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Original Article

Castigating intraoperative bleeding: Tranexamic acid, a new ally

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Abstract

Introduction: The field of instrumented spinal procedures is associated with substantial blood volume losses, which is one of the major hazards we encounter; this would lead to a greater need for blood products transfusions. The frequent use of these products can have negative consequences due to body fluid shifting, and donor-host rejection. Thus, it has become mandatory to establish strategies to maintain blood volume and minimize losses. Several strategies have been approved to control the disproportionate blood loss. **Objective:** This study aims to assess the effectiveness of tranexamic acid in reducing intraoperative bleeding during our spine instrumented surgeries, while addressing complications associated. **Methods:** In this retrospective analysis was steered of 153-consecutive patients treated in the neurosurgical- spine unit of King Hussein hospital, King Hussein Medical Center (KHMC), between April 2017 to January 2020, patients who underwent instrumented surgery for different spinal pathologies at our institute were reviewed. **Results:** During the analysis period, 153-patients who underwent interbody fusion, were allocated into two groups. The mean instrumented segments were 2.8 level (range 1-5 levels). The demographical data of patients of both groups analyzed. The mean span of operating time was (212.74 ± 41.85 min) for group I, while for the control group mean length was (208.09min ±42.03). Study showed that the mean drop in the hemoglobin concentration postoperatively was statistically significant comparing the two groups. Analysis of blood volume in suction container showed that group I had: 470 ml ±153.06 ml; while in control group volume was: 1560 ml ± 567.59 ml, which showed significant difference (p = 0.002). Comparing the drainage volumes at 12 hours postoperatively displayed no statistically significant differences (p = 0.69) concerning the two groups. Minor adverse effects allied with the tranexamic acid administration. **Conclusions:** In summary, perioperative bleeding deemed one of the most important threat for patients. Tranexamic acid is proved excellent in controlling perioperative bleeding, harboring few contraindications. Future large studies are still needed to elaborate on unanswered issues.

Keywords: *Antifibrinolytics, fibrinolysis, instrumented spine, intraoperative bleeding, tranexamic acid*

Introduction

The field of instrumented spinal procedures is associated with substantial blood volume losses, which is one of the major hazards we encounter; this would lead to a greater need for blood products transfusions. The frequent use of these products can have negative consequences, such as transmitted infections, acute cerebral or lung edema due to body fluid shifting, and donor-host rejection.[1,2] Thus, it has become mandatory to establish strategies to maintain blood volume and minimize losses, as encompassed within the concept of "patient blood management."[2] Several strategies have been approved to control the disproportionate blood loss from the preoperative period by applying blood function monitoring, while intraoperatively, methods have been established to decrease the need for blood products. Newly promoted antifibrinolytics agents are also available.[1-4]

In many fields of surgery, recent studies had advocated policies effective in lessening perioperative bleeding and decreasing the requirements for transfusion of blood products. Some of these studies are nowadays delving major spine surgeries.[4-7] Here we appraise the efficiency of tranexamic acid as a limiting agent of perioperative bleeding during our surgeries, while addressing complications associated.

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Methods

Patients

In this prospective, retrospective analysis, we gathered data from 153 consecutive patients treated in the neurosurgical spine unit of King Hussein Hospital, King Hussein Medical Center, between January 2016 and January 2020. All patients who underwent instrumented surgery for spinal pathologies at our institute were reviewed. Seventy-nine patients were enrolled in the final stage study. Thirty-one patients were excluded after applying the inclusion-exclusion criteria: 13 patients missed the 1 month follow-up, 11 patients had tumours, and 7 patients had posterior cervical instrumented surgery. Seventy-nine patients with spinal pathologies (namely: degenerative spine disease, spondylolisthesis, iatrogenic flat back, fractures, and infections) were recruited from the Spine centre for this study. All surgeries were conducted by a senior neurosurgeon. A control group (43 patients) was included consisting of our cases who had been previously operated and had lumbar spinal fusion procedure performed during the 16 months before tranexamic acid was introduced as an agent. Group I included 79 patients, enrolled in April 2017. Based on medical records, the intra- and post-operative blood losses were measured by evaluating the suction volume minus the irrigation fluids at the intraoperative period and drainage volumes 12, 24, and 48 h postoperatively. In addition, hemoglobin concentration was reviewed. Furthermore, the complications related to tranexamic acid administration were considered.

