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ORIGINAL ARTICLE

The Effect of Different Loading Doses of Tranexamic Acid with the Same Maintenance Dose on Total Blood Loss in the Operative Management of Adolescent Idiopathic Scoliosis: A Retrospective Cohort Study

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ABSTRACT

Background: Tranexamic acid is a known antifibrinolytic the decreases blood loss. However, there is a debate about its ideal routine of administration in idiopathic scoliosis surgeries which involves significant soft tissue dissection and excessive bleeding. The aim of this study is to determine the effect of different loading doses of tranexamic acid with the same maintenance dose on the total blood loss in idiopathic scoliosis surgeries.

Methods :A prospective cohort study performed at a single spine center. The first 79 patients who were indicated for AIS surgical correction who met our inclusion criteria were included in the study after obtaining informed consent. The patients were divided into 2 groups; group (A): 41 patients who received a loading dose of 10 mg/kg and group (B): 38 patients who received a loading dose of 50 mg/kg. Both had a maintenance dose of 1 mg/kg/h. **Results:** There were no statistically significant differences between the two studied groups in terms of total blood loss, blood loss per level, operative time, transfusion intraoperative, and transfusion post-operative.

Conclusion: There was no significant difference in blood loss between using a loading dose of 10 mg/kg and 50 mg/ kg of TXA while using a maintenance dose of 1 mg/kg/h. This may reflect the importance of paying attention to the maintenance dose as well as the loading dose of TXA as the high-loading dose seems to lose its superiority over the low-loading dose if the maintenance dose is not proportionally high.

Keywords: Tranexamic acid – Scoliosis – Bleeding

INTRODUCTION

Adolescence idiopathic scoliosis (AIS) is usually managed surgically via posterior spinal fusion (PSF) which involves significant soft tissue dissection and posterior vertebral segment osteotomies resulting in excessive bleeding and the need for blood transfusion. This procedure is a lengthy operation that usually lasts for at least 3-4 hours. Due to these circumstances, surgeons and anesthetists are worried about substantial blood loss during the intraoperative and postoperative phases[1]. It is considered that blood transfusion can be the best option to compensate for intraoperative blood loss and control postoperative anemia. However, this does not come without some risks. There are possible complications of blood transfusions such as viral transmission, transfusion related renal impairment, circulatory overload, and coagulopathy hazards associated with blood transfusion. Thus, there is a desire to lower the need for a blood transfusion by controlling blood loss intraoperatively to prevent the complications

mentioned above and to minimize the morbidity rate associated with significant blood loss [2].

Tranexamic acid (TXA) is a synthetic antifibrinolytic that stops the process of plasminogen activation into plasmin, thereby preventing fibrinolysis by inhibiting plasmin binding to fibrinogen. TXA was first used by patients with hereditary bleeding disorders or female patients with heavy menstruation. It can also decrease blood loss during scoliosis correction surgery and decrease the degree of platelet degradation process according to several studies that compared the safety and efficacy of different doses of TXA with a those of a placebo. It is utilized in pediatric patients and adults, with numerous studies demonstrating its application in cardiac, spine, obstetric, arthroplasty, and urological surgeries [3,4].

However, some complications of TXA are associated mainly with high doses such as nausea, vomiting, diarrhea, allergic dermatitis, giddiness, hypotension, renal impairment seizures, and thromboembolic events. TXA-induced seizures usually occur after very high doses, which are more than 5 folds of the recommended dose. In patients with any type of renal impairment, the lowest possible dose should be used while it is contraindicated in patients with active thromboembolic diseases [5]. It is proved in the clinical studies that TXA significantly lowers total blood loss in comparison with patients who did not take Tranexamic acid. However, there is still an ongoing debate in the literature about the ideal initial and maintenance doses of TXA to control bleeding without any drug-related complications [6,7]. This study aimed to evaluate whether there is a difference between a loading dose of 10 mg with a maintenance dose of 1 mg/kg/h and a loading dose of 50 mg with a maintenance dose of 1 mg/kg/h of TXA in reducing blood loss and minimizing the need for allogeneic blood transfusion in patients undergoing surgery for adolescent idiopathic scoliosis. The findings will help identify the minimum effective dose of TXA for controlling bleeding while avoiding higher doses and their associated side effects, particularly in high-risk patients such as those with renal impairment.

