

The Effect of Intravenous Tranexamic Acid on Blood Loss in Lumbar Hernial Disc Resection under Inhalation and Total Intravenous Anesthesia

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Abstract

Background: Tranexamic acid is a synthetic antifibrinolytic drug that reduces bleeding and transfusion requirements in cardiac surgery and total knee arthroplasty.

In this study, we evaluated the efficacy of the prophylactic tranexamic acid on intraoperative bleeding in patients undergoing lumbar hernial discs resection.

Methods: Eighty patients in ASA class I and II were randomized into 4 groups. In group 1, anesthesia was achieved by total intravenous anaesthesia and also the administration of tranexamic acid. The other groups were group 2, anesthetized by total intravenous anaesthesia without tranexamic acid; group 3, anesthetized by halothane and the administration of tranexamic acid and group 4, anesthetized by halothane without tranexamic acid. Blood loss and surgeon's satisfaction were registered.

Results: The amount of blood loss in group 1 was 267.1±177.3 ml; in group 2: 656±411.6 ml; in group 3: 357±307.2 ml and in group 4: 550±406.7 ml. The least bleeding was recorded in group 1 which had a significant difference with groups 2 and 4 for which tranexamic acid was not administered. Blood loss in groups 2 and 4 was more or less similar with no significant difference. The surgeon's highest satisfaction was with group 1. No complications were recorded in the 4 groups.

Conclusion: We concluded that administration of prophylactic tranexamic acid in patients undergoing hernial disc resection has the potential to reduce intraoperative bleeding and improving visualization of the surgical field especially when administered with total intravenous anesthesia.

Keywords: Tranexamic acid; Halothane; Total intravenous anesthesia; Propofol; Hernial disc resection

Introduction

Reduction of bleeding during operation has been one of the anesthesiologist's concerns for a long time. In major surgeries like cardiac surgery, transfusion of blood and blood products is inevitable in many cases. In other surgeries, bleeding leads to disturbed vision of the surgical field. So reduction of bleeding is favorable due to the decreased blood transfusion and its complications and the surgeon's improved vision.

Techniques commonly used to minimize bleeding are as follows:

A) Controlled hypotension which is well tolerated in healthy subjects but it has some disadvantages including long postanesthetic recovery for halothane, cyanide toxicity for nitroprusside, or the possibility of myocardial depression for esmolol.¹ B) Total intravenous anesthesia (TIVA) which is still controversial. For example, Chillemi et al.² reported no beneficial effects of remifentanyl and TIVA on the reduction of bleeding in hernial disc resection surgery, while in some studies,^{3,4,5} the use of TIVA techniques led to reduced blood loss in endoscopic sinus surgery. C) Use of antifibrinolytic drugs has also been reported as a means of reducing bleeding during operation. Wong

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et al.,⁶ Neilipovitz et al.,⁷ and Shapiro et al.⁸ showed that tranexamic acid (TXA) reduces intraoperative blood loss and transfusion in major spinal surgeries. TXA is a synthetic antifibrinolytic drug that competitively blocks the lysine-binding sites of plasminogen of plasmin and leads to blood clot degradation.⁹ Prophylactic TXA reduces blood loss and transfusion requirements after cardiac surgery.¹⁰⁻¹² Hippala et al.¹³ and Veien et al.¹⁴ have demonstrated similar benefits with TXA use in patients undergoing total knee arthroplasty.

Hernial disc resection which is a common neurosurgical procedure is associated with profound bleeding because of prone position and hyperemia of the spinal region. Bleeding in this region not only leads to disturbed surgeon's visual field but also may necessitate blood transfusion.

The aim of this study was to evaluate the effects of TXA and also of two different methods of anesthesia (inhalation and TIVA) on bleeding in patients undergoing hernial disc resection.

