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Propofol Infusion versus Combination of Isoflurane with Nitroglycerine for Controlled Hypotensive Anesthesia in Spine Surgery: A Randomized Controlled Study

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Abstract

Background: Several methods have been used to improve surgical field clarity and decrease blood loss intraoperative; one of them is the usage of hypotensive anesthesia. Spine surgery is one of the surgeries that need a clear field and a decreased amount of intraoperative bleeding which can impacton the ability of surgeons.

Aim of Study: Current study was designed to evaluate the effect of propofol versus isoflurane with nitroglycerine on blood loss, operative field clarity, extubation time and effect of both on tissue perfusion.

Settings and Design: This study design was a prospective randomized controlled double blinded clinical study.

Patients and Methods: 80 ASA or II patients undergoing elective spine surgery were randomly assigned to group P (n=40) that received propofol for induction and maintenance while group I (n=40) received thiopental for induction and isoflurane for maintenance with nitroglycerine. Heart rate, mean arterial pressure were recorded every 10min, amount of blood loss, grade of operative field clarity, extubation time and effect of both on liver and kidney function were recorded.

Results: Propofol group showed significant decrease in blood loss (p=0.01), better surgical field clarity (p=0.002) and shorter extubation time (p=0.001) than isoflurane group but there were no significant changes between the two groups regarding their effect on tissue perfusion (liver and kidney).

Conclusion: Propofol for elective spine surgery improved surgical condition and provided faster recovery compared to isoflurane even when we added an antihypertensive drug as nitroglycerine to isoflurane. Both of them had a comparable minor effect on liver and kidney functions.

Key Words: *Isoflurane – Propofol – Nitroglycerine – Hypotensive anesthesia – Spine surgery.*

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Introduction

INTRAOPERATIVE bleeding represents a challenge to spine surgeons. Reducing blood pressure intraoperatively has a positive impact on clarity of the surgical field; helping decrease bleeding from injured arteries and arterioles and decreases venous bleeding from cancellous sinusoidal channels. Controlled hypotensive anesthesia has been declared since the 1970s either alone or combined with other techniques for an optimal reduction of bleeding during elective spine surgeries **[1-3]**.

Various attempts have been used to improve the surgical field, such as proper positioning of the patient with the abdomen free of compression allows an important decrease in IVC pressure that adecreases the rate of epidural congestion and bleeding **[4]**.

Fast and meticulous surgery with expert hands is very essential in the reduction of blood loss. Use of bovie electrocautery and carefull subperiosteal dissection is paramount. Collagen, cellulose, and gelatin-based products are passive agents that promote platelet aggregation and formation of blood clot. On the other hand, active hemostatic agents like; thrombin or combination products allow de novo generation of a fibrin clot. They also provide hemostasis within 10 minutes of application **[5]**.

Propofol is the most known intravenous anesthetic drug used in Total Intravenous Anesthesia (TIVA); it produces marked decrease in blood pressure due to its vasodilator effect on blood vessels, it also decreases Cardiac Output (CO) as it has negative inotropic and chronotropic effects

on the heart **[6]**. Isoflurane decreases blood pressure as a result of a reduction in the systemic vascular resistance and this reduction in blood pressure is related to its concentration, also it decreases CO as it is a myocardial depressant **[7]**.

This study aimed at assessment of the efficacy of Total Intravenous Anesthesia (TIVA) using propofol in controlled hypotensive anesthesia in comparison to inhalational anesthetics using isoflurane with nitroglycerine in spine surgery and to detect the effect of hypotension produced by either methods on tissue perfusion (Liver & kidney).

Patients and Methods

This study was conducted at Fayoum University Hospital from February 2014 till April 2015. All patients were given full written informed consents before participation in this study. Eighty patients with American Society of Anesthesiologists Classification (ASA) I or II, from both sex groups, with age ranging from 20-60 years old, undergoing spine surgery were enrolled in a prospective, random, double blinded study to receive either propofol (Diprivan) infusion as Group P (n=40) or to receive isoflurane & nitroglycerine infusion as Group I (n=40). Randomization was done using opaque sealed envelopes by an assistant nurse that did not share in the anesthetic technique or data collection.

Patients with anemia (hemoglobin concentration <10gm/dl), systemic hypertension, significant cardiovascular diseases, renal diseases, diabetes mellitus and hepatic diseases were excluded. In anesthesia preparation room, IV line was inserted. On arrival to operating room, lactated ringer solution was infused at a rate of 4-6ml/kg/h. Standard monitoring devices (NIHON KHODN) were applied including Non-Invasive Blood Pressure (NIBP), ECG, pulse oximeter (SpO_2) before induction of General Anesthesia (GA), capnography for end-tidal CO_2 ($ETCO_2$) and Peripheral Nerve Stimulator (PNS) applied on the ulnar nerve for neuromuscular blockade after induction of GA.

