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Original Article

BIS feedback closed-loop target-controlled infusion of propofol or etomidate in elderly patients with spinal surgery

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Abstract: Objective: To investigate the safety of etomidate anesthesia induction combined with Bispectral index (BIS) feedback closed-loop target-controlled infusion of propofol for spinal surgery in elderly patients. Methods: Clinical data of 90 elderly patients who underwent elective spinal surgery were retrospectively analyzed. The patients were assigned to an etomidate group (n=48) and a propofol group (n=42) according to the different anesthesia methods. The etomidate group was anesthetized with etomidate combined with BIS feedback closed-loop target-controlled infusion, and the propofol group was anesthetized with closed-loop target-controlled infusion induced by propofol. The mean arterial pressure (MAP) and heart rate (HR) of the two groups were statistically analyzed 5 min after admission to the operating room (T0), the moment of the intubation (T1), 3 min after intubation (T2), 1 min before prone position (T3), 3 min after prone position (T4), the end of suture skin (T5) and 3 min after supine position (T6). In addition, the vasoactive drug application, awakening time, tracheal tube extraction time and incidence of postoperative complications were compared between the two groups. Results: There were significant changes in MAP and HR from T0 to T1 in both groups (MAP: etomidate group t=5.677, $P<0.001$, propofol group t=8.093, $P<0.001$; HR: etomidate group t=2.731, $P=0.008$, propofol group t=3.967, $P<0.001$). MAP changes in etomidate group from T0 to T1 were less (MAP: t=4.236, $P<0.001$; t=2.082, $P=0.040$), and there was no significant difference in HR between the two groups ($P>0.05$). There were fewer patients receiving vasoactive drugs in the etomidate group ($\chi^2=5.070$, $P=0.024$), but no significant difference was found in the incidence of complications between the two groups, $\chi^2=3.670$, $P=0.055$. Conclusion: Compared to propofol, the application of etomidate combined with BIS feedback closed-loop target-controlled infusion in spinal surgery anesthesia for elderly patients can keep hemodynamics in a stable state, without affecting postoperative resuscitation, showing high safety, so it is worthy of clinical application.

Keywords: Spinal surgery, etomidate, propofol, BIS, loop target controlled infusion, elderly patients, anesthesia

Introduction

Spinal diseases are mostly caused by an accumulation of long sitting time and improper sitting posture and are more common in the elderly due to the long-term formation process [1]. With the acceleration of the aging of China's population, there are an increasing number of elderly people with spinal diseases, so more and more spinal surgeries are needed. In elderly patients, the reserve and compensative functions of each organ are decreased, and the pharmacokinetics and pharmacodynamics have changed, so the depth of anesthesia is not easy to control. In addition, spinal surgery is performed in a prone position, so the anesthesia induction and position transformation are prone to cyclic adverse events [2]. Therefore, the selection of anesthetic drugs for spinal surgery in elderly patients has become a clinical concern. Studies have shown that etomidate has mild inhibition of circulatory function and is suitable for anesthesia induction in the elderly [3]. Bispectral index (BIS) feedback closed-loop target-controlled infusion system can stabilize hemodynamics, which is conducive to personalized drug use [4]. Our project team found that etomidate was used to stablize hemodynamics

in elderly patients during anesthesia induction in spinal surgery. Based on the above findings, we hypothesized that anesthesia induction with etomidate combined with anesthesia maintenance with BIS feedback propofol closed-loop target-controlled infusion could be used in elderly patients undergoing spinal surgery. We hope to understand if this combination could stabilize the anesthesia process and hemodynamics in elderly patients undergoing spinal surgery, thus speeding up patients' recovery and reducing postoperative complications. After collecting a large amount of literature, researchers found that there were only a few relevant studies reported at present. Therefore, the application of etomidate combined with BIS feedback for spinal surgery in elderly patients may become a new anesthesia method. In this study, a retrospective analysis was used to collect clinical data of elderly patients undergoing elective spinal surgery, aiming to explore the safety of etomidate combined with BIS feedback closed-loop target-controlled infusion, and to provide a reference for further improving the anesthesia safety in such patients.

Materials and methods

Sample size calculation

In this study, patients in the propofol group (control group) were selected by the pairing method. The iterative expanding radius matching method was applied to initiate pairing, and the matching ratio was 1:1 to 1:4. After the matching ratio reached 1:4, the number of matching cases was increased. There were 48 elderly patients undergoing elective spinal surgery who were anesthetized by etomidate combined with BIS feedback closed-loop target-controlled infusion. The paired factors of the propofol group were sex, age, weight and ASA to make the two groups comparable. Forty-two patients were selected as the propofol group from the patients who were anesthetized with closed-loop target-controlled infusion induced by propofol.

