의 학 석 사 학 위 논 문

주요 척추 수술 중 레미마졸람 또는 프로포폴 전정맥마취가 혈역학적 안정성에 미치는 영향의 비교

Effect of remimazolam versus propofol-based total intravenous general anesthesia on intraoperative hemodynamic stability in the prone position for major spine surgery : A randomized controlled trial.

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이 논문을 의학 석사 학위 논문으로 제출함

2023 년 8 월

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국문 요약

연구 배경

수술 전후 저혈압은 부정적인 수술 결과와 연관되어 있다. 이에 본 연구에서는 주요 척추 수술을 받는 환자들의 수술 중 혈역학적 안정성에 대한 레미마졸람과 프로포폴 기반의 전체 정맥 마취의 효과를 비교하였다.

연구 방법

본 무작위 대조 연구에서 척추 수술을 받는 환자들을 프로포폴 군과 레미마졸람 군으로 무작위로 배정했다. 프로포폴 군에서는 프로포폴을 1.5-3 μg/mL 으로 목표 제어 주입을 하였고 레미마졸람 군에서는 레미마졸람을 마취 유도 중 6 mg/kg/hr 로 주입하였으며, 그 후 0.5-2 mg/kg/hr로 유지하였다. 본 연구의 주요 결과는 저혈압과 심각한 저혈압 발생률, 그리고 혈압 안정성을 유지하기 위해 사용된 승압제 또는 혈관 수축제의 총량이었다. 기준 혈압은 휴식 상태에서 3회 측정한 병동 혈압의 평균으로 정의하였으며, 저혈압은 수축기 혈압이 기준치의 80% 또는 90 mmHg 미만, 평균 동맥압이 기준치의 80% 또는 65 mmHg 미만으로 정의하였다. 심각한 저혈압은 수축기 혈압이 기준치의 70% 또는 80 mmHg 미만, 평균 동맥압이 기준치의 70% 또는 55 mmHg 미만으로 정의하였다. 2차 결과변수로는 수축기 및 평균 동맥압, 심박수, 심장 지수, 심박출량, 일회 박출량, 일회 심박출량 변동지수, 파형변이지수를 비교하였다. 모든 변수들은 엎드린 자세 후 첫 10분간 매 분마다 기록했고, 이후 10분마다 기록하였다.

연구 결과

총 94명의 환자가 각 군에 47명씩 배정되었다. 엎드린 자세 후 첫 1시간 동안 두 군 간에 저혈압 또는 심각한 저혈압 사건의 발생률에 유의미한 차이가 없었고, 투여된 에페드린의 총량은 레미마졸람 군에서 적었다 (p=0.020). 엎드린 자세 후 초기 10분간 평균 동맥압과 (p=0.003) 심박수는 (p<0.001) 레미마졸람 군에서 높았으며, 일회 박출량은 (p=0.029) 프로포폴 군에서 더 높았다. 그 외 다른 혈역학적 변수는 차이가 없었다.

결론

위 결과들은 엎드린 자세 직후 척추 수술 중 평균 동맥압을 유지하는데 있어서 프로포폴보다 레미마졸람이 더 나은 선택일 수 있다는 것을 제안한다.

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Tables and figures

Introduction

Perioperative hypotension, particularly mean arterial pressure (MAP) is associated with cardiovascular events, acute kidney injury (AKI), and increased one-year mortality[1-3]. Even brief episodes of intraoperative hypotension can lead to negative consequences, highlighting the importance of timely treatment during general anesthesia[4].

Spinal surgery is commonly performed in the prone position, which decreases stroke volume and cardiac index, increasing the risk of hypotension[5]. Neurophysiologic monitoring is often required during spinal surgery, making total intravenous anesthesia (TIVA) more favorable than inhalation agents due to their minimal effects on latency or amplitude of somatosensory potentials (SSEP) and motor evoked potentials (MEP) during intraoperative patient monitoring. However, propofol, the most employed anesthetic agent for TIVA, increases the risk of intraoperative hypotension and often requires inotropic support[6 7].

Remimazolam is a novel ultrashort-acting benzodiazepine used in general anesthesia, which is rapidly hydrolyzed by carboxylesterase-1 into an inactive metabolite [8], therefore making it an appropriate agent for continuous infusion in general anesthesia [9]. Remimazolam exhibits the hemodynamic stability typical of benzodiazepines[9]. No studies have yet investigated the hemodynamic stability of remimazolam as a general anesthetic in patients undergoing prone position surgeries. Therefore, we investigated the effect of remimazolam versus propofol on intraoperative hemodynamic stability in patients in the prone position undergoing major spinal surgery.

