WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 3, 44-57. Research Article ISSN 2277– 7105

COMPARISON OF INTRAOPERATIVE BLOOD LOSS DURING SPINAL SURGERY USING EITHER ISOFLURANE, SEVOFLURANE AND COMBINATION PROPOFOL + REMIFENTANIL AS AN ADJUVANT TO GENERAL ANESTHESIA

Amir Salari[1], Farahzad Jannatmakan[1], Kaveh Behaeen[1]*, Ahmadreza Mohtadi[1], Homa Hamdan[2]

[1]Assistant Professor of Anesthesia, Department of Anesthesiology, Pain Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

[2]Anesthesiology Assistant, Department of Anesthesiology, Pain Research Center Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Article Received on
25 Dec. 2016,

Revised on 15 Jan. 2017,
Accepted on 05 Feb. 2017

DOI: 10.20959/wjpr20173-7863

***Corresponding Author**
Dr. Kaveh Behaeen
Assistant Professor of Anesthesia, Department of Anesthesiology, Pain Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz Iran.

ABSTRACT

Background: Decrease of bleeding is of significant importance in keeping the patient's hemodynamic stabilized, and also in creating a blood-free field with a good vision for the surgeon. The purpose of this study was to compare between the three Isoflurane, Sevoflurane and Propofol+ Remifentanil drugs in terms of hemodynamic status and also bleeding in controlled hypotension, during lumbar spine surgery.

Methods: This study was conducted as a randomized clinical trial among 90 patients undergone elective spinal surgery. The patients were randomly allocated into three groups. Group I: Patients received continuous infusion at a rate of 100-200 µg/kg/min propofol with 0.1 µg/kg/min Remifentanil. Group II: Patients received concentration of isoflurane between 1 to 2%. Group III: Patients received concentration of sevoflurane between 1 to 2%. The amount of hemorrhage, hemodynamic changes and Surgeon's Satisfaction were measured and recorded. **Results:** There was statistically significant decrease of the bleeding in both propofol and sevoflurane groups as compared to isoflurane group(360.83 ml, 302.50 ml and 690.00 ml respectively) ($p<0.001$). There was no significant difference seen in the heart rate in three groups except the last time. The surgeon had 23.3% and 20.0% complete satisfaction of the patients in Sevoflurane and Propofol groups but the Surgeon was not satisfied with surgical field in none

of the patients in Isoflurane group. **Conclusion:** The results show that, making use of Sevoflurane during spine surgery results in the least amount of hemorrhage, and non-occurrence of acute drop in hematocrit; and generally an appropriate hemodynamic stability is created without prescription of assisting drug, in comparison to application of Isoflurane, and Propofol+Remifentanil.

KEYWORDS: Isoflurane, Propofol+Remifentanil, Sevoflurane, bleeding.

INTRODUCTION

Spine surgeries are mostly associated with severe bleeding. Sometimes, transfusion of blood products is required due to the severity of the bleeding.[1] Decrease of bleeding is of significant importance in keeping the patient's hemodynamic stabilized and also in creating a blood-free field with a good vision for the surgeon. The bleeding is particularly sensitive in spine surgeries, because of proximity to important neural structures which are highly fragile. Surgeon's comfort results in short operation time which in turn reduces level of bleeding.[2] Decrease being made in bleeding is associated with reduction of prescription of blood product which in turn leads to reduction of related complications such as hemolytic and non-hemolytic reactions, acute lung injury, transfer of viral and bacterial infections, hypothermia, coagulation disorders, etc.[3]

Methods of saving blood products could be divided into two general groups, according to their target mechanism. These methods hemodynamically (through controlled hypotension, local vasoconstrictors and epidural block), or chemically/ biologically (such as Desmopressine, Aprotinin, Trans amine, Aminocaproic acid, estrogens, Bone wax, hemostatic sponges and Fibrin glue) make decrease in bleeding; or they may result in reduction of the need to homologous transfusion such as acute hemodilution, autologous transfusion, cell saver and erythropoietin.[4-6]