Data source

This study was approved by the Ethics Committee of The Second Affiliated Hospital of Xi'an Medical University and adopted a retrospective cohort study design. Through the electronic medical record system, 90 elderly patients who underwent elective spinal surgery in our hospital from February 2019 to February 2022 were selected according to the following inclusion criteria. 1) Patients underwent elective spinal surgery. 2) Patients were 60 years old or older, and without delirium, coma, or disturbance of consciousness before surgery. 3) Patients had no significant hearing impairment or loss, visual impairment, or dementia before surgery. 4) Patients were evaluated with American Standards Association (ASA) scale [5] and had Grade I-III. 5) Patients had complete and standardized medical records, including clinical data, preoperative examination results, surgical data, treatment data and complications records.

We excluded patients whose body mass index <18 or >28 kg/m^2, patients who underwent local anesthesia only, patients with incomplete data and required Statistical Analysis System (SAS) calculation, patients who underwent simultaneous surgery on other body parts, patients with an ASA rating higher than Grade IV, or patients who died within 24 hours after surgery.

Data collection

Clinical data included the mean arterial pressure (MAP) and heart rate (HR) of patients 5 min after admission to the operating room (T0), the moment of the intubation (T1), 3 min after intubation (T2), 1 min before prone position (T3), 3 min after prone position (T4), at the end of suture skin (T5) and 3 min after supine position (T6).

Treatment data included the vasoactive drug application, awakening time, tracheal tube extraction time, and incidence of postoperative complications.

Grouping and anesthesia methods

Grouping: Patients were assigned to an etomidate group and a propofol group according to the different anesthesia methods. The etomidate group was anesthetized by etomidate combined with BIS feedback closed-loop target-controlled infusion, and the propofol group was anesthetized by propofol-induced closed-loop target-controlled infusion.

Anesthesia induction: Patients in both groups received tracheal intubation and general anesthesia and used CONCERT-CLE closed-

loop target-controlled infusion pump (Guangxi Veryag Technology Co., LTD.). Both groups were given a target-controlled infusion of sufentanil 0.35 μg/L (Gepts model with pharmacokinetic parameters) and a T1 closed-loop target-controlled infusion of cisatracurium (0.16 mg/kg). After the plasma concentration was balanced, the etomidate group was treated with a target-controlled infusion of etomidate (Arden model, plasma target concentration 0.5 μg/mL, pharmacokinetic parameters), with a gradually increasing amplitude from 0.1 μg/mL until BIS was less than 60. The propofol group was treated with a target-controlled infusion of propofol (Marsh model with pharmacokinetic parameters, plasma target concentration of 1.5 μg/mL), with a gradually increasing amplitude from 0.5 μg/mL until BIS was less than 60. Mechanical ventilation of endotracheal intubation was performed when BIS was less than 60 and T1 was less than 10%.

Maintenance of anesthesia: Etomidate group: Before anesthesia induction, CONCERT-CLE closed-loop target-controlled infusion pump was connected to an empty syringe. The target BIS value was set as 50, and the target-controlled range was set as 45-55 according to etomidate (plasma target concentration 2.5 μg/mL), which was used as feedback target to automatically adjust the target-controlled concentration mode of etomidate (patients without intravenous access). About 15 minutes later, after plasma concentration balance was reached and the patient's BIS dropped to 60, etomidate was connected and the patient's intravenous channel to maintain anesthesia in the closed-loop mode mentioned above (this was the key step to achieve the maintenance of anesthesia in the closed-loop target-controlled infusion of etomidate and BIS feedback).

Propofol group: When the BIS of patients decreased to 60, the closed-loop target-controlled infusion was started. The target BIS value was set as 50, and the target range was set as 45-55, which was used as feedback target to automatically adjust the target-controlled concentration of propofol.

In both groups, target-controlled infusion of remifentanil (target-controlled concentration 3 ng/mL) and T1 closed-loop target-controlled infusion of cisatracurium were maintained for anesthesia. The infusion speed was adjusted according to the intraoperative stimulation intensity, heart rate and blood pressure of the patient. Besides, vasocontractile drugs (such as norepinephrine and norepinephrine) and antihypertensive drugs were used when necessary to maintain the patient's hemodynamics stable. After surgery, anesthesia was stopped, the patients were sent to the anesthesia recovery room, and the tracheal tube was immediately removed when the patient reached the extubation indication. Patients were sent back to the ward after their Aldrete score exceeded 9 points.