Methods

This single-center, prospective, randomized control trial was conducted at Asan Medical Center, a tertiary referral center in Seoul, South Korea. This study was conducted in accordance with the principles of the Declaration of Helsinki. The trial is registered at the ClinicalTrials.gov (NCT05644483) website. The study protocol was approved by the Institutional Review Board of Asan Medical Center (#2021-1514). All participants provided written informed consent before enrollment.

Study population

All patients undergoing major spinal surgery in the prone position between March 2022 and January 2023 at our center in the orthopedic department were considered eligible for the study and were screened. Patients aged between 19 and 80 years old and with an American Society of Anesthesiologists physical status score of 1-3, were included in the study. Patients were excluded if they had uncontrolled hypertension, hypothyroidism, moderate to severe cardiovascular or liver disease, acute narrow-angle glaucoma, shock, acute alcoholism, or a body mass index (BMI) below 15 kg/m^2 or over 35 kg/m^2. All included patients were randomly allocated into either the propofol group or the remimazolam group, without being made aware of their allocation. Randomization was conducted using a computer-gen erated randomization program (https://randomization.com). The participants were randomized to the propofol group or the remimazolam group in a 1:1 ratio. Group assignments were obscure d in sealed envelopes and opened immediately before anesthetic induction. Due to the color d ifference of the two study drugs, blinding was impossible for the investigators. However, the type of study anesthetic drug infused (propofol or remimazolam) was concealed to the patients.

Anesthesia

Upon patient arrival to the operating room, standard monitoring was performed, including pulse oximetry, pleth variability index, non-invasive blood pressure (NIBP), and electrocardiography. Non-invasive blood pressure was measured in the contralateral arm at 3-minute intervals before arterial cannula insertion. Electrocardiography, pulse oximetry, and pleth variability index were monitored continuously. Induction was achieved using either remimazolam at a rate of 6 mg/kg/hr in the remimazolam group or propofol target-controlled infusion at an effect-site concentration of 1.0-1.5 μg/mL in the propofol group. The propofol infusion rate was increased by 0.5 μg/mL every 30 seconds until loss of consciousness occurred. Remifentanil was infused at a rate of 3-5 ng/mL using target-controlled infusion in both groups. After loss of consciousness, the infusion rate was reduced to 0.5-2 mg/kg/hr for remimazolam or 1.5-3 μg/mL for propofol target-controlled infusion. Mask ventilation was applied using rocuronium at a dose of 0.6-0.8 mg/kg in both groups and tracheal intubation was performed after adequate relaxation. A 20-gauged arterial cannula was inserted into the radial artery and an 18-gauge intravenous cannula was inserted after anesthetic induction. Continuous hemodynamic variables were examined thereafter, including systolic and mean arterial pressure, cardiac index and output, stroke volume, and stroke volume variability. During induction, a crystalloid solution was administered at a rate of 6 mL/kg. During maintenance, the infusion rates of propofol (2-3 μg/mL) and remimazolam (1-2 mg/kg/hr) were adjusted to maintain a patient state index (PSI) value between 25 and 50, whereas the infusion rate of remifentanil was adjusted to maintain blood pressure (BP) within 20% of baseline (Figure 1).

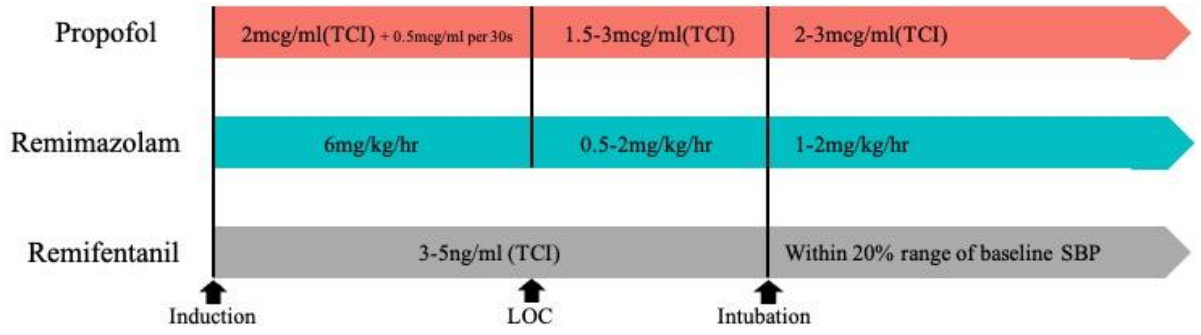

FIGURE 1. The research protocols. Abbreviation: TCI: target-controlled infusion, LOC: loss of consciousness, SBP: systolic