Anesthetic technique:

Group I: Anesthesia was initiated with fentanyl 2 gg/kg, thiopental Na 5mg/kg and atracurium 0. 5mg/kg then tracheal intubation was performed with the guidance of peripheral nerve stimulator. Anesthesia was achieved with 50% oxygen in air and 1-2% isoflurane, isoflurane concentration was adjusted according to hemodynamic responses to maintain MAP between 60 and 70mmHg, fentanyl infusion was started at the rate of 1gg/kg/h following intubation. The infusion of nitroglycerine was started at the rate of 0.1gg/kg/min and increased gradually till the target MAP was reached, increments of atracurium were given when necessary.

Group P: Anesthesia was initiated with fentanyl 2 gg/kg, propofol 2mg/kg and atracurium 0.5mg/kg then we performed tracheal intubation with the guidance of peripheral nerve stimulator. Anesthesia was secured with 50% oxygen in air, fentanyl infusion was started at the rate of 1gg/kg/h following intubation. Propofol infusion was started at a rate of 12mg/kg/h for 10min following intubation, then at 10mg/kg/h for next 1 0min and continued at a rate of 8mg/kg/h. The infusion rate was increased accounting on the patient's response and to maintain MAP between 60 and 70mmHg. However, it was decided not to surpass the maximal rate of propofol infusion above 12mg/kg/h, increments of atracurium were given when necessary. To provide increased convenience for the surgical team and to reduce the amount of bleeding. To estimate the effects of hypotensive agents on organ systems, Alanine Transaminase (ALT), Aspartate Transaminase (AST), urea and creatinine values that refer to hepatic and renal functions were measured and recorded during both the preoperative (one week before the operation) and postoperative periods (during 1st 24 hours).

Intraoperative measured parameters:

1- *Hemodynamics:* Heart Rate (HR), MAP every 10min interval.

2- *Intraoperative blood loss:* The blood loss from the surgical field was collected and measured.

3- *The extubation time:* Indicates the time from discontinuation of both (isoflurane or propofol infusion) till removal of the endotracheal tube.

If the MAP dropped below 60mmHg, the NTG infusion would be decreased in group I while propofol infusion would be decreased in group P, if the MAP was still below 60mmHg; ephedrine 6mg IV would be given and repeated after 3 minutes. Atropine 0.01mg/kg would be used if HR decreased below 50 beats/min and repeated after 3min if HR was still low. Once the surgery is terminated, isoflurane was discontinued and the NTG infusion was discontinued in group I, while propofol infusion was stopped in group P, residual atracurium was reversed with neostigmine 0.04 mg/kg IV and atropine 0.02mg/kg IV when the train of four (TOF) count is 2/4 i.e. the appearance of the 2nd twitch (<90% of receptor are blocked). Once the patient show eye opening and purposeful movement, trachea was extubated then the patient

was transferred to the Post Anesthesia Care Unit (PACU). In the PACU, the patients were monitored as NIBP, SpO_2, and ECG. Oxygen supplementation was provided via face mask (4-6L/h).

Post-operative measured parameters: In PACU:

1- MAP, HR and oxygen saturation were monitored every 10 minutes.

2- Sedation was assessed using Ramsay sedation score on arrival to PACU and then every 30min for 2 hours. Sedation scale (Ramsay Sedation Scale) is as follows:

1- Anxious, agitated or restless.

2- Cooperative, oriented and tranquil.

3- Responds to command.

4- Asleep but has a high response to light glabellar tap or loud auditory stimulus.

5- Asleep, has a low response to a light glabellar tap or loud auditory stimulus.

6- Asleep, no response.

3- Evaluation of liver and kidney functions (ALT, AST, serum creatinine and blood urea) were performed within 24 hours post-operative.

4- Recovery of the patients were evaluated using Modified Aldrete's Score **[8]** (MAS) on arrival to the PACU and every 30 minutes. Patients were discharged from the PACU after fulfilling a modified Aldrete's score of ≥9.

Table (1): Post anesthesia recovery score (modified aldrete score).