Statistical methods

Data were analyzed by statistical software SPSS 22.0. N (%) was used to express counting data, and the χ^2 test was used for comparison between groups. The measurement data conforming to normal distribution were expressed by $\bar{x}\pm sd$, and the comparisons between groups were processed using t-test, and data at multiple time points using repeated measure ANOVA. $P<0.05$ was considered statistically significant.

Results

General data and technical roadmap

There were 48 cases in the etomidate group and 42 cases in the propofol group. The comparison of general data between the two groups showed no statistical significance ($P>0.05$), indicating comparability. The data were shown in **Table 1**, and the technology roadmap of this study is shown in **Figure 1**.

Hemodynamic changes

MAP: Compared with those at T0, the MAP changed significantly at T1 in both groups, but MAP decreased more significantly in the propofol group (Etomidate group: t=5.677, $P<0.001$; Propofol group: t=8.093, $P<0.001$). The MAP values at T1 were significantly different between the two groups (t=4.236, $P<0.001$), but there was no significant difference in MAP between the two groups at T2-T4 ($P>0.05$). The data are shown in **Table 2**. Bonferroni's pair-to-pair comparison showed that the MAP at T0 was different from those at T1 to T6, the MAP at T1 was different from those at T2, T3, T5 and T6, the MAP at T2 was different from that at T4, the MAP at T3 was different from that at T5, and

Table 1. Comparison of general data

Group	Sex [n (%)]		Age ($\bar{x}$±s, year)	Weight ($\bar{x}$±s, kg)	BMI	ASA		
	male	female				grade I	grade II	grade III
Etomidate group (n=48)	28 (58.33)	20 (41.67)	69.19±4.93	66.43±10.69	22.46±2.58	15 (31.25)	22 (45.83)	11 (22.92)
Propofol group (n=42)	23 (54.76)	19 (45.24)	68.31±4.07	65.27±9.84	22.74±2.39	10 (23.81)	23 (54.76)	9 (21.43)
χ^2/t	0.116		1.456	0.533	0.532	-0.418		
P	0.733		0.149	0.595	0.596	0.676		

BMI, Body Mass Index; ASA, American Standards Association scale.

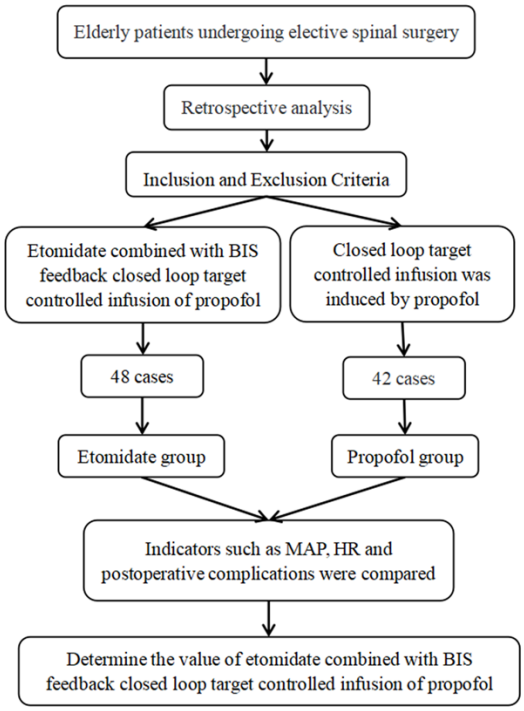

Figure 1. Technology roadmap.

the MAP at T4 was different from those at T5 and T6. See **Table 4**.

HR values: Compared with those at T0, HR values changed significantly at T1 in the two groups, but decreased more significantly in the propofol group (Etomidate group: t=2.731, *P*=0.008; Propofol group: t=3.967, *P*<0.001), and HR values were significantly different between the two groups at T1 (t=2.082 and *P*=0.040), but there was no significant difference in HR values between the two groups at T2-T4 (*P*>0.05). The data are shown in **Table 3**. The results of Bonferroni's pair-to-pair comparison showed that HR at T0 was different from those at T1 and T4, the HR at T1 was different from those at T5 and T6, the HR at T3 was different from that at T4, and the HR at T4 was different from those at T5 and T6, as shown in **Table 4**.

After analysis of variance by repeated measures, MAP and HR of the two groups had no interaction (MAP: $F_{interaction}$=1.629, *P*=0.137; $F_{intergroup}$=27.020, *P*<0.001; F_{time}=18.730, *P*< 0.001. HR: $F_{interaction}$=0.388, *P*=0.887; F=9.119, *P*<0.001; F_{time}=13.350, *P*=0.003).