blood pressure

Definition of hemodynamic events and management

Baseline systolic blood pressure (SBP) was defined as the average of three ward BP measurements at rest. Hypotension was defined as SBP <80% of baseline or <90 mmHg or MAP <80% of baseline or <65 mmHg. Severe hypotension was defined as SBP <70% of baseline or <80 mmHg, or MAP <70% of baseline or <55 mmHg. Post-positioning blood pressure was defined as the BP measured 10 minutes within prone positioning. Hypotension was treated by lowering the infusion rate of remifentanil, whereas severe hypotension was treated with phenylephrine (50-100 mcg) or ephedrine (5-10 mg) regardless of the trial drug. Continuous infusion of norepinephrine or phenylephrine was initiated if severe hypotensive episodes occurred three times within 15 minutes or five times within 30 minutes. The infusion rate of remifentanil was enhanced if SBP increased by > 20% from baseline. If SBP increased by > 30% from baseline, nicardipine (300 mcg) was considered. Bradycardia (heart rate <40 beats/min) was treated with atropine (0.5 mg), and esmolol (0.5 mg/kg) was administered for tachycardia (heart rate >100 beats/min).

Outcome measures

The primary outcomes of this study were the incidence of hypotensive and severe hypotensive episodes, as well as the total amount of inotropic or vasopressor medication used to maintain hemodynamic stability for one hour after prone positioning. Additionally, we analyzed continuous hemodynamic variables of systolic and mean arterial pressure, heart rate, cardiac index and output, stroke volume, stroke volume variation, and pleth variability index as secondary outcomes. All variables were recorded every minute for the first 10 minutes after prone positioning, and then every 10 minutes thereafter.

Statistical analysis

In a retrospective review, the incidence of hypotension during major spine surgery in the prone position under propofol based TIVA was approximately 56%. Assuming that using remimazolam instead of propofol could reduce this incidence by 28%, a power analysis indicated that a minimum of 44 subjects per group would be required to detect a difference in the incidence of hypotension with a power of 0.8 and an alpha error of 0.1. The final sample size was increased to 94 to account for potential dropouts from each group.

All statistical and graphical analyses were performed using R (version 4.1.2; http://www.rproject.org) and SAS®, version 9.4 (SAS Institute Inc., Cary, NC, USA). The significance of the outcome was defined as two-tailed p-value<0.05. Hypotensive episode, a primary outcome, was assessed by Student's t-test. Other continuous variables were evaluated by Student's t-test or Wilcoxon rank-sum test as appropriate, and Fisher's exact test was used to analyze categorical data. In addition, the linear mixed model was applied to evaluate the longitudinal changes of MBP and HR. In the model, we tested group and time effects and interactions of group and time.

Results

Patient characteristics and eligibility

Out of the 100 patients evaluated for eligibility, five declined to participate and one was excluded due to screening failure in the propofol group. The remaining 94 patients were included in the final analysis (Figure 2). Demographic data, co-morbid diseases, preoperative laboratory data, or surgery-related data of the propofol and remimazolam groups are illustrated in Table 1.

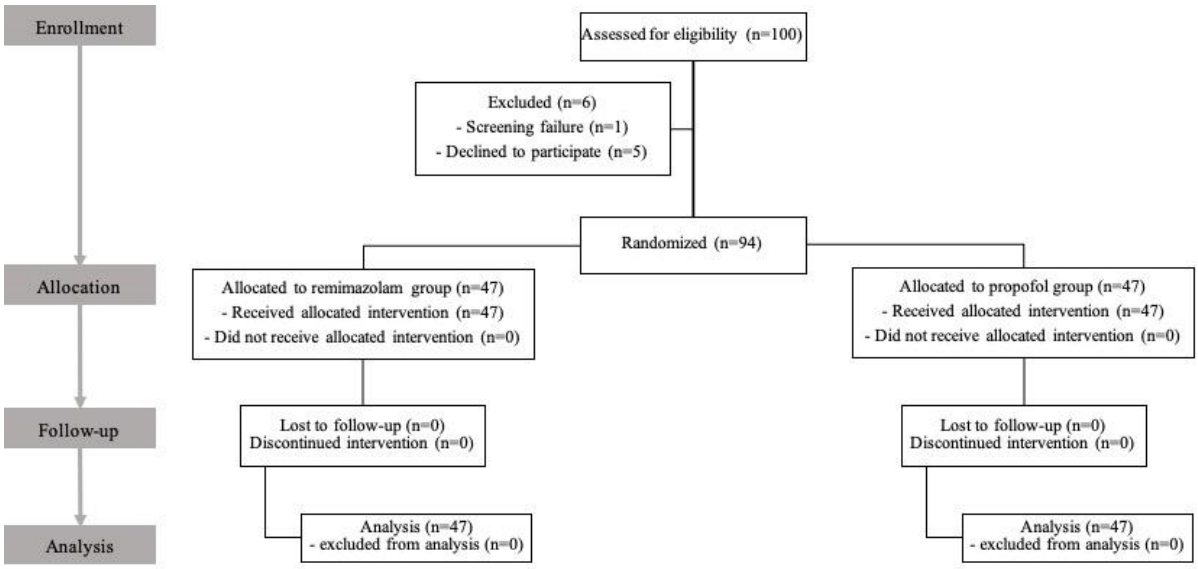

FIGURE 2. Flow chart of patient enrollment.