Materials and Methods

Eighty consecutive patients scheduled for lumbar hernial disc resection in Ghaem Hospital affiliated to Mashad University of Medical Sciences were enrolled. Medical Faculty Ethics Committee approval and informed written consent from all patients were obtained. All patients were in ASA class I and II. The exclusion criteria were a history of bleeding disorder, chronic renal insufficiency (serum creatinine > 2 mg/dL), perioperative anemia (Hb < 10 gr/dL), and warfarin medication. All patients were asked to stop taking NSAIDs one week before operation. The patients were randomly divided into four groups according to the method of anesthesia (halothane inhalation or TIVA) and administration of TXA or not. The envelope method with random numbers was used. These groups were as follows:

Group TIVA and TXA: In this group, anesthesia was induced by propofol (2 mg/kg), alfentanil (20 µg/kg) and atracurium (0.5 mg/kg) and maintained by propofol (80-120 µg/kg/min), alfentanil (0.3-0.4 µg/kg/min) plus a mixture of N₂O and O₂ to preserve blood pressure and heart rate in a constant range. The patients in this group were slowly given 15 mg/kg of TXA intravenously, 20-30 minutes before skin incision and then continued for 0.1 mg/kg/min during the operation. **Group TIVA:** Induction and maintenance of anesthesia was similar to the first group but TXA

was not administered. **Group Hal+ TXA:** In this group, anesthesia was induced by propofol (2 mg/kg), alfentanil (20 µg/kg) and atracurium (0.5 mg/kg) and maintained by halothane (0.6-0.8%) plus mixture of N₂O and O₂. TXA was administered identical to TIVA+TXA group. **Group Hal:** Induction and maintenance of anesthesia was similar to Hal+TXA group but TXA was not administered.

Controlled ventilation was applied on all patients as V_t=12 ml/kg, Rate=12, I:E=1:2, PEEP=0. The patients were situated in prone position after induction of anesthesia and intubation. Two roles were located on two sides of the thorax, in such a way that the patients' ventilation was accomplished easily. Routine monitoring including temperature, ECG, pulse oximetry and non-invasive blood pressure measurement were applied on all patients. Perioperative transfused fluid volume was lactated ringer's solution in both groups, 500 ml as compensatory volume expansion, followed by 5 ml/kg/h as basic needs and 5 mL/kg as third space loss. Substitution for intraoperative blood loss was 3 times the amount of bleeding in both groups. No routine investigations for deep venous thrombosis or pulmonary embolism were done, but clinical signs of thromboembolic complications were investigated. Intraoperative blood loss was measured by weighing sponges and the amount of suction drainage. All the operations were performed by one surgeon who was blind to the patients. The surgeon was asked to rate the operative condition in regard to bleeding on a visual analog scale score, with anchors of 0 (negligible bleeding and high surgeon's satisfaction) and 10 (massive bleeding and poor surgeon's satisfaction). We rated the operative condition as excellent when VAS ≤ 2, good when VAS = 3, 4, 5, intermediate when VAS = 6, 7, 8 and bad when VAS = 9, 10. The patients' characteristics and intraoperative variables including the amount of blood loss, duration of the surgery, hemodynamic changes, the time of awareness, duration of recovery period were collected in a questionnaire. Statistical analysis of the data was performed with SPSS version 11.5. Comparison between groups was performed with ANOVA, student t and the Mann-Whitney tests. Chi-square test was used regarding gender and the *p* < 0.05 was chosen as the significant level.

Results

The patients' characteristics were shown in Table 1. There was no significant difference in relation to age,

Table 1: Demographic characteristics (Mean±SD)

Variable	Age (yr)	Sex (M/F)	BMI (kg/m ²)
	Mean±SD		Mean±SD
TIVA+TXA	40.4 ± 7.64	10/10	25.56 ± 2.53
TIVA	40.5 ± 12.48	9/11	25.67 ± 4.19
Hal+TXA	42.0 ± 17.31	8/12	22.79 ± 3.75
Hal	42.6 ± 10.42	9/12	26.09 ± 4.55

sex, and body mass index (BMI). The factors that might affect the amount of blood loss including duration of surgery, number of disc spaces and mean arterial pressure were identical in all groups (Table2). Our focus was on the amount of bleeding in each group (Table 3 and Figure1).

There was a significant difference between TIVA+TXA and TIVA groups regarding the amount of bleeding ($p=0.007$). There was also a significant difference between TIVA+TXA and Hal groups ($p=0.040$). However, there was no significant difference between TIVA+TXA and Hal+TXA groups ($p=0.280$), TIVA and Hal groups for which no TXA was used ($p=0.300$), Hal+TXA and Hal groups ($p=$

0.300), and TIVA and Hal+TXA groups ($p=0.052$).

The results of the surgeon's satisfaction were registered according to visual analog scale (VAS) score (Table 4). In this study, the highest rate of satisfaction was registered in TIVA+TXA group, which had a significant difference with the other groups ($p=0.037$).