Controlled hypotension has been used successfully in orthopedic and endoscopic surgeries.[7-8] This method is widely applied and various studies.[9-12] have shown it to be helpful, in spine surgeries. Those drugs individually used for induction of controlled hypotension include inhaled anesthetics, Propofol, Sodium nitroprusside, Nitroglycerin and Beta-blockers (Propranolol, Esmolol). Nowadays, the preferred method is a combination of Remifentanil and Propofol, or an inhaled anesthetic (Isoflurane, Desflurane, or Sevoflurane).[13-16]

Ideal drug for blood pressure reduction has to be easily applicable and bear predictable level of response; quick start and ending time of medication with no toxic intermediates.[17] It seems that, inhaled anesthetics featuring vasodilatation are considered as appropriate drugs for controlled hypotension.[18] Moreover, it has been shown that these drugs have protective effects on brain and heart.[19] From among these drugs, Isoflurane with suitable vasodilation characteristic and poor effect on myocardial activity of the heart appropriately maintains cardiac markers during hypotension at the time of operation.[20] Sevoflurane is also one of relatively new inhaled anesthetics which in many ways resembles other inhaled anesthetics such as isoflurane[21]; however, there are some differences between the two: increase of heart rate is less observed during anesthesia with sevoflurane.[22] Various studies have proved the effect of these two drugs on controlled hypotension in different surgeries.[21,23-24] however, up to this moment there have been few studies to compare Isoflurane, Sevoflurane, and Propofol+ Remifentanil, in lumbar spine surgeries. Therefore, this research has been performed to the aim of comparison between the three Isoflurane, Sevoflurane and Propofol+ Remifentanil drugs in terms of hemodynamic status and also bleeding in controlled hypotension, during lumbar spine surgery.

Method

After confirmation by ethics committee in Ahvaz Jundishapour University of Medical Science, 90 patients selected for spine surgery. Before operations, the patients knowingly provided us with letter of consent. Their names were filled in a list previously prepared upon random blocking, according to their order of entrance to the operating room. The list contained: name, family name, and file number; and A, B, C codes were replaced the drug they were consuming. The inclusion criteria were: spine surgery to the aim of laminectomy; spine surgery to the aim of fixation of the fracture; patients being between 18 to 65 years old; and ASA≤ II. Criteria for exclusion from the research were: patient's lack of consent; bei allergic to Propofol, soya, egg, Isoflurane; record of malignant hyperthermia in the patient and his family; patients with record of coagulation complications or consumption of coagulation-related drugs; any record of diseases such as stroke, coronary artery diseases, hypertension, deep veins thrombosis, pulmonary embolism, and peripheral vascular diseases. Gender, age and weight of the patients were written down using their files; and their heart rate, systolic and diastolic pressure as basic values before induction of anesthesia were determined by arterial line previously improvised, and mentioned in the form also. The patients were randomly divided into three groups of receiving Propofol+Remifentanil,

Isoflurane, and Sevoflurane. At the beginning of anesthesia all of the patients were hyperventilate for 3 minutes, and then put under general anesthesia similarly through 2 µg/kg Fentanyl, 5 mg/kg thiopental, and 0.5 mg/kg Atracurium. Nitros Oxide 50% and Oxygen 50% were also prescribed during anesthesia, similarly for the patients in all three groups. In the group prescribed with Propofol, anesthesia was maintained through (100-200 µg/kg/min) dose of it and 0.1 µg/kg/min of remifentanil. In the group prescribed with Isuflurane, anesthesia was maintained through 1-2% dose, and in the group prescribed with Sevoflurane, anesthesia was maintained through 1-2% dose of MAC.

In order to determination the amount of hemorrhage to be examined, all blood volumes retained after the surgery from suction chamber, additional weight of bloody gauzes and level of blood in hemovac drain chamber were used. The patients' hematocrit was recorded both before and after operation, through dispatch of laboratory sample. Level of prescribed liquid during surgery and also level of diuresis of the patients were also recorded. Mean blood pressure and heart rate in seven different time intervals (before and after induction, after change of position, 30, 60 and 90 minutes after start of the operation, and at the end of operation) were measured and recorded.

