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Compared to Conventional Dressing Techniques, Tranexamic Acid Injection Provide Better Surgical Outcomes in Spinal Fusion Surgery

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The use of mechanical and chemical hemostatic control techniques in spinal fusion surgery is common in Indonesia. However, there has been no study comparing the two in a single clinical trials. This study aims to find out which best of tranexamic acid injection, a bulky compression dressing and a standard dressing in providing surgical outcomes in spinal fusion surgery. Thirty patients were grouped into three, 10 patients each. To Group 1, tranexamic acid at a dose of 500 mg/ml was administered pre operation and 2 hours later. For Group 2, a bulky compression dressing was performed by covering the surgical wounds with a low-adherent dressing, overlaid with four layers of sterile gauze and then sealed with a conformable adhesive retention tape. Standard dressing was applied to the patients of Group-3 using the same type of bandage and adhesive tape given to the Group-2, but only overlaid with two layers of sterile gauze. There is no statistical difference among trials groups for preoperative ($P > 0.220$) and postoperative ($P > 0.380$) hemoglobin levels and the level of perioperative blood loss ($P > 0.110$). With respect to number of transfusion required, the tranexamic acid group was significantly lower compared to the standard dressing group ($P = 0.018$). No abnormality of wound seen in all three trials groups and only 2 patients of bulky compression dressing group reported experience of headache. In conclusion, tranexamic acid is better to promote hemostasis compared to conventional dressing techniques.

Keywords: Spine surgery, surgical outcomes, tranexamic acid, compression dressing.

Substantial blood loss in orthopedic surgery, not only has clinical but also financial implications for patients, because of a higher incidence of morbidity as well as a longer time of hospitalization. That is why safe and effective measures to reduce blood loss in spinal fusion surgery is indispensable [Huang and Ou, 2015). In Indonesia, surgeons make hard effort to minimize blood loss in any type of surgery, in order to avoid allogeneic blood transfusion. In this country blood transfusion faces not only a low level of blood safety, but also a limited blood availability [WHO, 2017]. As indicated, in countries with a low human development indexes (HDIs), typical for developing countries, the risks of allogeneic blood transfusions are including viral, bacterial and parasitic infections [Marcucci *et al*., 2004].

Apart from these challenges orthopedic spine surgeons in Indonesia have adopted a variety of recommended methods for surgical bleeding management including mechanical and chemical hemostatic control techniques [Jahja, 2017].

However, so far there has been no study comparing surgical outcomes between the use of mechanical and chemical hemostatic control techniques in a single clinical experiment. Such a comparison is necessary due to no any bleeding control technique that is free from limitations affecting the success of the procedure and patient outcomes.

Tranexamic acid (TXA) injection is recognized as highly effective in reducing the needs for blood transfusion in spine surgery [Sethna *et al*., 2005; Zhang *et al*., 2014; Sadaqa, 2016). However, this antifibrinolytic agent is potential to cause some complications such as thromboembolic phenomena, seizures, headache, back pain, nasal disorders and gastrointestinal disorders [Reed and Woolley, 2015; Tranexamic Acid Injection]. On the other hand, mechanical control of hemostasis is also not fully effective in reducing postoperative complications. Hemostatic control using compression dressing, for example, is known to increase incidence of hematoma, blister, nausea and other types of discomfort such as itchiness and irritation (Botti *et al*., 1998; Bunick and Aasi, 2011; Dobbelaere *et al*., 2015).

This study is an attempt to find the most effective and safest technique for bleeding control with the best outcomes clinically and financially. Three hemostatic control measures, i.e. tranexamic acid (TXA) injection, a bulky compression dressing and a standard dressing, were performed to compare their impact on surgical outcomes.

METHODS

Research subjects

Research subjects were all patients underwent spinal fussion surgery in four hospitlas namely Academic Hospital of Gajah Mada University (RS UGM), Hidayatullah Islamic Hospital of Yogyakarta, Yogyakarta Islamic Hospital PDHI, and Soeharso Hospital of Solo, between May 2016 and June 2017. The inclusion criteria of the subjects were: patients with a maximally two-level spinal fusion in the case of degenerative spine condition, spinal instability, canal stenosis and willing to signed informed consent. The informed consent was approved by Ethics Committee for Medical and Health Research the Faculty of Medicine, University of Lampung, Indonesia (Appointed by Decree No: 155/UN26/8/KP/2014). Patients with blood clotting disorders, tranexamic acid (TXA) allergy, heart disorders, kidney disorders, history of thromboembolism and prolonged blood clotting were excluded.