Vasoactive drug application, awakening time and tracheal tube extraction time

In the etomidate group, the application of vasoactive drugs, awakening time and tracheal tube extraction time were 42.86%, (9.05±2.37) min and (12.36±3.03) min, respectively. In the propofol group, the data were 18 cases (42.86%), (9.58±3.05) min and (13.66±3.91) min, respectively.

There were fewer patients receiving vasoactive drugs in the etomidate group than those in the propofol group, χ^2=5.070, *P*<0.05. There was no significant difference in the awakening time and tracheal tube extraction time between the two groups (t=0.926, 1.774; *P*=0.357, 0.079). See **Figure 2**.

Incidence of postoperative complications

There was 1 case of myoclonus, 3 cases of postoperative agitation, 8 cases of emesis in the etomidate group, and 4 cases of postoperative agitation in the propofol group, as shown in **Table 5**. There was no significant difference in total postoperative complications between the two groups (χ^2=3.670, *P*=0.055), as shown in **Figure 3**.

Discussion

The elderly undergo degenerative changes of body functions, which reduce their tolerance and adjustment ability to anesthesia and surgical stimulation. Therefore, the stress response of elderly patients during surgery may be greater than that of young patients, which brings higher anesthesia risk to elderly patients [6]. In addition, the position for spinal surgery is

Table 2. MAP at different time points ($\bar{x}\pm s$)

Time	MAP (mmHg)		t	*P*
	Etomidate group (n=48)	Propofol group (n=42)		
T0	91.08±9.16	91.21±9.29	0.067	0.947
T1	82.03±6.17	75.41±8.59	4.236	<0.001
T2	86.33±7.62	84.25±8.19	1.248	0.215
T3	84.15±7.52	81.19±7.05	1.918	0.058
T4	81.65±6.09	79.39±8.17	1.499	0.137
T5	87.56±6.98	85.33±7.08	1.502	0.137
T6	86.39±6.05	84.28±6.19	1.633	0.106

MAP, Mean Arterial Pressure.

Table 3. HR at different time points ($\bar{x}\pm s$)

Time	HR (times/min)		t	*P*
	Etomidate group (n=48)	Propofol group (n=42)		
T0	76.39±10.18	75.92±11.06	0.210	0.834
T1	71.06±8.90	67.05±9.36	2.082	0.040
T2	74.95±11.33	71.26±10.97	1.564	0.121
T3	75.37±9.42	72.10±9.58	1.630	0.107
T4	70.36±8.52	66.38±9.17	2.134	0.036
T5	76.92±9.24	74.59±10.88	1.099	0.275
T6	75.84±8.59	73.66±9.07	1.170	0.245

HR, Heart Rate.

prone, so position conversion easily causes adverse circulatory events. Therefore, the selection of anesthetic drugs and their application in spinal surgery for elderly patients are focuses in this type of surgery.

In this study, clinical data of elderly patients undergoing elective spinal surgery were analyzed. The etomidate group used etomidate combined with BIS feedback closed-loop target-controlled infusion for surgical anesthesia, while the propofol group used BIS feedback propofol-induced closed-loop target-controlled infusion. The closed-loop target-controlled infusion was an intelligent and individualized anesthesia auxiliary method [7, 8]. By setting the BIS value, the closed-loop target-controlled infusion could also avoid deep anesthesia [9].

Propofol is an alkyl acid anesthetic, which is a common anesthetic induction and maintenance drug. Because of its rapid and stable induction of anesthesia, rapid metabolism in the body and good controllability, patients can recover quickly and smoothly after drug withdrawal, and patients usually do not have vertigo and drowsiness and can maintain clear consciousness. This made propofol an alternative to inhalation anesthesia and the drug of choice among the same class of intravenous anesthetics [10, 11]. However, with the deepening of medical studies on propofol, it was found that propofol could inhibit the respiratory and circulatory systems, leading to related adverse reactions [12]. We conducted a literature review and clinical observation and analyzed etomidate as an alternative anesthesia induction drug, it was found that etomidate could reduce the adverse effects of propofol. Etomidate is a non-barbiturate drug that leads to stable hemodynamics and light respiratory inhibition, which is different from propofol [13, 14]. For elderly patients, their physical conditions can lead to cardiovascular and cerebrovascular issues, such as myocardial ischemia and valvular heart disease. Etomidate had a wider safety range than propofol [15]. However, at present, etomidate was rarely used in the maintenance of anesthesia clinically, because etomidate had a certain impact on the adrenal cortex of the body [16, 17]. Propofol had no significant effect on liver function, kidney function and corticosteroid synthesis.

