD group ($p < 0.001$).

Conclusion: Prophylactic use of large dose of TA (50 mg/kg loading dose then 20 mg/kg maintenance dose) provides an effective, safe and cheap method for reduction of blood loss during and after spine operations than the use of small dose (10 mg/kg loading dose then 1 mg/kg maintenance dose).

Keywords: Tranexamic Acid, Perioperative blood loss, Spine surgery

Introduction

Degenerative spinal stenosis and instability requiring multilevel spine surgery can be associated with considerable blood loss. The association of increased intra- and postoperative blood loss during reconstructive spine surgery with higher complication rates has been established. [1,2]. Dealing with cancellous bone with its rich blood supply is often associated with significant perioperative blood loss and usually requires multiple blood transfusions [3,4]. Allogeneic blood transfusion carries the significant risk of transmitting infections (viral and bacterial), hemolytic transfusion reactions, transfusion-related lung injury, and increases hospital costs [5,6]. A variety of strategies have already been proposed in attempts to diminish the dependence on allogeneic blood transfusion in major surgery. These include storage of autologous blood before the operation, normovolemic Hemodilution, hypotensive anesthesia, use of a cell recovery machine and the use of drugs with antifibrinolytic properties, such as aprotinin, epsilon-aminocaproic acid and tranexamic acid [7,8].

Tranexamic acid (4- [amino methyl] cyclohexanecarboxylic acid; trade name Kapron; AMOUN, Cairo, Egypt) is a synthetic derivative of the amino acid lysine that exerts its antifibrinolytic effect through the reversible of the blockade of lysine binding sites on plasminogen molecules. As a result, plasminogen is unable to bind to the lysine residue on fibrin, and fibrinolysis is suppressed [9,10]. This suppression of fibrinolysis results in reductions in D-dimer levels but has no impact on blood coagulation parameters (e.g., platelet count, a PTT, and PT times). Therefore, TXA reduces the rate at which

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hemostatic fibrin is dissolved, allowing for stabilization of the fibrin clot and decreased blood loss. Because of its low cost and because its side effects are small, studies have been conducted in different parts of the world in attempts to evaluate its efficacy for controlling perioperative bleeding in major surgery [11,12]. TXA doses of up to 100 mg/kg have been recommended. However, a significant increase in clinical seizures in the early postoperative period was noted in 2 institutions after introduction of routine TXA infusions for high-risk cardiac surgical patients [13].

The objective of this study was to document the influence of tranexamic acid in high dose (50 mg/kg) and low dose (10 mg/kg) on the bleeding in thoracic spine surgery and to ascertain whether the expected reduction in bleeding was capable of reducing the need for blood transfusion.

Patients and Methods

This study was conducted at Benha university hospitals (tertiary hospital) between April 2014 and Oct. 2016.

After local ethical committee approval and patients informed written consent, this prospective, randomized, double blind and controlled clinical trial was conducted on 60 patients in Benha university hospitals, their ages ranged between 28- 65 years, ASA I and II, BMI < 35 kg/m² underwent Posterior thoracic vertebrae arthrodesis with fusion of one or two levels under general anesthesia.

Patients with uncontrolled hypertension, liver or renal impairment, congenital or syndromic scoliosis, fixation of more than 2 levels, Previous spinal surgery, coagulopathies or patients who received anticoagulant or any drug that may interfere with the study drugs were excluded from the study.

These patients were randomly allocated into three equal groups:

Group C (control): patients did not receive tranexamic acid and received normal saline.

Group HD (High Does): patients received tranexamic acid in which tranexamic acid was used at loading dose of 50 mg/kg of body weight, administered over the 30-minute period prior to making the skin incision. After the incision has been made,

continual infusion is maintained at the rate of 20 mg/kg/h until the end of the procedure, i.e. when the skin has been closed.

Group LD (Low Does): patients received tranexamic acid in which tranexamic acid was used at loading dose of 10 mg/kg of body weight, administered over the 30-minute period prior to making the skin incision, continual infusion is maintained at the rate of 1 mg/kg/h until the end of the procedure, i.e. when the skin has been closed.

All patients were admitted to Benha university hospital one day before the operation. Preoperative visit was conducted to explain the maneuver, history taking and check the investigations. In the pre-anesthetic room, IV line was inserted and midazolam 0.01-0.2 mg/kg was administered.