As to awareness and recovery of the patients, the period between the end of the operation till extubation was 6.75 ± 2.5 minutes in TIVA group and 9.55 ± 2.34 minutes in halothane groups, showing a significant difference ($p=0.001$). The time of recovery stay was 5.6 ± 3.5 in TIVA group and 12.3 ± 2.9 in halothane groups ($p<0.0001$) (Table 5).

Table 2: Duration of surgery, number of disc spaces, mean arterial pressure and PR during operation

Variable	TXA+TIVA	TIVA	Hal+TXA	Halothane	Total	P value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Duration of surgery	53.9 ± 14.45	56.0 ± 15.23	48.6 ± 7.36	55.9 ± 11.14	53.6 ± 12.33	0.51
Number of disc spaces	1.2 ± 0.42	1.1 ± 0.31	1.1 ± 0.31	1.1 ± 0.31	1.12 ± 0.33	0.88
Mean arterial pressure	90.76 ± 15.81	85.23 ± 13.16	86.60 ± 11.58	99.89 ± 13.76	90.62 ± 14.35	0.09
Pulse rate	66.44 ± 15.02	71.67 ± 12.83	75.94 ± 16.85	73.87 ± 11.73	71.98 ± 14.15	0.49

Table 3: The amount of blood loss in each group

Variable	TXA +TIVA	TIVA	Hal+TXA	Halothane	Total	P value
	Mean± SD	Mean± SD	Mean± SD	Mean± SD	Mean± SD	
The amount of blood loss	267.1±177.3	656.0±411.6	357.0 ±307.2	550.5±406.7	457. ±6 375.5	0.027

Table 4: Surgeon's Satisfaction in each group

Group	TXA + TIVA		TIVA		Hal+TXA		Halothane		Total	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Incidence										
Surgeon's opinion										
Excellent	14	70.0	6	30.0	10	50.0	4	20.0	34	42.5
Good	6	30.0	4	20.0	6	30.0	6	30.0	22	27.5
Moderate	0	0.0	8	40.0	4	20.0	6	30.0	18	22.5
Poor	0	0.0	2	10.0	0	0.0	4	20.0	6	7.5

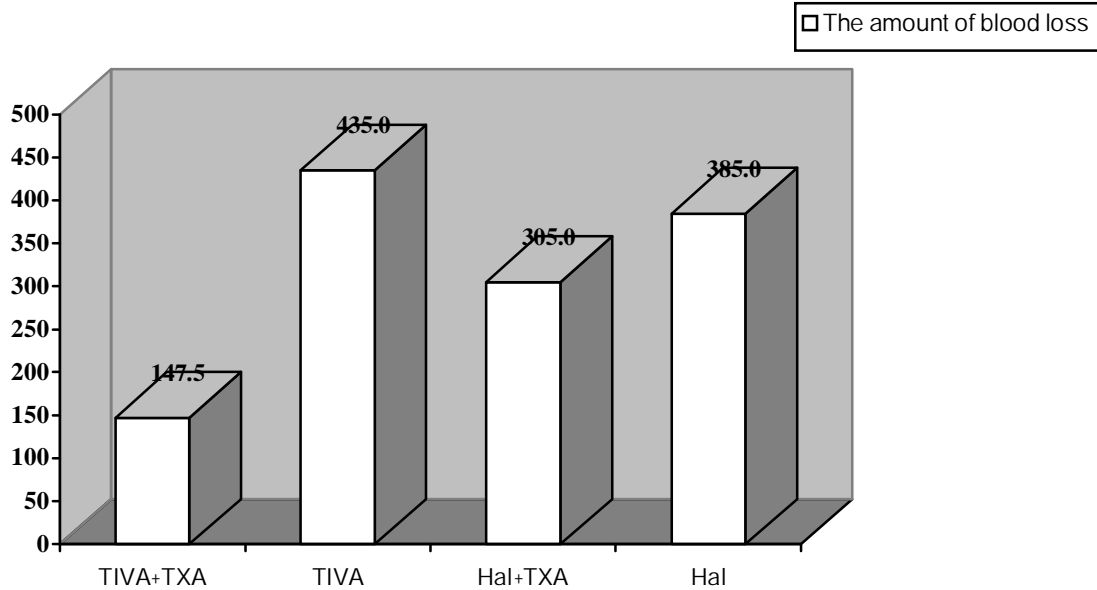


Figure 1: The amount of blood loss

Table 5: Extubation and recovery times in two groups of halothane or TIVA

Variable	TIVA	Halothane	P value
	Mean±SD	Mean±SD	
Time to extubation	6.75 ± 2.5	9.55 ± 2.39	0.001
Recovery stay (min)	5.6 ± 3.5	12.3 ± 2.9	0.001

The incidence of bucking, laryngospasm and complications in the recovery room were shown in Table 6 and there was no significant difference between TIVA and Halothane groups. No major thrombotic event and no evidence of deep vein thrombosis were recorded in either group.