METHODS

This was a prospective cohort study performed at a single spine center. The first 79 patients who were indicated for AIS surgical correction who met our inclusion criteria were included in the study between January 2022 and October 2022. Informed consent was obtained from all participants involved in the study. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki and received approval from the Ethics Committee of Zagazig University Hospitals (IRB). The patients were divided into 2 groups; group (A): the first 41 patients who were admitted to the study received a loading dose of 10 mg/kg and group (B): the next 38 patients who received a loading dose of 50 mg/kg. Both had a maintenance dose of 1 mg/kg/h.

The mean age of our study group A was 14.19± 2.37 years (range 10-19), whereas that of group B was 13.52± 1.8 (range 11-18). The sex distribution of group A was 35 females and 6 males, whereas that of was 30 females and 8 males. The inclusion criteria were adolescent idiopathic scoliosis (AIS) patients requiring surgical correction who were otherwise healthy. Exclusion criteria included the presence of autoimmune diseases, chronic infections, cancer or a positive history of epilepsy ot thromboembolic manifestations.

All the patients were managed by posterior spinal fusion via pedicular screws and bilateral facetectomies at each level included in the fusion. Autogenous bone graft from the removed facets were mixed with 1 gm Vancomycin powder and applied the spine after shingling of the lamina of the spine between the upper instrumented vertebra and the lower instrumented vertebra. For the postoperative care, we are using the enhanced recover protocol with a special team of doctors and nurses.

The data were collected preoperatively through history taking, clinical exams, and laboratory investigations. The data intraoperatively were collected through ABG and intraoperative blood loss

measurement, whereas the postoperative data were collected through clinical and laboratory investigations. The data were initially entered into Microsoft Excel and then imported into the Statistical Package for the Social Sciences (SPSS version 20.0) for analysis. Qualitative data were represented as numbers and percentages, while quantitative continuous data were expressed as mean ± standard deviation (SD). The following statistical tests were employed to assess differences for significance. Differences between quantitative pairs by paired t test, correlation by Pearson's correlation, or Spearman's. P value was set at <0.05 for significant results and <0.001 for highly significant results.

RESULTS

79 Seventy-nine patients were included in our study. All the patients did not experience any intraoperative neurological or vascular complications. All our patients were discharged at the third day postoperative. None of our patients had any complications related to TXA as there were no nausea, vomiting, thromboembolic manifestations or renal function laboratory impairment even after one year follow up. Regarding fusion levels, there was statistically no significant difference between the two studied groups as group A: 11.19± 2.08 (7-15) & group B: 11.05± 2.09 (6-14). Regarding total blood loss (ml), there was no statistically significant difference between the two studied groups as group A: 583.33± 208.7 ml, while group B: 586.84± 220.3 ml. Regarding blood loss per level, there was no statistically significant difference between the two studied groups as group A showed 53.23 ± 20.65 ml/level (31-114) while group B showed 53.57 ± 18.86 ml/ level(٣٢-١٠٩) . There was no statistically significant difference between the two studied groups in terms of operative time, transfusion intraoperative, and transfusion post-operative. The mean operative time for group A was 4.19 ± 0.78 hours ranging from 3-6 hours, whereas that for group B was 3.73 ± 0.83 hours ranging from 2.5-6 hours. As for intra-operative blood transfusion, group A included 16 out of 41 patients who received a transfusion, and group B included 14 out of 38 patients who received a transfusion. As for postoperative blood transfusion in Group A, 24 patients received a transfusion whereas in group B, 18 patients received a transfusion as shown in (Figure 1). There was a significant positive correlation between blood loss per level and age in both groups with a P value = 0.032 making it statistically significant as shown in (Figure 2).