Surgical field was scored using the scale that was originally described by Fromme et al. and then subsequently adapted by Boezaart et al.[25-26]

Grade 0 -No bleeding (cadaveric conditions)

Grade 1 -Slight bleeding - no suctioning required

Grade 2 -Slight bleeding - occasional suctioning required

Grade 3 -Slight bleeding -frequent suctioning required; bleeding threatens surgical field a few seconds after suction is removed

Grade 4 -Moderate bleeding -frequent suctioning required and bleeding threatens surgical field directly after suction is removed

Grade 5 -Severe bleeding -constant suctioning required; bleeding appears faster than can be removed by suction; surgical field severely threatened and surgery usually not possible.

The surgeon was asked about the condition with the expression of dissatisfaction, poor satisfaction, partial satisfaction and complete satisfaction. An expert not being aware of the type of prescribed drugs filled out the related form. The data analyses were obtained by using SPSS software. The quantitative variables were compared between two groups by t-test and changes were assessed using repeated measurement ANOVA; qualitative variables were

compared between two groups by chi-square test. Statistically P<0.05 was considered significant.

RESULTS

The results show that, in the three groups of Propofol, Isoflurane and Sevoflurane, the number of male and female patients were: (30%, 70%), (23.23%, 76.67%) and (40%, 60%), respectively. Chi-square test was applied for comparing two groups and a significant level of (p=0.37) was obtained. Again, in order for ASA class of the patients to be determined in all three groups, the same test was performed and there was no significant difference observable (P=0.19). To determine other demographic information such as age, weight, and height of the patients in all three groups, T-test was applied with no significant difference observed (P>0.05). None of the patients in Sevoflurane and Propofol groups were required nitroglycerin for control of blood pressure, whereas, nitroglycerin was required in 36.6% of the patients of the group prescribed with Isoflurane (P<0.001). In terms of anesthesia and operation time periods, it was significantly less in Sevoflurane group (P=0.01). During surgery, least level of liquid was used in Sevoflurane group, and a significant difference was seen in comparison to the other two groups. Of course, Isoflurane group received significantly higher level of liquid, compared to the Propofol group. The highest level of urine output during surgery was belonging to Isoflurane group, which was also significantly higher than the two other groups (P<0.001). During surgery, Sevoflurane group experienced lower amount of hemorrhage, with significant difference in comparison to the other groups. Those patients prescribed with Propofol had significantly lower amount of hemorrhage during surgery, compared to Isoflurane group (P<0.001).

In Table 2, examination of two levels of the surgeon's satisfaction regarding hemorrhage is illustrated. The Surgeon was not satisfied with surgical field in none of the patients in Isoflurane group; however his complete satisfaction was 23.3% and 20.0% of the patients in Sevoflurane and Propofol groups, respectively. Dissatisfaction of surgical field was recorded for 13.3% of isoflurane group; however the surgeon was not dissatisfied with any of the patients in Sevoflurane and Propofol groups. As far as hemorrhage is concerned, those patients receiving Sevoflurane and Propofol have not had severe or average blood loss; however, 16.7% of Isoflurane group had average blood loss, which was significantly different from the other two groups. Most patients in Isoflurane group (80%) frequently needed

suction; however more than half of the patients in Sevoflurane and Propofol groups occasionally were in need of surgical field suction.

The hematocrit changes in the patients of all three groups are shown in Figure 1; and it is statistically significant after surgery, the greatest decrease of hematocrit is seen in Isoflurane group.

Mean arterial pressure changes are compared in Figure 2, in three groups during surgery in seven times. There has been significant difference observed between groups during surgery: after induction, after change of position, 30 and 60 minutes after start of operation (P<0.05). Figure 3, shows heart rate changes in various time intervals; and in neither of them except for the latest time interval, there is a difference between the groups.