	Propofol (N=47)	Remimazolam (N=47)
Sex (male)	20 (42.6%)	15 (31.9%)
ASA classification		
- 2	42 (89.4%)	43 (91.5%)
- 3	5 (10.6%)	4 (8.5%)
Age (years)	67.2 ± 7.5	67.4 ± 8.0
Height (m)	1.6 ± 0.1	1.6 ± 0.1
Weight (kg)	64.9 ± 9.2	61.1 ± 9.0
Diabetes mellitus	7 (14.9%)	16 (34.0%)
Hypertension	27 (57.4%)	23 (48.9%)
Ischemic heart disease	4 (8.5%)	2 (4.3%)
Cerebrovascular accident	2 (4.3%)	0 (0.0%)
Pulmonary disease	4 (8.5%)	4 (8.5%)
Renal disease	1 (2.1%)	4 (8.5%)
Hemoglobin (g/dL)	13.0 ± 1.4	12.7 ± 1.6
White blood cell (10^3/μL)	6.4 ± 1.5	6.3 ± 2.1
Platelet (10^9/μL)	235.6 ± 49.8	235.8 ± 53.8
Albumin (g/dL)	3.8 ± 0.3	4.5 ± 4.7
Creatinine (mg/dL)	0.8 ± 0.2	0.8 ± 0.2
Aspartate aminotransferase (IU/L)	23.1 ± 7.1	23.1 ± 6.3
Alanine aminotransferase (IU/L)	21.8 ± 11.5	20.3 ± 8.0
C-reactive protein (mg/dL)	0.2 ± 0.6	0.3 ± 0.8
Anesthetic time (min)	194.0 ± 39.3	189.5 ± 34.6
Operation time (min)	140.4 ± 38.4	137.5 ± 33.7
Total amount of remifentanil (mcg)	1649.1 ± 665.4	1737.1 ± 722.7

TABLE 1. Patient baseline characteristics.

Continuous variables are expressed as mean ± standard deviation or as median (1st quartile and 3rd quartile) and categorical variables as n (%). Abbreviation: ASA, American Society of Anesthesiologist

Primary outcomes

The primary outcomes of this study, the number of patients experiencing hypotensive or severe hypotensive events, as well as the number of episodes per patient during the first hour after prone positioning, were not different between the study groups. The total amount of ephedrine administered during the first hour after prone position was greater in the propofol group (p=0.020). No significant differences were observed for any of the other drugs (Table 2).

	Propofol (N=47)	Remimazolam (N=47)	***p*-value**
Intraoperative adverse events			
Patients with hypotensive event (1 hour)	45 (95.7%)	39 (83.0%)	0.091
Hypotensive event per individual (1 hour)	4.7 (2.4%)	4.1 (2.7%)	0.366
Patients with severe hypotensive event (1 hour)	36 (76.6%)	31 (66.0%)	0.254
Severe hypotensive event per individual (1 hour)	2.8 (2.3%)	2.1 (2.1%)	0.128
Administration of inotropics or vasopressors			
Total amount of ephedrine (mg)	7.6 ± 9.1	4.1 ± 6.9	0.020
Total amount of phenylephrine (mcg)	1684.3 ± 1961.7	1069.5 ± 1552.2	0.239
Total amount of norepinephrine (mcg)	21.2 ± 112.5	0	0.164

TABLE 2. Intraoperative hypotensive and severe hypotensive events of patients allocated randomly to propofol and remimazolam groups.

Continuous variables are expressed as mean ± standard deviation or as median (1st quartile and 3rd quartile) and categorical variables as n (%).

Secondary outcomes

In the first hour after prone positioning, the remimazolam group exhibited a significantly elevated heart rate (p=0.003) and a significantly reduced stroke volume (p=0.046) compared to the propofol group, with no significant differences in other secondary outcome hemodynamic parameters (Figure 3).