Parameter	Score		
	2	1	0
• Activity	• Moves all extremities voluntarily or on command.	• Moves two extremities voluntarily or on command.	• Unable to move extremities
• Respiration	• Breathes deeply and coughs freely.	• Dyspnea, shallow or limited breathing.	• Apneic.
• Circulation	• BP ±20mm of preanesthetic level.	• Bp ±20-50mm of preanesthetic level.	• BP ±50mm of preanesthetic level
• Consciousness	• Fully awake.	• Arousable on callig.	• Not responding.
• Oxygen saturation		• Supplemental O_2 required to maintain SpO_2 >90%.	• SpO_2 <90% with O_2 supplementation

Total Score = 10; A score of ≥9 required for discharge.

Complications were managed accordingly. If the patient suffered from post-operative pain; paracetamol preparation "perfalgan" 1gm would be given as IV infusion over 15min.

Statistical analysis:

Sample size calculated using G* Power© software version 3.1.7 (Institute of experimental psychology, Heinrich Heine University, Dusseldorf, Germany) **[9]**.

Data was gathered, coded to make manipulation of data easier, and double entered into Microsoft Excel and data analysis was performed using Statistical Package for the Social Sciences (SPSS) software version 19 under windows 7. Qualitative data were analysed in a simple descriptive way in the form of numbers and percentages, and quantitative parametric data were analysed by arithmetic means as standard deviations as measure of dispersion, central tendency measurement, and inferential statistic test: For quantitative parametric data: Independed student *t*-test used to compare measures of two independent groups of quantitative data. For qualitative data: Chi square used test to compare two of more than two qualitative groups. The level *p*-value <0.05 was considered the cut-off value for significance.

Results

Regarding the demographic data, there was no statistically significant difference between the two study groups: (Sex, age, weight, height, ASA) as shown in (Table 2).

Table (2): Demographic data (age, weight, height, gender & ASA).

Data	Isoflurane Group (N=40)		Propofol Group (N=40)		*p*-value
	Mean	±SD	Mean	±SD	
Age (years)	27.70	5.97	30.10	7.13	0.163
Weight (Kg)	71.33	8.30	68.97	6.78	0.231
Height (cm)	165.33	7.54	166.23	6.03	0.611
Gender (male/female)	21/19		22/18		0.795
ASA (I/II)	27/ 13		28/12		0.770

N : Number.
SD: Standard Deviation.
Hemodynamic variable: (HR, MAP).

Heart rate: The baseline HR showed no significant difference between two groups. After induction, HR significantly decreased (about 25%) from the base line measurements in the two groups, then increased again after tracheal intubation. The HR had almost constant course during the intraoperative period in both groups but propofol group showed a lower decrease in heart rate than isoflurane group and the difference was statistically significant (Table 3) and Fig. (1).

Table (3): Heart rate changes in both groups.

HR(beats/minutes)	Isoflurane Group (N=40)		Propofol Group (N=40)		*p*-value
	Mean	±SD	Mean	±SD	
Pre-operative	84.17	9.81	85.50	9.09	0.587
At induction	74.77	6.18	69.50	7.40	0.004*
At intubation	77.77	7.21	73.53	5.44	0.013*
At 10min	77.20	9.98	71.23	5.16	0.005*
At 20min	75.27	8.11	70.93	5.73	0.020*
At 30min	75.90	6.09	70.17	5.52	0.001*
At 40min	74.13	5.37	70.93	5.91	0.032*
At 50min	76.23	4.78	70.87	4.95	0.001*
At 60min	74.60	4.66	71.57	5.90	0.031*
At 70min	75.43	5.29	70.70	6.31	0.003*
At 80min	75.70	6.83	69.20	3.14	0.001*
Post-extubation	77.93	7.03	75.07	8.24	0.153

N: Number. * : Significant difference.
SD: Standard Deviation. HR: Heart Rat.

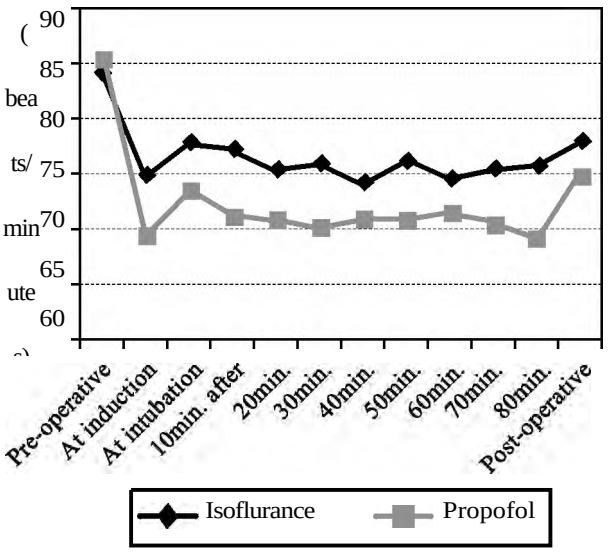

Fig. (1): Heart rate changes in both groups.