Inclusion/exclusion criteria

Inclusion criteria

1. One or more levels of instrumented spine disease
2. Treatment by posterior interbody fusion and/or reconstructive osteotomies
3. Thoracic and lumbar segments (from T1 to S1)
4. A minimum follow-up of 2 months.

Exclusion criteria were

1. Inadequate documentation of follow up
2. Oncology cases scheme
3. The presence of severe systemic disease (heart disease, thromboembolism, bleeding tendency, renal malfunction)
4. Age <18 years
5. Cervical spine surgeries
6. Patients with 360° surgical approach.

Demographic features

All adult patients operated by our team at the neurosurgical department from January 2016 to January 2020 were evaluated. The medical reports of patients were retrieved from our database and reviewed; clinical follow-up data were collected in cooperation with the investigators.

Table 1: Demographic details of all patients

Parameter	Patients number
Gender	
Male	48
Female	31
Age	
<60	72
>60	7
Instrumented level	
1–2 level	56
3–5 levels	23

Table 2: Demographic distribution regarding gender

Parameter	Males	Females
Age		
<60	45	27
>60	3	4
Instrumented level		
1–2 levels	30	26
3–5 levels	18	5
Primary diagnosis		
Degenerative disc disease	25	13
Spondylolisthesis	7	7
Iatrogenic flat back	5	8
Fractures	7	2
Infections	4	1

The mean age of our patient was 54.6 years (27–69 years), and there were 48 men and 31 women. The mean symptom duration before surgery was 1.3 years (range: 1 week to 2.5 years), and patients were monitored for of 12.3 months on an average (range: 2–15 months). The demographic data of Group I are summarized in Tables 1 and 2.

Our protocol of tranexamic acid includes a loading dose of 20 mg/kg introduced intravenously on induction, followed by an intravenous infusion of rate 5 mg/kg/h until skin closure. No added oral doses are given postoperatively, nor intravenous administrations.

Operations/instrumentations

There are many alternative available procedures to address the different spinal pathologies, such as Posterior lumbar interbody fusion, transforaminal lumbar interbody fusion with and without osteotomies, either minimally invasive or open. The enrolled patients underwent open instrumented surgery of thoracic and/or lumbar spine segments, using a conventional posterior midline approach, while patients operated at the cervical segment or that had the 360° approach were excluded. All valid options of instrumentations and techniques were used. There was no preselected method of surgery nor a specific type of cages, screws, or rods. The surgical technique included subperiosteal discussion of paraspinal muscles, exposure of posterior neural arches, decompression, spinal osteotomies,