In Figure 3, there were no significant differences between the three groups as regards the heart rate at all times, except for the last time

Table 1. Demographic Data in two groups

Variable	Propofol (N=30)	Isoflurane (N=30)	Sevoflurane (N=30)	P.Value
Sex **Male** **Female**	 9 21	 7 23	 12 18	0.37
Age(Year)	45.93(5.64)	44.60(4.70)	43.10(9.55)	0.36
Weight(Kg)	84.06(5.51)	83.03(7.08)	81.96(6.35)	0.74
Height(cm)	167.43(10.99)	166.93(10.28)	169.73(11.84)	0.28
ASA Class **Class 1** **Class 2**	 15 15	 11 19	 18 12	0.19
Nitroglycerin **Yes** **No**	 0 30	 11*,∞ 19	 0 30	<0.001
Anesthesia Time(min)	184.00(34.09)	185.66(27.87)	147.62(34.04)†,∞	0.01
Surgery Time(min)	146.50(34.71)	144.16(32.27)	123.50(34.04)†,∞	0.01
Water Vol Added(ml)	3693.33(662.24)*	4233.33(504.00)	2550.00(711.36)†,∞	<0.001
Urine Output(ml)	688.33(227.68)*	918.66(194.86)	331.66(124.21)†,∞	<0.001
Bleeding Vol(ml)	360.83(182.14)*	690.00(301.97)	302.50(133.47)∞	<0.001

Values are expressed as mean (standard deviation).

* $p < 0.05$ propofol vs isoflurane

† $p < 0.05$ propofol vs sevoflurane∞ $p < 0.05$ isoflurane vs sevoflurane

Table 2 Comparison of surgeon's satisfaction and Surgical Field Bleeding in three groups.

Variable	Propofol (N=30)	Isoflurane (N=30)	Sevoflurane (N=30)	P.Value
Surgeon's Satisfaction No Satisfaction Poor Satisfaction Partial Satisfaction Complete Satisfaction	0(0%) 6(20.0%) 18(60.0%) 6(20.0%)	4(13.3%) 22(73.3%) 4(13.3%) 0(0%)	0(0%) 4(13.3%) 19(63.3%) 7(23.3%)	<0.001
Surgical Field Bleeding No bleeding No suctioning required Occasional suctioning required Frequent suctioning required Moderate bleeding Severe bleeding	0(0%) 0(0%) %)7.56(71 %)3.43(31 0(0%) 0(0%)	0(0%) 0(0%) 1(3.3%) 24(80.0%) 5(16.7%) 0(0%)	0(0%) 0(0%) 19(63.3%) 11(36.7%) 0(0%) 0(0%)	<0.001