Study design

Thirty patients fulfilled inclusion criteria were grouped into three, according to the types of hemostatic control technique applied, 10 patient's each. Group 1 is a group of patients whose bleeding control is done by injecting tranexamic acid. Group 2 is the patients whose surgical hemorrhage is controled by using a bulky compression dressing. Group 3 is the research subjects underwent hemostatic control using a standard dressing.

Hemostatic control measures

TXA were given intravenously to the patients of Group-1 with a loading dose of 500 mg/ml pre operation and 2 hours later by assuming the operation will take 4 or 5 hours. Bulky compression dressing was performed on patients of Group-2 by covering the surgical wounds with a low-adherent dressing made of open weave cotton gauze impregnated with soft paraffin, with a size of 10 x 10 cm (from Cuticell classic® BSN, Ref. No.72538-02), overlaid with four layers of sterile gauze and then sealed with a conformable adhesive retention tape, 15 cm x 10 m, (from Hypafix BSN®). Standard dressing was applied to the patients of group-3 using the same type of gauze given to the Group-2 (Cuticell classic® BSN, Ref. No.72538-02), but only overlaid with two layers of sterile gauze, which then also sealed with Hypafix dressing retention tape.

Surgical outcomes measurement

Surgical outcomes measured in this study were: pre- and postoperative hemoglobin, intra- and postoperative blood loss, intra- and postoperative blood transfusion and postoperative complication. Intraopterative blood loss were estimated based on the amount of blood soaked by surgical sponges and blood volume in the suction drain. Postoperative blood loss were calculated by measuring blood volume within drainage bags in the first 72 h. The needs of blood transfusion were quantified based on the total number of blood bags transfused during intra- and postoperative. The surgical complication noted in the study included all possible discomforts experienced by the patients and all observed abnormalities of the surgical wounds.

Statistical analysis

Descriptive statistics were applied to describe demographic characteristics of the subjects and possible postoperative complications. For quantitative parameters, the one-way analysis of variance (ANOVA) was used to determine variance among groups followed by Fisher's Least Significant Difference (LSD) to test the difference of mean values between groups.

RESULTS

Demographic characteristics of the research participants (N=30) are shown in Table 1. All subjects belong to Mongoloid race, aged between 48 – 71 years, height ranged 152 – 170 cm, and weighing between 59 – 85 kg.

Table 2 shows surgical outcomes for patients underwent three different hemostasis control measures applied in the study. Based on the one-way ANOVA analysis, there is no statistical difference among trials groups for preoperative ($P > 0.220$) and postoperative ($P > 0.380$) hemoglobin levels and the level of perioperative blood loss ($P > 0.110$). However, with respect to the number of transfusions, the *P*-value obtained is 0.056. Because it is only slightly above the limit of significance, the post hoc test (LSD test) has been

Table 1. Pre trials demographic characteristics of study subjects

Characteristics		Values		
		Tranexamic Acid	Bulky Compression Dressing	Standard Dressing
Patients	N	10	10	10
Sex	Male	8	3	6
	Female	2	7	4
Race (%)	Mongoloid	100	100	100
	Others	0	0	0
Age (years)	Min	48	53	48
	Max	71	70	66
	Mean	61.3	60.9	57.4
	SE	2.48	1.7	2.03
Height (cm)	Min	155	152	153
	Max	165	169	170
	Mean	159.6	157.8	160.5
	SE	1	1.6	1.8
Weight (kg)	Min	64	60	59
	Max	82	82	85
	Mean	71.4	70.4	74.9
	SE	2	2.2	3.1

Table 2. Surgical outcomes by type of hemostasis control measures

Variables	Outcomes (mean ± SE)			*P value*
	Tranexamic Acid	Bulky Compression Dressing	Standard Dressing	
Pre Operative Hb (g/dl)	12,6 ± 0,31	13,07 ± 0,26	12,28 ± 0,37	0,225
Post Operative Hb (g/dl)	9,08 ± 0,47	9,01 ± 0,21	8,47 ± 0,26	0,383
Blood Loss (ml)	495 ± 60,30	475 ± 30,05	605 ± 40,45	0,112
Transfusion (n)	1 ± 0,26	1,3 ± 0,21	1,8 ± 0,20	0,056*

*Although *P value* of ANOVA is slightly above the significance threshold, post hoc test (LSD) has been attempted with the results shown in Table 3

performed. The LSD test results for the transfusion number variables are presented in Table 3.