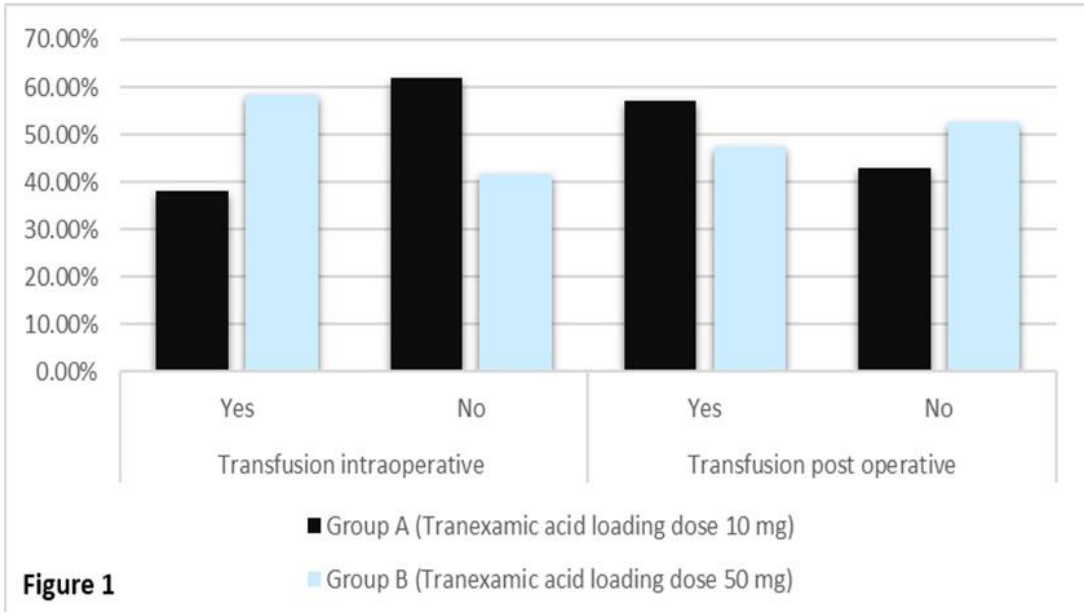

Figure (1): Distribution of blood transfusion intraoperative and postoperative between the studied groups

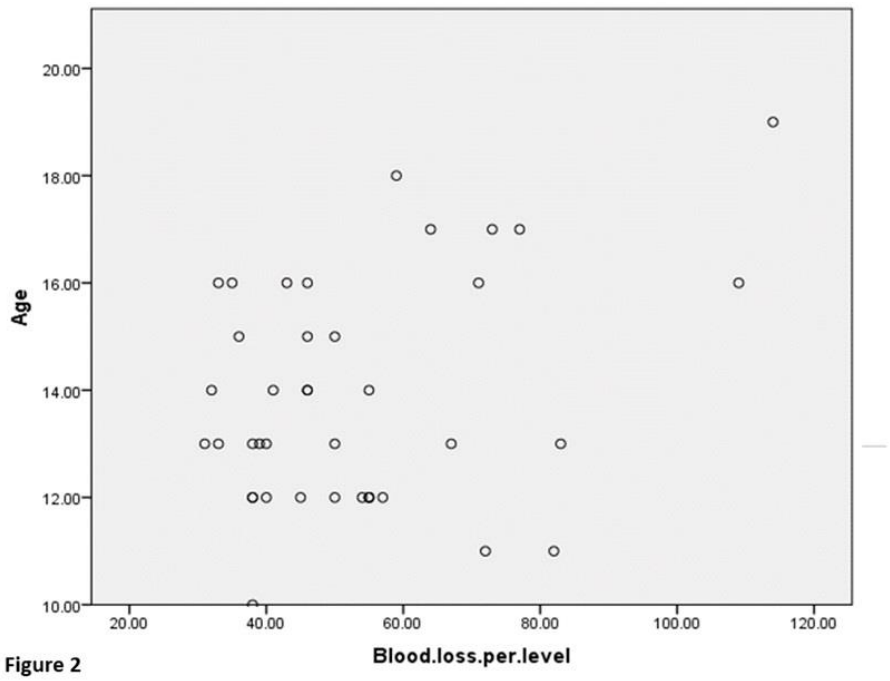

Figure (2): Correlation between blood loss per level and age in both groups

DISCUSSION

Management of AIS with PSF is a major surgery with extensive soft tissue dissection that is associated with a remarkable amount of blood loss even in the hands of a skilled surgeon with good hemostasis and a qualified anesthesiologist who maintains a controlled mean arterial blood pressure and heart rate during the operation. Significant blood loss intraoperatively is associated with increased risks of hypoperfusion of important structures such as the kidney leading to acute kidney injury or the spinal cord itself, which may even lead to signal loss during correction of the deformity intraoperatively. Postoperative hematoma collection is also a disturbing complication of excessive bleeding that may lead to neural tissue compression requiring a second operation to evacuate the hematoma. The need for a blood transfusion with all its hazards increases proportionally with the increase of bleeding. Therefore, it has always been a very concerning matter to control the perioperative bleeding in spine surgeries [8].