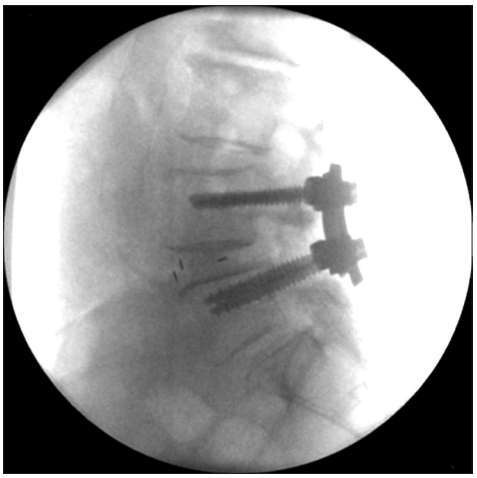

Figure 1: Single instrumented level

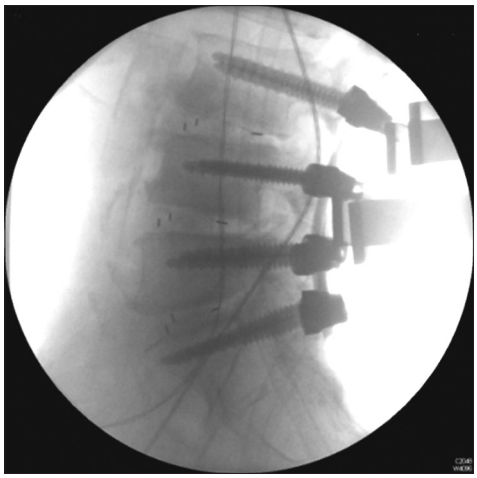

Figure 2: Three instrumented level

posterolateral fusion techniques utilizing autologous graft, interbody fusion, and stabilization using pedicle screws. Our technique included inferior facet partial resection and a foraminotomy in all patients. Procedures were performed by a senior spine surgeon (Al. R). Subfascial suction drains were inserted and were retained for at least 48 h postoperatively. The study had 56 patients with one or two instrumented levels [Figure 1]. We also had 23 patients who underwent 3–5 levels instrumentation [Figure 2].

Statistical analysis

The main baseline cardinal characteristics of the patients are plotted as means and standard deviations for definite variables. We compared the baseline characteristics between the two groups using the analysis of variance method. Correlation analyses were done using the Pearson correlation coefficient. A value of $P < 0.05$ was defined as statistically significant.

Results

During the analysis period, our study included 153 patients who underwent instrumented spinal interbody fusion. After applying inclusion criteria, the population were allocated into two groups, 79 patients were recruited for the final stage of study as Group I, while 43 patients were reviewed as the control group (group II). In Group I, 37 patients had a primary procedure, whereas 42 cases were revision surgeries. The mean level of instrumented segments was 2.8 (range: 1–5 levels). The demographical data of patients of both groups analyzed are given in Table 3. Group I comprised 31 females and 48 males (mean age: 58.6 ± 7.45 years, range: 27–69 years). In group II, 27 males and 16 females were recruited, with a mean age of 61.4 years. The mean operating time was 212.74 ± 41.85 min for a group I and 208.09 ± 42.03 min in the control group.

In group I and II, the fluid volumes infused intraoperatively were 2254.40 ± 237.60 ml and 2563.33 ± 782.30 ml,

Table 3: Demographical features of patients recruited in both groups compared

	Group I	SD	Group II	SD	*P*
Groups population	79		43		
Gender (*n*)					
Male	48		27		
Female	31		16		
Weight (kg)	79.98	1253	76.18	12.76	0.449
Height (cm)	166.04	6.77	171.35	7.47	0.023
Age	67	9.5	69	9.8	0234
Coagulation-PTT (s)	27	3.93	26	4.2	0.352
Procedure length (min)	212.74	41.85	208.09	42.03	0.587
Number of levels					
1 segment TLIF	35		17		0.286
2 segments TLIF	21		13		
3 segments TLIF	16		8		
4 segments TLIF	4		3		
5 segments TLIF	3		2		

PTT – Partial thromboplastin time; TLIF – Transforaminal lumbar interbody fusion; SD – Standard deviation

Table 4: Comparing the perioperative results of the population analyzed

	Group I	SD	Group II	SD	*P*
Groups population	79		43		
Haemoglobin levels (g/dl)					
Preoperation levels	13.91	1.1	14.51	1.28	0.103
Levels postoperation (1 day)	11.28	1.68	10.24	1.39	0.013
Mean drop	2.63	0.89	4.27	0.9	0.012
Drain (ml)					
Intra operation (suction)	470	153.06	1560	567.59	0.0002
Postoperation 12 h	101.25	72.7	110	81.6	0.69
Postoperation 24 h	161.25	111.01	258.75	121.8	0.002
Postopeative total 48 h	286	180	368.75	211.4	0.016