The results of observations made for possible postoperative complications in patients are summarized in Table 4. No abnormality of wound seen in all three trials groups and only 2 patients of pressed dressing group reported experience of headache.

DISCUSSION

The demographic characteristics of patients presented in Table 1 show that the study subjects consisted of mixed sex with an unequal number between men and women. This is because of the difficulty of the researcher in getting participants from the same gender who meet the inclusion criteria of the study. Despite the limited number of samples, this study is still carried out, because in orthopedic surgery the amount of blood loss in male and female is generally comparable (Gombotz *et al*., 2016). In scoliosis surgery there was also report suggesting that the need for red blood cell transfusion is not associated to the sex. (Cristante *et al*., 2009).

The findings of this study indicate that the difference of hemostasis control techniques have no significant clinical effect on the postoperative hemoglobin (Hb) levels as well as the amount of perioperative blood loss. Hb levels and blood loss in principle are interrelated with each other. If a surgical measures causes greater blood and body fluid requirements, it is generally accompanied by a signficant decrease in postoperative Hb levels. Because the amount of blood loss between experimental groups is relatively the same, it is natural that Hb levels are not different between groups (Grant *et al*., 2014).

Bulky compression dressings and standard dressings also do not give a different effect on hemoglobin levels and blood loss. This may be due to no difference in pressure forces arisen by the retention tape on the surface of the surgical wound in the two groups even though the layers number of the sterile gauze is different. As has been described in methodology section, the type and size of the Hypafix retention tape used in both groups were the same. Another factor that allegedly causing no surgical outcomes difference in the three groups was because the length of surgery in the

Table 3. Results of LSD test against the mean number of transfusion between groups

(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Tranexamic	Standard Dressing	-0.8	0.319	.018*	-1.45	-0.15
	Bulky Pressed Dressing	-0.3	0.319	0.355	-0.95	0.35
Bulky Compression Dressing	Tranexamic	0.3	0.319	0.355	-0.35	0.95
	Standard Dressing	-0.5	0.319	0.128	-1.15	0.15
Standard Dressing	Tranexamic	0.8	0.319	.018*	0.15	1.45
	Bulky Pressed Dressing	0.5	0.319	0.128	-0.15	1.15

*Sig. value less than 0.05 *(P*<0.05)

Table 4. Surgical complication by type of hemostasis control measures

Type of Complications	Tranexamic Acid	Bulky Compression Dressing	Standard Dressing
None	10	8	10
Discomfortness	0	2*	0
Abnormalities of wound	0	0	0
Total	10	10	10

*Patients experience a headache

three groups in this study did not exceed 6 hours. As has been reported that the duration of surgical measures affects surgical outcomes, such as a high risk of postoperative infection (Veeravagu *et al*., 2009).

While the Anova *P value* for postoperative Hb levels and perioperative blood loss actually exceeded 0.05, the *P value* for the number of transfusions was 0.056. Driven by curiosity, we conducted a post hoc test on the average number of transfusions between experimental groups. As presented in Table 3, it is quite surprising that apparently the number of transfusions for the TXA group was significantly lower compared to the standard dressing group ($P = 0.018$). Considering the number of transfusions in the TXA group was also lower when compared to the bulky compresion dressing group, it is worthy to infer that chemical hemostasis control using TXA is much better. In this study the preoperative dose of TXA given is 500 mg/ml and followed by the same dosage two hours later. This measures make the TXA loaded is relatively high. As has been revealed, hemostatic effect of tranexamic is doses-related. For patients with idiopathic scoliosis a higher dose of TXA (20 mg/kg) resulted in a 50% reduction of transfusion requirements compared with those of lower dose (10 mg/kg). (Tse *et al*., 2011).

Table 4 descriptively showed postoperative complication experienced by patients of bulky compression dressing group. Unfortunately, there has no literature provide a plausible explanation for the relationship between the incidence of postoperative headaches and the surgical wound dressing applied. Very likely, the incidence of postoperative headaches is related to the anesthetic and surgical measures. As indicated by Solis and Dorian (2012) that in orthopedic surgery anesthetic techniques are very influential on the incidence of postoperative headaches.

CONCLUSION

The absence of postoperative complications in patients of tranexamic acid group in addition to the lowest transfusion requirements reinforces the belief that tranexamic acid is better to promote hemostasis compared to the mechanical techniques.

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