TXA is a homolog of lysine so it has a high affinity for the lysine binding sites of fibrinogen. This binding blocks the interaction between the plasmin and the fibrinogen and then limits the destruction of fibrin by fibrinolytic enzymes leading to a hemostasis by preservation of the formed clots [9]. Over the past decade, there has been an increase in the use of TXA in scoliosis surgeries with very good results in controlling blood loss in comparison to surgeries without TXA usage [10].However, TXA has its side effects, especially at high doses like any other medications that may pose serious risks to patients' lives, such as thromboembolic events, seizures, or renal impairment. Multiple studies have been performed on different doses and their effect on controlling the bleeding without any drug-related side effects)[11,12].

Several studies have investigated the effect of the use of Tranexamic acid with different protocols of loading doses and maintenance doses on bleeding control in comparison with control groups. Unfortunately, there are not many studies comparing the effect of different doses in bleeding control. Our study compared the use of a loading dose of 10 mg/kg vs 50 mg/ kg as bolus doses preoperative and followed by 1 mg/ kg/ hour as a maintenance dose intraoperatively. There was no significant difference

between the two groups in total blood loss, blood loss per level, operative time, or blood transfusion intraoperatively and postoperatively. The results were very similar between the two groups. There were no recorded drug-related complications in the two groups.

Our results differ from those of Johnson et al., who reported that there were significant differences between the 10 mg/kg loading dose and the 50 mg/kg loading dose in terms of total blood loss, operative time, and blood transfusion. However, in their study, the maintenance dose of the 50 mg/ kg loading dose group was 5 mg/ kg/ hour, unlike that in our study which was 1 ml/ kg/ hour. This may be a reason for the different results [13].

These findings are also different from those of Grant et al. They reported a significant difference in the amount of blood transfusion between the low-dose and high-dose TXA groups. Their study also differed from ours in utilizing a high-dose protocol, which included a loading dose of 20 mg/kg and a maintenance dose of 10 mg/kg/hour [14].Tumber et al. studied two groups; A (loading dose > 30 mg/kg) and B (loading dose < 30 mg/ kg) with the same maintenance dose of 10 mg/kg/h. There was a significant difference in total blood loss as group A had an average blood loss of 1000 ml whereas group B had an average of 1600 ml blood loss. There was a significant difference between the 2 groups in the need for blood transfusion with only 19% receiving a blood transfusion in group A and 67% in group B. They used a much higher maintenance dose (10 mg/kg/h) compared to our study (1 mg/ k/h) [15].

In terms of the significance of the low dose of TXA in reducing bleeding, our results are similar to those published by Verma et al. & Neilipovitz et al., who reported a significant decrease in total blood loss. They used loading and maintenance doses similar to the low dose used in our study [16,17]. In terms of the significance of high doses of TXA in reducing bleeding, our results are similar to those published by Goobie et al in terms of total blood loss, blood loss per level, and blood transfusion. They had the same loading dose as our high-dose group (50 mg/ kg) but had a different maintenance dose of 10 mg/ kg/ hour [18]. Limitations: A limited number of cases were included. There were limited variations in the dose protocols which we compared in this study. There may be a need for more comprehensive studies with more dose-protocol comparisons.

CONCLUSION

There was no significant difference in blood loss between using a loading dose of 10 mg/kg and 50 mg/ kg of TXA while using a maintenance dose of 1 mg/kg/h. This may reflect the importance of paying attention to the maintenance dose as well as the loading dose of TXA as the high-loading dose seems to lose its superiority over the low-loading dose if the maintenance dose is not proportionally high.

Disclosure of Conflict of interests: there is no conflict of interests

List of Abbreviations: TXA= Tranexamic acid, AIS= Adolescence idiopathic scoliosis, PSF= posterior spinal fusion.

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