Mean arterial blood pressure (MAP): MAP showed no significant difference between both groups in the pre-operative period and after induction of General Anesthesia (GA). MAP showed significant decrease in propofol group than isoflurane group after intubation. Intraoperatively, MAP showed no significant difference between the two groups (Table 4) and Fig. (2).

Table (4): MAP changes in both groups.

MAP (mmHg)	Isoflurane Group (N=40)		Propofol Group (N=40)		*p*-value
	Mean	±SD	Mean	±SD	
Pre-operative	81.83	7.05	82.47	4.68	0.684
At induction	70.07	6.33	68.43	3.89	0.234
At intubation	75.30	4.54	70.13	2.96	0.001*
At 10min	70.83	2.65	71.83	2.35	0.128
At 20min	68.33	2.68	69.70	2.88	0.062
At 30min	67.83	2.98	69.77	4.44	0.053
At 40min	66.63	2.39	68.63	5.33	0.068
At 50min	68.43	1.99	70.00	3.88	0.055
At 60min	70.03	1.40	70.80	3.55	0.278
At 70min	69.97	2.27	71.53	3.68	0.052
At 80min	70.23	2.03	71.30	2.97	0.111
Post-extubation	79.53	7.23	81.07	3.68	0.306

N : Number.
SD : Standard Deviation.
* : Significant difference.
MAP : Mean Arterial Pressure.

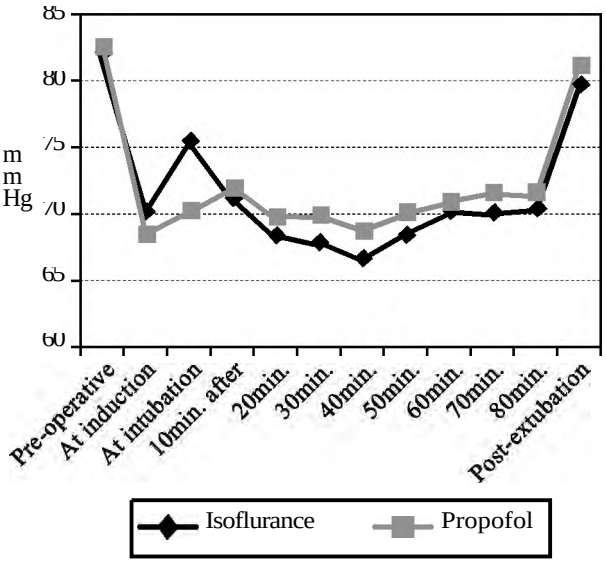

Fig. (2): Intra operative MAP.

Blood loss: The amount of blood loss was statistically significant lower in propofol group when compared to isoflurane group as shown in (Table 5).

Table (5): Blood loss in both groups.

Data	Isoflurane Group (N=40)		Propofol Group (N=40)		*p*-value
	Mean	SD	Mean	SD	
• Amount of blood loss (ml)	698.8	291.6	376.4	138	0.002*

N : Number.
SD : Standard Deviation.
* : Significant.

Extubation time: There was a statistically significant difference between the two study groups regarding extubation time being longer in the isoflurane group (Table 6).

Table (6): Comparison of the extubation time between the two study groups.

Data	Isoflurane Group (N=40)	Propofol Group (N=40)	*p*-value
	Mean ±SD	Mean ±SD	
Extubation time (min)	15.43 2.03	10.53 1.11	0.001*

N : Number.
SD : Standard Deviation.
* : Significant.

Liver & kidney function: Regarding liver and kidney function (ALT, AST, Creatinine & urea); there was no statistically significant difference between the two study groups (Table 7).

Table (7): Comparison of ALT, AST, Urea & Creatinine pre-operative & post-operative between the two study groups.

Data	Isoflurane Group (N=40)	Propofol Group (N=40)	*p*-value
	Mean ±SD	Mean ± SD	
• ALT pre-operative IU/L	18.97 6.14	21.97 7.96	0.108
• ALT post-operative IU/L	21.10 6.34	24.07 7.75	0.110
• AST pre-operative IU/L	19.27 7.28	20.97 6.64	0.349
• AST post-operative IU/L	22.83 7.48	23.80 7.13	0.610
• Creatinine pre-operative mg/dl	0.79 0.26	0.70 0.06	0.097
• Creatinine post-operative mg/dl	0.88 0.29	0.77 0.11	0.060
• Urea pre-operative mg/dl	24.43 6.23	26.67 6.36	0.175
• Urea post-operative mg/dl	27.40 6.46	29.53 6.33	0.202

N : Number.
SD : Standard Deviation.