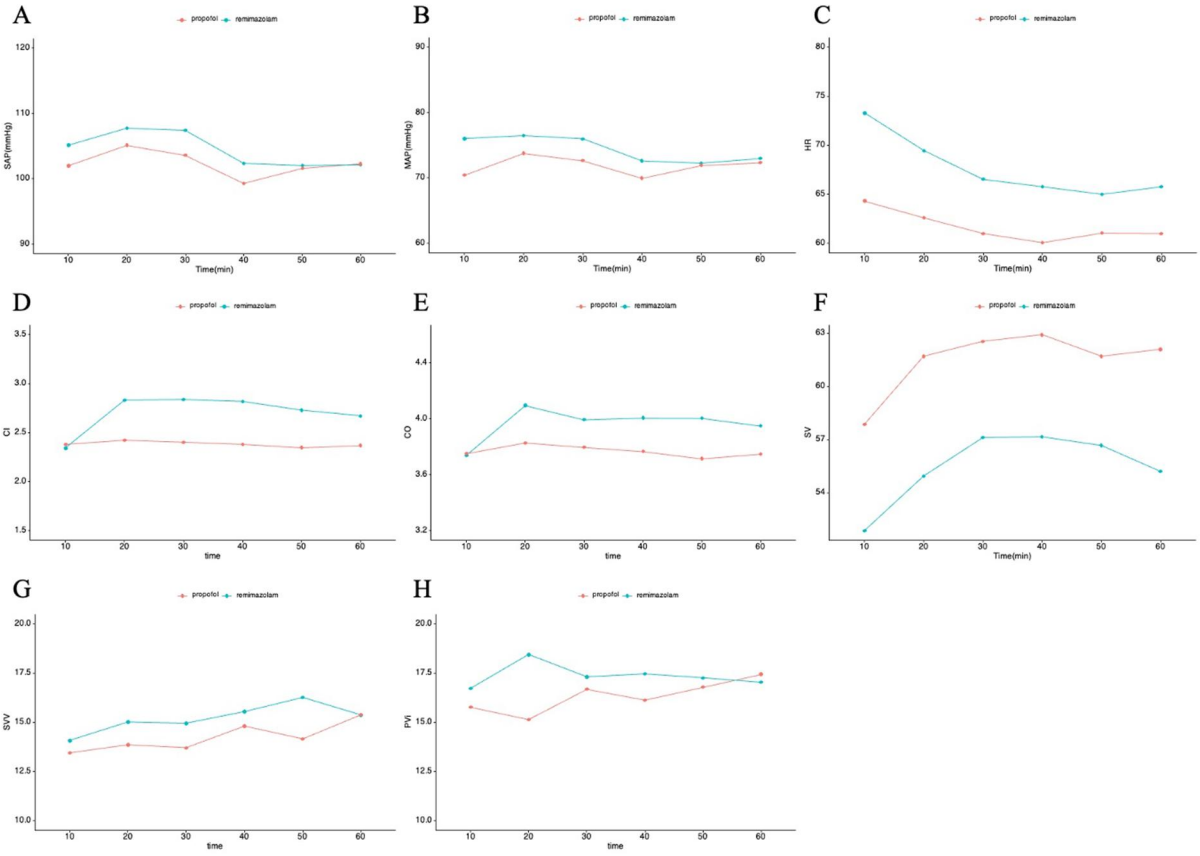

Figure 3A~H. Serial changes in systolic arterial pressure (A), mean arterial pressure (B), heart rate (C), cardiac index (D), cardiac output (E), stroke volume (F), stroke volume variant (G) and pleth variability index (H) during the initial one hour after prone position. In comparison to the propofol group, the remimazolam group showed higher heart rate (p=0.003) and lower stroke volume (p=0.046). No significant difference was observed in mean arterial pressure between the two groups.

Abbreviation: SAP, systolic arterial pressure; MAP, mean arterial pressure; HR, heart rate; CI, cardiac index; CO, cardiac output; SV, stroke volume; SVV, stroke volume variant; PVi, pleth variability index

In the initial 10 minutes after prone positioning, as compared to the propofol group, the remimazolam group had significantly higher mean arterial pressure (p=0.003) and heart rate (p<0.001). Stroke volume was significantly increased in the propofol group as compared with the remimazolam group (p=0.029)

during the first 10 minutes following prone position (Figure 4).