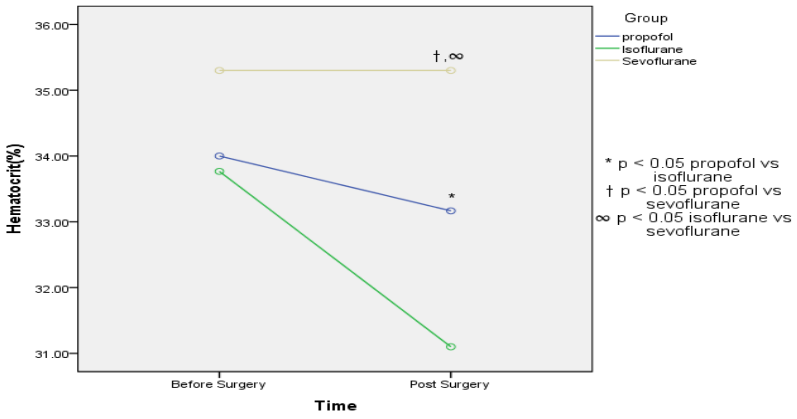

Figure 1. Hematocrit changes before and post surgery in three Groups

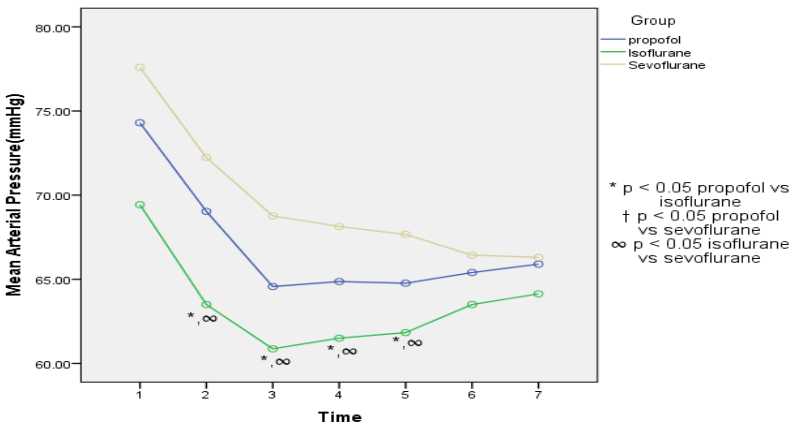

Figure 2. Mean Arterial Pressure changes at different times in three groups

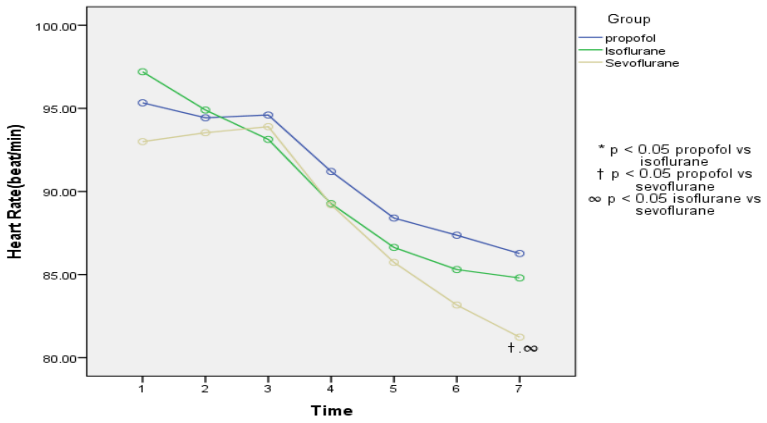

Figure 3. Heart Rate changes at different times in three groups

DISCUSSION

In the present study, the effect of Isoflurane, Sevoflurane and combination of Propofol+ Remifentanil on amount of hemorrhage (subsequent to hypotension induction) in lumbar spine surgery are compared. Data gathered have shown that, amount of hemorrhage in those patients receiving Sevoflurane and Propofol was significantly less than Isoflurane group. Also patients receiving Sevoflurane and Propofol had also less blood loss in surgical field. Milon′ski et al. have compared the effects of application of Sevoflurane and Propofol on hemorrhage during surgery and contrary to the results of present study, they have found that amount of hemorrhage in Propofol group is significantly less than Sevoflurane group.[27-28] They have attributed this to lower heart rate in the Sevoflurane group which has caused prolongation of diastolic time, resulting in increase of blood supply in blood vessels and consequently higher heart output. However, in present study except the last time, there has been no difference observed in heart rate of the patients, and applying nitroglycerin in 36.6% of Isoflurane group could be attributed to higher amount of hemorrhage during surgery in comparison to the Sevoflurane and also Propofol groups. It also seems that, vasodilatation resulted from nitroglycerin application has caused increase of bleeding of the patients in Isoflurane group.

In another study, Marzban et al. have shown that in comparison to Isoflurane, applying Propofol in combination with Remfentanil causes lower hemorrhage in surgical field, in a way that surgeons have been significantly more satisfied with the results in Propofol group. In our research also, surgeon has had complete satisfaction of surgical field in 20% of Propofol group; however in none of the patients in Isoflurane group complete satisfaction was achieved. The surgeons were dissatisfied with 13.3% of the patients in Isoflurane group

and the difference may be indicative of the direct influence of hemorrhage on surgeon's satisfaction from surgical field, in both Propofol and Isoflurane groups.[29]

Salama also has made use of Propofol and Isoflurane for induction of anesthesia and also making controlled hypotension in his research concerning those patients nominated for lumbar spine fixation. Similar to present study, lower amount of hemorrhage and higher satisfaction of the surgeon of surgical field has been achieved in Propofol group, compared to Isoflurane group. In Isoflurane group 45% of the patients were requiring blood transfusion, while in Propofol group only 10% have been delivered blood and the difference between the groups was significant. The difference may be indicative of better effects of Propofol on these patients.[30]