Discussion

Collaboration between spine surgeon and the anesthesiologist helps achieving an optimum surgical procedure with clear visualization of the surgical field. Maintaining a minimal intraoperative blood loss has an excellent impact on lowering the length of surgery, patient morbidity and the total cost of the surgical procedure **[10,11]**.

Propofol is the most common intravenous anesthetic drug used in Total Intravenous Anesthesia (TIVA); it produces marked reduction in blood pressure due to its vasodilator effect on blood vessels, it also decreases Cardiac Output (CO) as it has negative inotropic and chronotropic effects on the heart **[12]**. Isoflurane decreases blood pressure as a result of a reduction in the systemic vascular resistance and this reduction in blood pressure related to its concentration, also it decreases CO as it is a myocardial depressant.

In the current study propofol was associated with less amount of blood loss and better surgical field than isoflurane due to its effect on heart rate.

In a study conducted by Marzaban et al., **[13]** propofol was compared with isoflurane for endoscopic sinus surgery and results showed that less blood loss and better surgical score in patients given propofol than those given isoflurane (p= 0. 003).

Another study conducted by Salama HF et al., **[14]** propofol-remifentanyl intravenous anesthesia for lumbar fixation was beneficial and improve surgical visibility compared with isoflurane and this agree with our results.

On the other hand a study conducted by Haghbin MA **[15]** and Ankichetty PS, **[16]** total intravenous anesthesia using propofol for endoscopic sinus surgery offered no significant advantage over isoflurane in term of blood loss and operative field.

In the current study, propofol group show significant decrease in extubation time than isoflurane (p=0.001). The current study agrees with Khalid A et al., **[17]** who reported that propofol provided faster recovery than isoflurane for laparoscopic cholecystectomy. A study conducted by Haki KB et al., **[18]** reported that propofol-remifentanyl had short recovery time than isoflurane-remifentanyl for septorhinoplasty.

On the other hand, the study done by LD Mishra et al., **[19]** who compared between propofol based anesthesia and conventional inhalational general anesthesia for spine surgery, show that there was no significant difference in the recovery time between propofol group and inhalational group.

In the current study, there was insignificant between two group as regard the effect of hypotension on liver and kidney function. The current study agrees with Kim SH et al., **[20]** who compared the effect of enflurane, isoflurane & propofol on liver functions in tympanomastoidectomy and there was no significant difference in post-operative hepatic functions between the three group (p>5).

A study conducted by Saricaoglu F et al., **[21]** who compared the effect of propofol infusion, isoflurane, sevoflurane and halothane on renal functions after coronary artery bypass surgery,

reported that there was no significant difference between propofol and isoflurane on renal functions.

Also Wook Kim et al., **[21]** who compared hepatic and renal functions between inhalational with sevofluraneremifentanyl and TIVA with propofol-remifentanyl for thyroidectomy, reported that the changes of hepatic and renal functions between two groups were clinically insignificant, and there was no difference between the two methods which consistent with this study.

Conclusion:

Propofol for spine surgery improve surgical condition and provide faster recovery compared to isoflurane even when we added antihypertensive (nitroglycerine) to isoflurane. Both of them have a comparable minor effect on liver and kidney functions.

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الحقن الوريدى لعقار البروبوفول مقابل مزيج من عقارى الآيزوفلورين والنيتروجلسرين للتخدير الخافض للضغط الخاضع للتحكم فى جراحات العمود الفقرى: دراسة عشوائية خاضعة للرقابة

هناك أساليب كثيرة تستخدم لتقليل النزف أثناء الجراحة وضوح المجال الجراحى. من هذه الأساليب تقليل الضغط أثناء التخدير. جراحات العمود الفقرى من الجراحات التى تحتاج مجال جراحى واضح لتحسن قدرة جراح الأعصاب على التعامل مع الأنسجة العصبية. هدف هذه الدراسة هو تقييم تأثير عقار البروبوفول بالمقارنة بعقارى الآيزوفلورين مع النيتروجلسرين معاً على كمية النزف أثناء الجراحة ووضوح المجال الجراحى ووقت نزع الأنبوبة الحنجرية ومعدل إرواء الأنسجة. خلصت هذه الدراسة إلى تفوق عقار البروبوفول فى تحسين الأجواء الجراحية وإعطاء إستشفاء أسرع بالمقارنة بعقارى الآيزوفلورين مع النيتروجلسرين معاً.