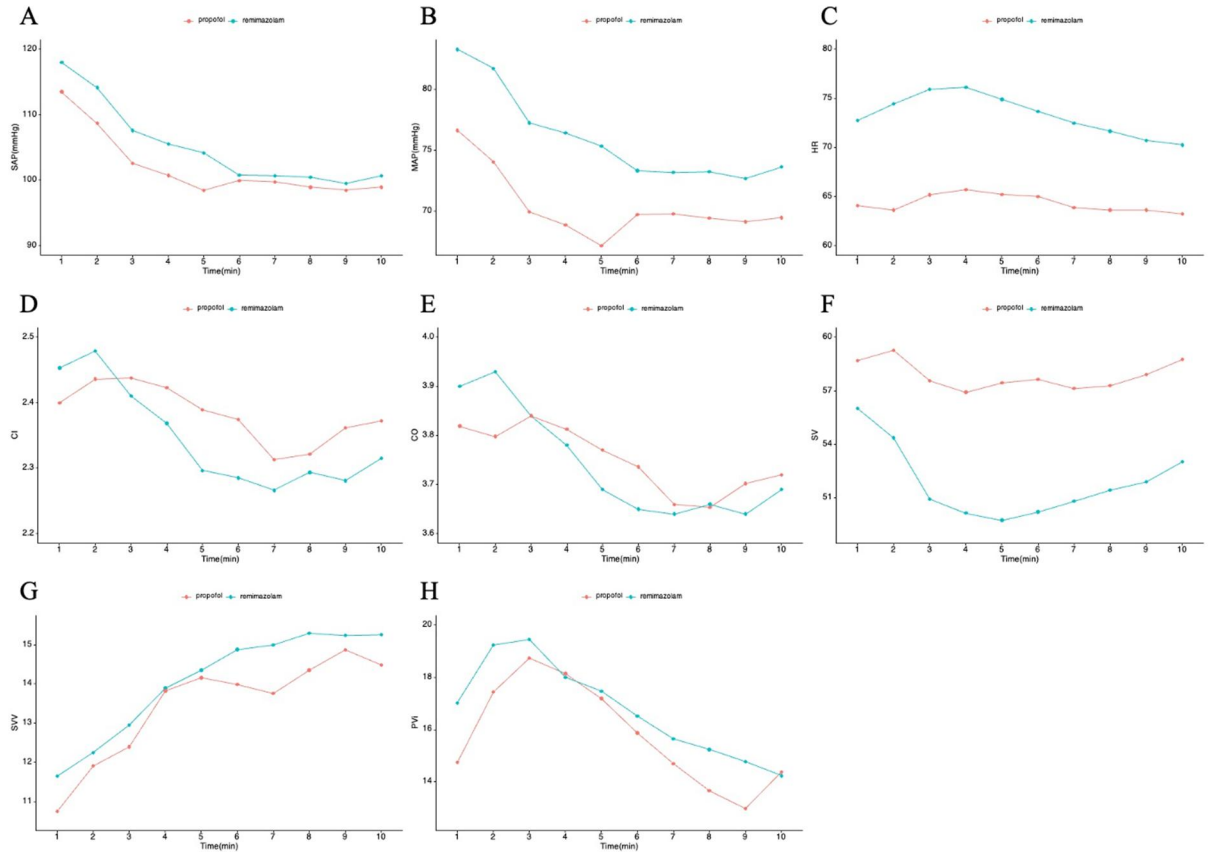

Figure 4A~H. Serial changes in systolic arterial pressure (A), mean arterial pressure (B), heart rate (C), cardiac index (D), cardiac output (E), stroke volume (F), stroke volume variant (G) and pleth variability index (H) during the initial 10 minutes after prone position. In comparison to the propofol group, the remimazolam group exhibited significantly higher mean arterial pressure (p=0.004) and heart rate (p<0.001) during the first 10 minutes after assuming a prone position. Stroke volume was significantly higher in the propofol group than in the remimazolam group (p=0.029).

Abbreviation: SAP, systolic arterial pressure; MAP, mean arterial pressure; HR, heart rate; CI, cardiac index; CO, cardiac output; SV, stroke volume; SVV, stroke volume variant; PVi, pleth variability index

Other secondary outcome hemodynamic parameters including cardiac output and index, stroke volume variation, and pleth variability index were not different between the study groups during the initial 10 minutes after prone positioning.

Discussion

In this randomized controlled study, we compared the effects of remimazolam and propofol-based total intravenous general anesthesia on intraoperative hemodynamic stability during major spine surgery in the prone position. Our study revealed no significant difference in the incidence of hypotensive or severe hypotensive events between the two groups. However, the mean arterial pressure during the initial 10 minutes was higher in the remimazolam group.

Previous studies have reported a lower incidence of decreased blood pressure for remimazolam as compared to propofol [10]. However, these previous trials compared the two drugs in supine positioned patients, which is the major difference among them versus the current study. The prone position itself has a significant impact on physiology, particularly on respiratory and cardiovascular systems. When a patient is turned prone during anesthesia, there can be a decrease in cardiac output due to a reduction in stroke volume. This decline in arterial pressure is partially countered by an escalation in heart rate and peripheral vascular resistance. The reduction in stroke volume is thought to be due to a reduction in pre-load, which can be caused by factors such as blood sequestration, caval compression, amplified intra-thoracic pressure, and the use of positive pressure ventilation and positive end expiratory pressure[5]. Therefore, our study result demonstrated that the prone position itself has a greater effect on the incidence of hypotensive events during major spinal surgery. However, there was a difference between the two groups in the total amount of ephedrine administered during the first hour after assuming a prone position. This can be attributed to the dominant parasympathetic effect of propofol and the dominant sympathetic effect of midazolam during sedation[11 12]. The propofol group exhibited a lower heart rate due to the drug's parasympathetic effect, resulting in a lower heart rate during hypotensive events and more frequent administration of ephedrine. Therefore, the difference in ephedrine dose suggests that remimazolam provides hemodynamic stability during TIVA in prone-positioned patients.