A number of studies have obtained different results, e.g. in Haghbin studies, there has been no significant difference in the amount of surgical bleeding through application of Propofol and Isoflurane, in those patients nominated for sinus endoscopic surgery.[31]

In another study by Ankichetty et al., 40 patients in the two groups of receiving Propofol and Isoflurane were examined for the time consumed for achieving desirable MAP, status of surgical field and amount of hemorrhage during surgery. The results were indicate that no difference between the two drugs. Lack of difference in amount of hemorrhage between groups under study by Ankichetty, could be attributed to significant and higher usage of Fentanil by Isoflurane groups, which has been capable of creating appropriate blood pressure during surgery, with no differentiation with Propofol group in terms of hemorrhage.[32]

In the present study also, hemodynamic status of the patients in all three groups was examined. Since in previous studies, ideal blood pressure during surgery of spine has been set as 60-70 mmHg, no additional drug such as nitroglycerin was required in any of Sevoflurane and Propofol groups; however, in more than one third of patients in Isoflurane group, this assisting drug was used in order for ideal blood pressure to be obtained. Samantaray et al. also made use of Sevoflurane and Propofol in two groups of patients nominated for spine surgery, to induce anesthesia and create controlled hypotension. They suggested that, application of both drugs has created ideal blood pressure during surgery with no difference in the two groups. Again, there has been no difference in terms of applying assisting drugs such as Thiopentone and Fentanil.[33]

In case of application of Propofol and Isoflurane, Haghbin et al. have reached different results compared to us: no difference being found in MAP during surgery, no relationship between MAP and depth of anesthesia, and no difference in terms of hemorrhage in the patients of both groups.[31] In a similar study, Yoo et al. have also found some results in disagreement to ours: no difference in terms of blood pressure and status of surgical field was seen in all the three groups under prescription with Propofol+Remifentanil, Isoflurane and Desflurane, which is also opposed to our results.[34]

Orhon et al. have also examined the effects of applying Propofol and Sevoflurane on hemodynamic and recovery status of patients during and after operation, using BIS (*technology to monitor depth of anesthesia*). Contrary to our study, they have found some differences in terms of blood pressure and heart rate of the two groups. In their study, they have referred to advantages of BIS monitoring to evaluate the effect of depth of anesthesia on the level of consumption of anesthetics. They believe that, patients could be monitored in similar conditions, through application of BIS. They also suggested that, depth of anesthesia affects cardio-vascular parameters. It is possible that in the present study in contradiction to their use of Remifentanil in infusion form along with Propofol has prevented the difference between the effects of Propofol and Sevoflurane on hemodynamic status of the patients to become clear; this way, both groups have experienced a good hemodynamic stability during surgery.[35]

Changes in the level of hematocrit from before to after surgery with significant difference between various groups, is considered as another result of the present study. Isoflurane group had the highest level of hematocrit drop, in comparison to the other groups. Cho et al. have compared changes made in the hemoglobin level of those patients under sinus endoscopic surgery, through application of Propofol and Desflurane. In both groups, changes were less than 1g/dl and in contradiction to the present study no difference was found between the groups. It seems that in our study, differences in hematocrit changes is stemmed from consumption of more liquids, creation of more hemodilution, and also higher hemorrhage during surgery in Isoflurane group, which has resulted in this huge hematocrit drop comparing to Propofol and Sevoflurane group. However, in the research performed by Cho, there has been no difference between the liquid amount prescribed during surgery between both receiver groups (Desflurane and Propofol), and no significant difference observed in hemoglobin changes of the patients of both groups.[36]

CONCLUSION

The results show that, making use of Sevoflurane during spine surgery results in the least amount of hemorrhage, and non-occurrence of acute drop in hematocrit; and generally an appropriate hemodynamic stability is created without prescription of assisting drug, in comparison to application of Isoflurane, and Propofol+Remifentanil.

ACKNOWLEDGMENTS

This paper is base on thesis No: PAIN_9505 approved by Ahvaz Jondishapur University of Medical Sciences, Ethnic Committee No: IR@AJUMS.REC.1395.557 . We acknowledge the vice chancellor of Deputy of Research and Technology Affairs of Ahvaz Jundishapour University of Medical Sciences.