General anesthesia was induced by propofol 2 mg/kg, fentanyl 1-2 micg/kg, and tracheal intubation was facilitated by atracurium 0.5 mg/kg. Anesthesia was maintained by isoflurane 1-2 MAC and top up doses of atacurium 0.1 mg/kg every 20 min. respiratory parameters were adjusted to keep the end tidal Co₂ between 35-40 mmHg.

The following parameters were recorded:

- Demographic characteristics (Age, sex, weight, height, BMI and ASA physical status.)
- Time of surgery (time from skin incision till removal of surgical drapes)
- The total amount of blood loss intraoperative and in the first 24 hours postoperative: Intraoperative blood loss was measured by adding the volume of blood in the suction bottles to the weight of sponges. All fluids added to the surgical field intraoperatively were quantified and deducted from the measured blood loss. Postoperative blood loss was measured from wound drainage of the surgical drain for the first 24 h.
- Hemoglobin concentration (preoperative and one day postoperative).

Statistical analysis

(1) Data were analyzed by using SPSS (IBM, New York, USA), version 16.

		Group C	Group HD	Group LD	p-value
Age (years)		46.05 ± 12.04	44.35 ± 12.2	44.7 ± 12	0.895
Weight (Kg)		76.95 ± 11.2	74 ± 11.7	76.45 ± 11	0.6745
Height (cm)		169.7 ± 10	170.05 ± 10.3	171.8 ± 10.8	0.7903
Sex	M	11	13	9	0.44
	F	9	7	11	
BMI (Kg/m ²)		29.9±3.5	29.8 ± 3.2	29.98 ± 3.14	0.9938
ASA	I	6	7	7	0.9277
	II	14	13	13	
Time of surgery (min.)		172.3 ± 18	170.85 ± 17.5	168.8 ± 19.2	0.8318
Blood loss (ml)		1073.9 ± 119	689.75 ± 67†	892.15 ± 75	<0.001**
Hb %		13.3 ± 1.16	13.295 ± 1.23	13.2 ± 0.86	0.3175
	Post-op.	10.265 ± 1.15	12.26 ± 1.19	11.325 ± 1.04	<0.001
Duration of hospital stay (day)		6.1±0.78	5.65±0.81	5.85±0.67	<0.17

** Significant deference between groups

†Significant deference between Group HD and group LD

Table 1: Demographic characteristic, time of surgery, blood loss, Hb% and duration of hospital stay.