As a secondary finding, we compared the continuous hemodynamic variables such as systolic and

mean arterial pressure, heart rate, cardiac index, cardiac output, stroke volume, stroke volume variability and pleth variability index between the two groups. Our results indicated that the propofol group had a significantly reduced mean arterial pressure as compared to the remimazolam group, along with a lower heart rate and elevated stroke volume in the immediate post-positioning period. Due to the dominant parasympathetic effect of propofol and the dominant sympathetic effect of midazolam during sedation[11 12], the propofol group exhibited a declined heart rate and a greater stroke volume as a result of compensatory venous relaxation[13]. As cardiac output is the product of stroke volume and heart rate, the changes in these two factors may have resulted in no significant difference in cardiac output between the two groups.

The primary objective of perioperative blood pressure management is to ensure adequate organ perfusion. Organ perfusion pressure is determined by the difference between inflow and outflow pressures, with MAP serving as the inflow pressure for most organs and acting as a clinically available surrogate for perfusion pressure[14]. Although there is an ongoing debate regarding whether hypotension should be defined based on absolute or relative blood pressure [14-17], there is consensus that mean arterial pressure below absolute thresholds is progressively associated with both myocardial and kidney injury, with prolonged exposure at any given threshold increasing the odds of injury[3 16]. It is important to note that transient episodes of hypotension, falling below MAP thresholds of 50-65 mmHg, have been associated with renal and myocardial injury[16]. Furthermore, a study by Maheshwari et al. stated that during elective non-cardiac surgery, one-third of hypotension episodes occurred before incision and was significantly associated with acute kidney injury [18]. In our study, we observed that the group receiving propofol had a lower mean arterial pressure as compared to the group receiving remimazolam in the immediate post-positioning period. These findings are noteworthy because maintaining mean arterial pressure above a certain threshold is important in preventing adverse outcomes such as acute kidney injury and myocardial injury. Given that hypotension between anesthetic induction and surgical incision is preventable and is associated with ischemic injuries, it is imperative to consider it as a modifiable risk factor and take steps to avoid it. Our results suggest that remimazolam may be a better option to

propofol for preserving mean arterial pressure during spinal surgery in the immediate period following prone positioning, which is particularly significant because even brief episodes of hypotension have been associated with renal and myocardial injury.

Our study has several limitations. We did not investigate whether the difference in mean arterial pressure between the two groups had an impact on long-term major postoperative complications. Additionally, we did not recognize a specific cutoff value for meaningful hypotensive episodes and blood pressure thresholds related to postoperative myocardial or kidney injury. The generalizability of our findings may be limited due to the study being conducted at a single center and having a relatively small sample size.

In conclusion, our study described no significant differences in the incidence of hypotensive events during the first hour after prone positioning between remimazolam and propofol-based total intravenous general anesthesia. However, the remimazolam group had an increased mean arterial pressure during the initial 10 minutes after prone positioning.

References

1. Roshanov PS, Sheth T, Duceppe E, Tandon V, Bessissow A, Chan MTV, Butler C, Chow BJW, Khan JS, Devereaux PJ: Relationship between Perioperative Hypotension and Perioperative Cardiovascular Events in Patients with Coronary Artery Disease Undergoing Major Noncardiac Surgery. Anesthesiology 2019, 130(5):756-766.

2. Bijker JB, van Klei WA, Vergouwe Y, Eleveld DJ, van Wolfswinkel L, Moons KG, Kalkman CJ: Intraoperative hypotension and 1-year mortality after noncardiac surgery. Anesthesiology 2009, 111(6):1217-1226.

3. Walsh M, Devereaux PJ, Garg AX, Kurz A, Turan A, Rodseth RN, Cywinski J, Thabane L, Sessler DI: Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. Anesthesiology 2013, 119(3):507-515.

4. Wesselink EM, Kappen TH, Torn HM, Slooter AJC, van Klei WA: Intraoperative hypotension and the risk of postoperative adverse outcomes: a systematic review. Br J Anaesth 2018, 121(4):706-721.

5. Edgcombe H, Carter K, Yarrow S: Anaesthesia in the prone position. Br J Anaesth 2008, 100(2):165-183.

6. Clapcich AJ, Emerson RG, Roye DP, Jr., Xie H, Gallo EJ, Dowling KC, Ramnath B, Heyer EJ: The effects of propofol, small-dose isoflurane, and nitrous oxide on cortical somatosensory evoked potential and bispectral index monitoring in adolescents undergoing spinal fusion. Anesth Analg 2004, 99(5):1334-1340.

7. Monk CR, Coates DP, Prys-Roberts C, Turtle MJ, Spelina K: Haemodynamic effects of a prolonged infusion of propofol as a supplement to nitrous oxide anaesthesia. Studies in association with peripheral arterial surgery. Br J Anaesth 1987, 59(8):954-960.