We are indebted to all physicians, staff, nurses and patients who participated in this study.

REFERENCES

1. Cole, J.W., et al., *Aprotinin reduces blood loss during spinal surgery in children.* Spine, 2003; **28**(21): 2482-2485.
2. Ialenti, M.N., et al., *Predicting operative blood loss during spinal fusion for adolescent idiopathic scoliosis.* Journal of Pediatric Orthopaedics, 2013; **33**(4): p. 372-376.
3. Szpalski, M., R. Gunzburg, and B. Sztern, *An overview of blood-sparing techniques used in spine surgery during the perioperative period*, in *Haemostasis in Spine Surgery*. 2005; Springer. p. 18-27.
4. McNicol, E.D., et al., *Antifibrinolytic agents for reducing blood loss in scoliosis surgery in children.* The Cochrane Library, 2016.
5. Ker, K., D. Prieto-Merino, and I. Roberts, *Systematic review, meta-analysis and meta-regression of the effect of tranexamic acid on surgical blood loss.* British Journal of Surgery, 2013; **100**(10): 1271-1279.
6. Yao, H.H., M.K. Hong, and K.J. Drummond, *Haemostasis in neurosurgery: what is the evidence for gelatin-thrombin matrix sealant?* Journal of Clinical Neuroscience, 2013; **20**(3): 349-356.
7. Bajwa, S.J.S., et al., *Nitroglycerine, esmolol and dexmedetomidine for induced hypotension during functional endoscopic sinus surgery: A comparative evaluation.* Journal of Anaesthesiology, Clinical Pharmacology, 2016; **32**(2): 192.
8. Jans, Ø., et al., *Oral Midodrine Hydrochloride for Prevention of Orthostatic Hypotension during Early Mobilization after Hip ArthroplastyA Randomized, Double-blind, Placebo-*

controlled Trial. The Journal of the American Society of Anesthesiologists, 2015; (6)123: 1292-1300.

9. Nazir, O., et al., *Dexmedetomidine and Esmolol as Agents to Induce Hypotension in Lumbar Spine Surgery.* Trauma Monthly, 2016 (In Press).
10. Degoute, C.-S., *Controlled hypotension.* Drugs, 2007; **67**(7): 1053-1076.
11. Snidvongs, K ,.et al., *Dexmedetomidine improves the quality of the operative field for functional endoscopic sinus surgery: systematic review.* The Journal of Laryngology & Otology, 2015; **129**(S3): S8-S13.
12. Nowak, S., et al., *Impact of Controlled Induced Hypotension on Cognitive Functions of Patients Undergoing Functional Endoscopic Sinus Surgery.* Medical science monitor: international medical journal of experimental and clinical research, 2016; **22**: 898.
13. Mireskandari, S.M., et al., *The Effectiveness of Intravenous Magnesium Sulfate for Deliberate Hypotension in Rhinoplasty.* Archives of Anesthesiology and Critical Care, 2015; **1**(4): 112-115.
14. Saleh, Z.T., et al., *controlled hypotension in endoscopic sinus surgery: comparative study between the efficacy of esmolol, sodium nitroprusside and magnesium sulphate.* Zagazig University Medical Journal, 2015; **17**(4).
15. Skurić, J., et al. *The influence of different anesthetic techniques on intraoperative bleeding during endoresection of choroidal melanoma*. in *4th International symposium of critical bleeding*. 2013.
16. Bayram, A., et al., *Comparison between magnesium sulfate and dexmedetomidine in controlled hypotension during functional endoscopic sinus surgery.* Revista brasileira de anestesiologia, 2015; **659(1):** 61-67.
17. .17 Ullrich Jr, P., et al., *Results of hypotensive anesthesia in operative treatment of thoracolumbar fractures.* Journal of spinal disorders, 1990; **3**(4): 329-333.
18. .18 Obal, D., et al., *Cardioprotection against reperfusion injury is maximal with only two minutes of sevoflurane administration in rats.* Canadian Journal of Anesthesia, 2003; **50**(9): 940-945.
19. Koerner, I.P. and A.M. Brambrink, *Brain protection by anesthetic agents.* Current Opinion in Anesthesiology, 2006; **19**(5): 481-486.
20. Kurt, F., et al., *Old method, new drugs: comparison of the efficacy of sevoflurane, isoflurane, and desflurane in achieving controlled hypotension in spinal surgery.* Advances in therapy, 2005; **22**(3): 234-240.