Discussion

The beneficial effects of TXA on the reduction of bleeding in cardiac surgery and total knee arthroplasty and major spinal surgeries have been determined. In some studies, the effect of the method of

anesthesia on the amount of bleeding during operation has been proposed. For instance, one of the methods used for reduction of bleeding in endoscopic sinus surgery is TIVA.^{3,4}

In this study, we demonstrated that the method of anesthesia had no effect on the amount of bleeding during hernial disc resection, and there was no significant difference between the two methods of inhalation and TIVA. Our findings are in agreement with those of Chillemi et al.², indicating that adding TXA to TIVA causes significant reduction in bleeding in comparison with TIVA alone. The difference between TIVA+TXA and Hal groups was significant. Although adding TXA to halothane anesthesia causes

Table 6: Comparison of different complications in two groups of halothane or TIVA

Variable	TIVA		Halothane		P value
	No.	%	No.	%	
Bucking	10	25.0	6	15.0	0.19
Laryngospasm	1	2.5	1	2.5	1
Complications in recovery	3	7.5	8	20.0	0.07

reduction in bleeding in comparison with halothane alone, but the difference was not significant. Therefore, it seems that a combination of TIVA and TXA would have a synergistic effect on the reduction of bleeding in lumbar hernial disc resection which causes improved surgeon's visual field. Our study showed the beneficial effect of TXA in reducing bleeding in hernial disc resection.

Wong et al.,⁶ Neilipovitz et al.⁷ and Shapiro et al.⁸ also demonstrated that TXA reduced blood loss and blood transfusion in major spinal surgeries. The primary concern when administering an antifibrinolytic drug is the potential increased incidence of thromboembolic events. No patients in this study experienced any complications from the use of TXA, including deep vein thrombosis and pulmonary emboli. No investigations beyond physical examination and history taking like venography and ventilation-perfusion scan were indicated. However, in other studies such as Benoni et al.¹⁵ where venography and ventilation-perfusion lung scanning were performed, the incidence of positive findings on the venography was comparable between non-TXA and TXA groups. None of these had positive findings on the lung scanning. Benoni et al.¹⁵ suggested that TXA was not as-

sociated with thromboembolic events because the effects of TXA are more pronounced in operative wounds than in the peripheral venous blood, indicating that TXA does not induce a general prothrombotic state. In other studies in cardiac surgery, no thrombotic effect of TXA was reported, either.^{16,17}

Generally, it is concluded that although the beneficial effect of TXA on reducing blood transfusion has been approved in cardiac surgery and major spinal surgeries, it can be used in surgeries with less tissue trauma like hernial disc resection. In addition to the reduction effect on bleeding and blood consumption, it leads to a better surgeon's visual field and surgical condition. To investigate the beneficial effect of TXA in minor surgeries and its complications, we recommend the use of TXA in a larger population of the patients.

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Conflict of interest: None declared.