8. Kilpatrick GJ, McIntyre MS, Cox RF, Stafford JA, Pacofsky GJ, Lovell GG, Wiard RP, Feldman PL, Collins H, Waszczak BL et al: CNS 7056: a novel ultra-short-acting Benzodiazepine. Anesthesiology 2007, 107(1):60-66.

9. Kim KM: Remimazolam: pharmacological characteristics and clinical applications in anesthesiology. Anesth Pain Med 2022, 17(1):1-11.

10. Doi M, Morita K, Takeda J, Sakamoto A, Yamakage M, Suzuki T: Efficacy and safety of remimazolam versus propofol for general anesthesia: a multicenter, single-blind, randomized, parallel-group, phase IIb/III trial. J Anesth 2020, 34(4):543-553.

11. Win NN, Fukayama H, Kohase H, Umino M: The different effects of intravenous propofol and midazolam sedation on hemodynamic and heart rate variability. Anesth Analg 2005, 101(1):97-102, table of contents.

12. Hasegawa G, Hirata N, Yoshikawa Y, Yamakage M: Differential effects of remimazolam and propofol on heart rate variability during anesthesia induction. J Anesth 2022, 36(2):239-245.

13. de Wit F, van Vliet AL, de Wilde RB, Jansen JR, Vuyk J, Aarts LP, de Jonge E, Veelo DP, Geerts BF: The effect of propofol on haemodynamics: cardiac output, venous return, mean systemic filling pressure, and vascular resistances. Br J Anaesth 2016, 116(6):784-789.

14. Saugel B, Sessler DI: Perioperative Blood Pressure Management. Anesthesiology 2021, 134(2):250-261.

15. Futier E, Lefrant JY, Guinot PG, Godet T, Lorne E, Cuvillon P, Bertran S, Leone M, Pastene B, Piriou V et al: Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery: A Randomized Clinical Trial. Jama 2017, 318(14):1346-1357.

16. Salmasi V, Maheshwari K, Yang D, Mascha EJ, Singh A, Sessler DI, Kurz A: Relationship between Intraoperative Hypotension, Defined by Either Reduction from Baseline or Absolute Thresholds, and Acute Kidney and Myocardial Injury after Noncardiac Surgery: A Retrospective Cohort Analysis. Anesthesiology 2017, 126(1):47-65.

17. Cohen B, Rivas E, Yang D, Mascha EJ, Ahuja S, Turan A, Sessler DI: Intraoperative Hypotension and Myocardial Injury After Noncardiac Surgery in Adults With or Without Chronic Hypertension: A Retrospective Cohort Analysis. Anesth Analg 2022, 135(2):329-340.

18. Maheshwari K, Turan A, Mao G, Yang D, Niazi AK, Agarwal D, Sessler DI, Kurz A: The association of hypotension during non-cardiac surgery, before and after skin incision, with postoperative acute kidney injury: a retrospective cohort analysis. Anaesthesia 2018, 73(10):1223-1228.

Abstract

Introduction: Perioperative hypotension has been linked to negative perioperative outcomes. In this study, we compared the effects of remimazolam and propofol-based total intravenous general anesthesia on intraoperative hemodynamic stability in patients undergoing surgeries in the prone position.

Methods: In this randomized controlled study, patients undergoing major spinal surgery in the prone position were randomly assigned to the propofol and remimazolam groups. Target-controlled infusion (1.5-3 μg/mL) was used for the induction and maintenance of anesthesia in the propofol group and continuous infusion (6 mg/kg/hr for induction and 0.5-2 mg/kg/hr for maintenance) was used in the remimazolam group, with target-controlled infusion of remifentanil at a rate of 3-5 ng/mL in both groups. The primary outcomes of this study were the incidence of hypotensive and severe hypotensive episodes, and the total amount of inotropic or vasopressor medication used to maintain hemodynamic stability for one hour after prone positioning. The secondary outcomes included systolic and mean arterial pressure, heart rate, cardiac index and output, stroke volume, stroke volume variation, and pleth variability index. All variables were recorded each minute for the first 10 minutes after prone positioning, and every 10 minutes thereafter.

Results: Among the 94 enrolled patients (47 patients in each group), the results indicated no significant difference in the incidence of hypotensive or severe hypotensive events between the two groups during the first hour after prone positioning. The total amount of ephedrine administered during the first hour after prone positioning was less in the remimazolam group (p=0.020) and the mean arterial pressure during the initial 10 minutes after prone positioning was higher in the remimazolam group (p=0.003).

Conclusion: These findings suggest that remimazolam may be a better option than propofol for preserving mean arterial pressure during spinal surgery in the immediate period following prone positioning.

Keywords: spinal surgery; perioperative hypotension; remimazolam