SD – Standard deviation

respectively (P = 0.3). The study showed that the mean drop in the hemoglobin concentration postoperatively was statistically significant when comparing the two groups, results revealed that the Group I was superior (2.63 g/dl versus 4.27 g/dl) in Group II (P = 0.012). The blood volume in the suction container was 470 ± 153.06 ml for group I and 1560 ml ± 567.59 ml for the control group (P = 0.002). The drainage volume at 24 h postoperatively was 161.25 ± 111.01 ml in Group I and 258.75 ± 121.8 ml in the control group (P = 0.002); there was less blood loss in group I than in Group II. At 12 h postoperatively, we detected no difference in drainage volumes when comparing groups (P = 0.69).

This review observed minor adverse effects allied with tranexamic acid administration: three cases of an allergic reaction, there were two cases developed deep-vein thromboses (DVTs), complications were tackled effectively without any further morbidity by administrating conventional anticoagulation therapy. There were no major complications in terms of intracranial embolic infarcts; seizure myocardial infarction or acute renal shut-down. General outcomes are shown in Table 4.

Discussion

Tranexamic acid, as an indirect antifibrinolytic, was developed in Shosuke Okamoto's lab in the early 1960s. It was initially introduced for patients with heavy menstrual cycles, then used for cases with hereditary bleeding disorders. Tranexamic acid was also used for programmed operations because of its blood preservation abilities, and its contraindications were few, including venous/arterial thrombosis and allergy.[3,7]

Such emerging haemostatic agents had a huge impact on controlling perioperative bleeding necessitating allogenic blood products transfusions. Predominantly, major instrumented spinal surgeries are associated with massive perioperative bleeding.[8-12] The need for transfusions of blood can lead to potential long-term morbidity and even mortality.[13,14] There is an economic burden associated with perioperative blood loss, in terms of direct costs of the blood products salvage technology and indirectly due to extended patient hospitalization.[15]

Constant efforts have been aimed at achieving healthier perioperative blood preservation. Prophylactic intravenous administration of antifibrinolytic agents is a principal method that can be used either before or during major surgery. Currently, intravenous administration of the low-cost but vastly efficient lysine analogue tranexamic acid diminishes perioperative hemorrhage and the demand for blood transfusions by one-third in major surgery, including extensive instrumented spinal surgery.[16-22]

This study was conducted to investigate whether tranexamic acid can diminish perioperative blood loss in our set-up. Taking into consideration all previously reported data, we introduced this agent in action with tremendous precautions, registering all available data. Results were in line and comparable with all studies reported. This might be subject to bias, as we introduced the tranexamic acid bases on previous studies and reports. Furthermore, we followed the guidelines strictly. However, during tranexamic acid usage, many questions were not addressed and remained unanswered, such as when to start intravenous administration (e.g., 24 h preoperatively, on induction, during surgery, or just after), the optimal dose, and the route of administration.

Unfortunately, these challenges remain.[8] Finally, this was a small-size retrospective analysis; although large studies might reveal different results, our results indicate that tranexamic acid is a drug of great value to reduce almost most kinds of bleeding. The efficacious concomitant factors controlling perioperative bleeding are well-established.

Future studies with larger sample sizes and further evaluating the concomitant parameters will have higher precision and stronger conclusions in terms of timing, safety, related complications, patient quality of life, impact on the cost, dosage, and route of administration. Also, this might help in the development of further treatment strategies.

Conclusion

In synopsis, perioperative bleeding is deemed one of the most important threats for patients needing extensive surgeries mandating blood transfusion. Tranexamic acid is proved as a drug of excellent benefit in controlling perioperative bleeding; it is cheap and convenient to use and has few contraindications.

Among parameters, the cost-effective and applicability are important for broadening the indications for any treatment. Future studies are now needed to address the remaining unanswered questions.

Informed consent

Patient's informed consent was waived as this is a retrospective study.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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