References

- 1 Degoute CS, Ray MJ, Manchon M, Dubreuil C, Banssillon V. Remifentanyl and controlled hypotension; comparison with nitroprusside or esmolol during tympanoplasty. *Can J Anaesth* 2001;**48**:20-7. [11212044] [doi:10.1007/BF03019809]
- 2 Chillemi S, Sinardi D, Marino A, Mantarro G, Campisi R. The use of remifentanyl for bloodless surgical field during vertebral disc resection. *Minerva Anesthesiol* 2002;**68**:645-9. [12370680]
- 3 Blackwell KE, Ross DA, Kapur P, Calcaterra TC. Propofol for maintenance of general anesthesia: a technique to limit blood loss during endoscopic sinus surgery. *Am J Otolaryngol* 1993;**14**:262-6. [8214320] [doi:10.1016/0196-0709(93)90072-F]
- 4 Sivaci R, Yilmaz MD, Balci C, Erinciler T, Unlu H. Comparison of propofol and sevoflurane anesthesia by means of blood loss during endoscopic sinus surgery. *Saudi Med J* 2004;**25**:1995-8. [15711683]
- 5 Pavlin JD, Colley PS, Weymuller EA Jr, Van Norman G, Gunn HC, Kerschgen ME. Propofol versus isoflurane for endoscopic sinus surgery. *Am J Otolaryngol* 1999;**20**:96-101. [10203159] [doi:10.1016/S0196-0709(99)90018-2]
- 6 Wong J, El Beheiry H, Rampersaud YR, Lewis S, Ahn H, De Silva Y, Abrishami A, Baig N, McBroom RJ, Chung F. Tranexamic acid reduces perioperative blood loss in adult patients having spinal fusion surgery. *Anesth Analg* 2008;**107**:1479-86. [18931202] [doi:10.1213/ane.0b013e3181831e44]
- 7 Neilipovitz DT, Murto K, Hall L, Barrowman NJ, Splinter WM. A randomized trial of tranexamic acid to reduce blood transfusion for scoliosis surgery. *Anesth Analg* 2001;**93**:82-7. [11429344] [doi:10.1097/0000539-200107000-00018]
- 8 Shapiro F, Zurakowski D, Sethna NF. Tranexamic acid diminishes intraoperative blood loss and transfusion in spinal fusions for duchenne muscular dystrophy scoliosis. *Spine* 2007;**32**:2278-83. [17873823] [doi:10.1097/BRS.0b013e31814cf139]
- 9 Hardy JF, Desroches J. Natural and synthetic antifibrinolytics in cardiac surgery. *Can J Anesth* 1992;**39**:353-65. [1373346] [doi:10.1007/BF03009046]
- 10 Zabeeda D, Medalion B, Sverdlow , Ezar S, Schachner A, Ezri T, Cohen AJ. Tranexamic acid reduces bleeding and the need for blood transfusion in primary myocardial revascularization. *Ann Thorac Surg* 2002;**74**:733-8. [12238832] [doi:10.1016/S0003-4975(02)03784-0]
- 11 Reid RW, Zimmerman AA, Laussen PC, Mayer JE, Gorlin JB, Burrows FA. The efficacy of tranexamic acid versus placebo in decreasing blood loss in pediatric patients undergoing repeat cardiac surgery. *Anesth Analg* 1997;**84**:990-6. [9141920] [doi:10.1097/0000539-199705000-00008]
- 12 Fremes SE, Wong BI, Lee E, Mai R, Christakis GT, McLean RF, Goldman BS, Naylor CD. Metaanalysis of prophylactic drug treatment in prevention of postoperative bleeding. *Ann Thorac Surg* 1994;**58**:1580-8. [7526811]
- 13 Hiiipala ST, Strid LJ, Wennestrand MI, Arvela JVV, Niemelä H, Mantylas K, Kuismar P, Ylinen JE. Tranexamic acid radically decreases

- blood loss and transfusion associated with total knee arthroplasty. *Anesth Analg* 1997;**84**:839-44. [9085968] [doi:10.1097/00000539-199704000-00026]
- 14 Veien M, Sørensen JV, Madsen F, Juelsgaard P. Tranexamic acid given intraoperatively reduces blood loss after total knee replacement: a randomized controlled study. *Acta Anaesthesiol Scand* 2002;**46**:1206-11. [12421192] [doi:10.1034/j.1399-6576.2002.461007.x]
- 15 Benoni G, Fredin H. Fibrinolytic inhibition with tranexamic acid reduces blood loss and blood transfusion after knee arthroplasty: a prospective, randomised, double-blind study of 86 patients. *J Bone Joint Surg Br* 1996;**78**:434-40. [8636182]
- 16 Ruel MA, Wang F, Bourke ME, Dupuis JY, Robblee JA, Keon WJ, Rubens FD. Is tranexamic acid safe in patients undergoing coronary endarterectomy? *Ann Thorac Surg* 2001;**71**:1508-11. [11383791] [doi:10.1016/S0003-4975(01)02459-6]
- 17 Vanek T, Jares M, Fajt R, Straka Z, Jirasek K, Kolesar M, Brucek P, Maly M. Fibrinolytic inhibitors in off-pump coronary surgery: a prospective, randomized, double-blind TAP study (tranexamic acid, aprotinin, placebo). *Eur J Cardiothorac Surg* 2005;**28**:563-8. [16125959] [doi:10.1016/j.ejcts.2005.06.027]