21. Wakasugi, Y., N. Matsuura and T. Ichinohe, *Intraoperative Blood Loss During Orthognathic Surgery: A Comparison of Remifentanil-Based Anesthesia With Sevoflurane or Isoflurane.* Journal of Oral and Maxillofacial Surgery, 2015; **73**(12): 2294-2299.
22. Nishiyama, T., *Changes in heart rate variability during anaesthesia induction using sevoflurane or isoflurane with nitrous oxide.* Anaesthesiology Intensive Therapy, 2016.
23. Tantry, T.P., et al., *Target-controlled infusion (Propofol) versus inhaled anaesthetic (Sevoflurane) in patients undergoing shoulder arthroscopic surgery.* Indian journal of anaesthesia, 2013; **57**(1): 35.
24. Gupta, P., et al., *Comparison between sevoflurane and desflurane on emergence and recovery characteristics of children undergoing surgery for spinal dysraphism.* Indian journal of anaesthesia, 2015; **59**(8): 482.
25. Boezaart, A.P., J. van der Merwe, and A. Coetzee, *Comparison of sodium nitroprusside- and esmolol-induced controlled hypotension for functional endoscopic sinus surgery.* Canadian journal of anaesthesia :(5)42 .1995p. 373-376.
26. Fromme, G.A., et al., *Controlled hypotension for orthognathic surgery.* Anesthesia & Analgesia, 1986; **65**(6): 683-686.
27. Nair, S., et al., *The Effect of β-Blocker Premedication on the Surgical Field During Endoscopic Sinus Surgery.* The Laryngoscope, 2004; **114**(6): 1042-1046.
28. Simpson, P., *Perioperative blood loss and its reduction: the role of the anaesthetist.* British journal of anaesthesia, 1992; **69**(5): 498-507.
29. Marzban, S., et al., *Comparison of surgical conditions during propofol or isoflurane anesthesia for endoscopic sinus surgery.* Anesthesiology and pain medicine, 2013; **3**(2): 234-238.
30. Salama, H.F., *Remifentanil/propofol total intravenous anesthesia versus remifentanil/isoflurane inhalation anesthesia for controlled hypotension in lumbar spine fixation surgery.* Ain-Shams Journal of Anaesthesiology, 2014; **7**(2): 134.
31. Haghbin, M.A., H. Hakimzadeh, and M. Shabani, *Evaluating the efficacy of remifentanil-propofol versus isoflurane in reducing blood loss with considering depth of anesthesia during endoscopic sinus surgery.* 2013.
32. Ankichetty, S.P., et al., *Comparison of total intravenous anesthesia using propofol and inhalational anesthesia using isoflurane for controlled hypotension in functional endoscopic sinus surgery.* Journal of Anaesthesiology Clinical Pharmacology, 2011; **27**(3): 328.

33. Samantaray, A. and M. Rao, *Comparative effects of propofol infusion versus sevoflurane for maintenance of anesthesia for spine surgery.* Internet J Anesthesiol, 2007; **11:** 2.
34. Yoo, H.-S., et al., *Comparison of surgical condition in endoscopic sinus surgery using remifentanil combined with propofol, sevoflurane, or desflurane.* Korean journal of anesthesiology, 2010; **59**(6): 377-382.
35. Orhon, Z.N., et al., *Comparison of recovery profiles of propofol and sevoflurane anesthesia with bispectral index monitoring in percutaneous nephrolithotomy.* Korean journal of anesthesiology, 2013; **64**(3): 223-228.
36. Cho, K., et al., *Comparison of surgical conditions during propofol or desflurane anesthesia for endoscopic sinus surgery.* Korean journal of anesthesiology, 2012; **63**(4): 302-307.