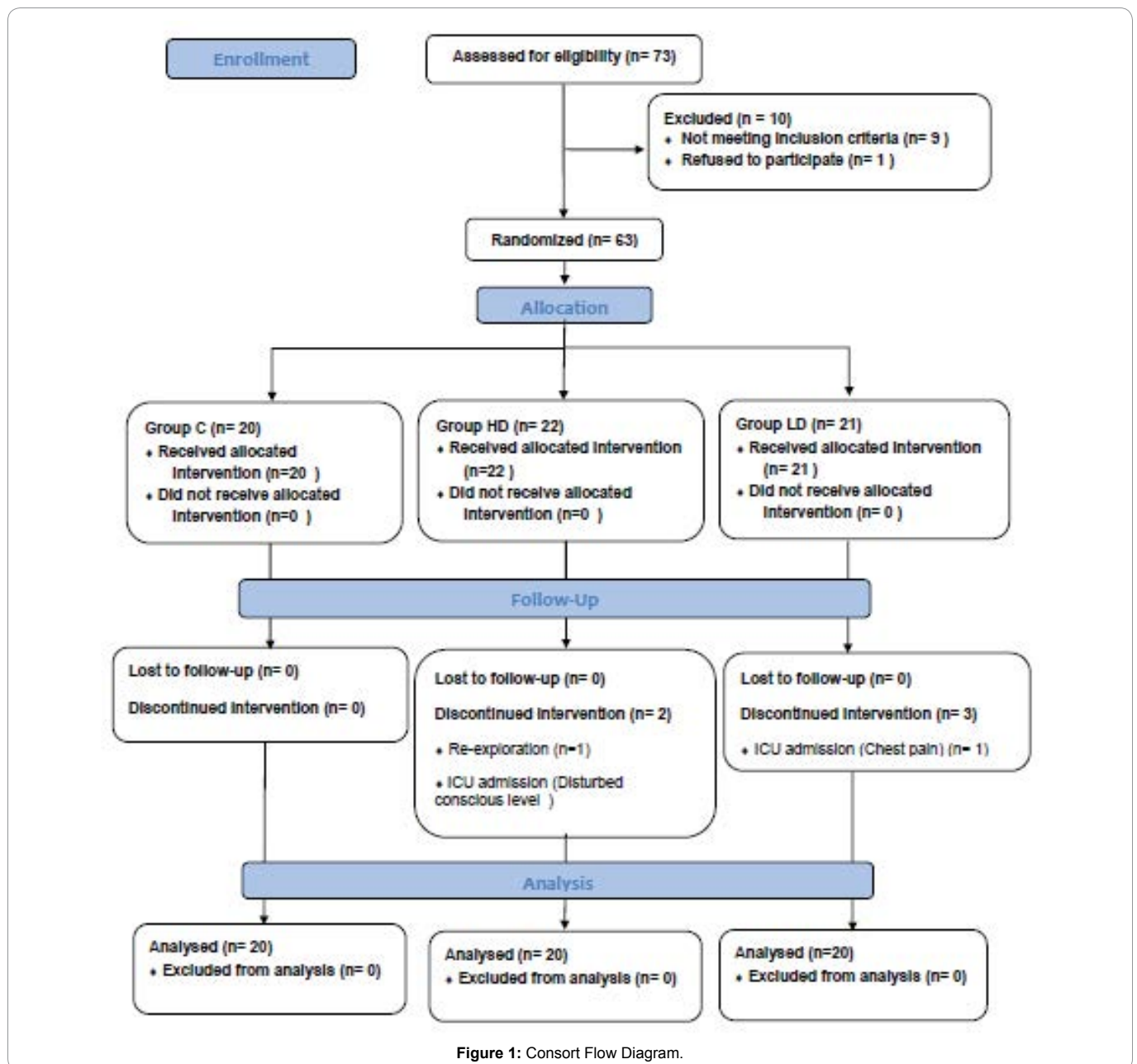


Figure 1: Consort Flow Diagram.

- (2) Quantitative data were presented as mean and SD and were analyzed using the analysis of variance (ANOVA) test.
- (3) Significant ANOVA test was further analyzed using the post-hoc test to determine the significant group.
- (4) Qualitative data were presented as number and percentages and were analyzed using the χ^2 -test.
- (5) A P-value less than 0.05 was considered statistically significant, whereas a P-value less than 0.01 was considered statistically highly significant.

Results

From 73 patients assessed for eligibility, 9 patients not met

the inclusion criteria and 1 patient refused to participate. 63 patients were enrolled in the study but 3 more patients were excluded shortly thereafter because 2 patients were admitted to ICU and one patient re-explored. So in total 60 patients completed the study protocol (Figure 1).

Discussion

In the current study, we demonstrated that administration of tranexamic acid in high dose in HD group (50 mg/kg bolus followed by 20 mg/kg/h) reduce the total perioperative blood loss significantly in comparison with the administration of tranexamic acid in low dose in LD group (10 mg/kg bolus followed by 1 mg/kg/h) Both groups (High dose and low dose) had a significantly less blood loss in comparison with the control group. The patients in the TXA groups also had higher

postoperative hemoglobin levels than the control group with significant decrease in hemoglobin levels in low dose group in comparison with the high dose group.

The high dose of tranexamic acid used in the current study was the dose recommended by Vinícius and his colleagues [14] who follow a protocol in which tranexamic acid was used at an attack dose of 100 mg/kg of body weight, administered over the 30-minute period prior to making the skin incision followed by infusion of 30 mg/kg/h until the end of the procedure. The low dose of tranexamic acid used in the current study was the recommended by John and his colleague [15,16].

Our findings of reduced blood loss, are consistent with Jean Wong [16]. Who concluded that TXA significantly reduce the estimated and calculated total amount of perioperative blood loss in adult patients having elective posterior thoracic/lumbar instrumented spinal fusion surgery. Also, Sethna, et al. [17] found that TXA reduce intraoperative blood loss in pediatric patients undergoing scoliosis surgery. Kushagra Verma, et al. [18] found that TXA significantly reduce the estimated and calculated total amount of perioperative blood loss in adult patients having elective posterior thoracic/lumbar instrumented spinal correction of deformities [19-21].

Conclusion

Prophylactic use of large dose of tranexamic acid (50 mg/kg loading dose then 20 mg/kg maintenance dose) provides an effective and cheap method for reduction of blood loss during and after thoracic spinal operations than the use of small dose of tranexamic acid (10 mg/kg loading dose then 1 mg/kg maintenance dose). Hence TA may help in reducing not only transfusion related complications but also operative expenses. Considering the limited number of patients in this study, our results need to be validated on a larger number of patients.

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