Hemodynamics mainly reflects the state of blood flow and whether the blood vessels are deformed, including ventricular ejection velocity in the systolic phase, blood filling degree in the diastolic phase, blood discharge time and cardiac output. It is an important objective of surgical anesthesia to maintain hemodynamic stability. Therefore, this study selected MAP and HR, which can indicate the stability of hemodynamics, for observation. Statistically, there were significant changes in MAP and HR in both groups immediately after intubation, but the etomidate group showed less change in the MAP than the propofol group did, and the changes in HR were not significantly different between the two groups. These results suggest that the use of etomidate combined BIS feed-

Table 4. *P* values of Bonferroni pairwise comparisons

Time	MAP						HR					
	T1	T2	T3	T4	T5	T6	T1	T2	T3	T4	T5	T6
T0	<0.001	<0.001	<0.001	<0.001	0.009	<0.001	<0.001	0.671	1.000	<0.001	1.000	1.000
T1	-	<0.001	0.004	1.000	<0.001	<0.001	-	0.334	0.094	1.000	<0.001	<0.001
T2	-	-	0.484	0.001	1.000	1.000	-	-	1.000	0.069	1.000	1.000
T3	-	-	-	0.876	7	0.237	-	-	-	0.01	1.000	1.000
T4	-	-	-	-	<0.001	<0.001	-	-	-	-	<0.001	<0.001
T5	-	-	-	-	-	1.000	-	-	-	-	-	1.000

MAP, Mean Arterial Pressure; HR, Heart Rate.

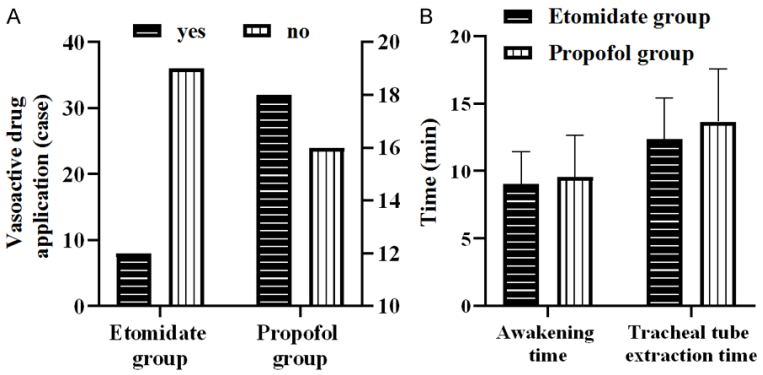

Figure 2. Vasoactive drug application, awakening time and tracheal tube extraction time. Note: The number of cases was 48 in the etomidate group and 42 in the propofol group.

Table 5. Incidence of postoperative complications [n (%)]

Group	Myoclonus	Postoperative agitation	Emesis
Etomidate group (n=48)	1 (2.08)	3 (6.25)	8 (16.67)
Propofol group (n=42)	0 (0.00)	4 (9.52)	0 (0.00)
Z		-1.905	
P		0.057	

back under closed-loop target-controlled infusion of propofol anesthesia could make stable hemodynamics in elderly patients, and the combination of etomidate induction and propofol maintenance was superior to propofol induction and maintenance alone. The possible reason was that propofol had a significant inhibitory effect on sympathetic nerve activity, which could directly dilate blood vessels and inhibit the myocardium, leading to a significant decrease in HR and blood pressure, resulting in significant fluctuations in the hemodynamics of patients [18]. In addition, studies [19] had shown that the older patients were, the more sensitive their central nervous system was to propofol, that is, propofol had stronger cardiovascular inhibition and sedation effect on elderly patients. Etomidate had no direct inhibitory effect on the respiratory and circulatory systems [20], no significant effect on the tension discharge of sympathetic nerves and baroreceptors and did not affect the reflex of the autonomic nervous system. Therefore, this drug could maintain the blood pressure in a stable state and keep the patient's hemodynamics stable [21]. In this study, the number of patients in the etomidate group receiving vasoactive drugs was less than that in the propofol group, indicating that the cardiovascular inhibition of etomidate was weaker than that of propofol, therefore resulted in more stable hemodynamics in patients. The awakening time and tracheal tube extraction time in the etomidate group were not significantly different from those in the propofol group, suggesting that surgical anesthesia performed by etomidate combined with BIS feedback propofol closed-loop target-controlled infusion did not affect the postoperative resuscitation of elderly patients.

There was 1 case of myoclonus, 3 cases of postoperative agitation and 8 cases of emesis in the etomidate group, and 4 cases of postoperative agitation in the propofol group, but no significant difference was found in the total number of complications between the two groups ($P>0.05$). Agitation during postoperative recovery was a common adverse reaction in patients with general anesthesia. It can be

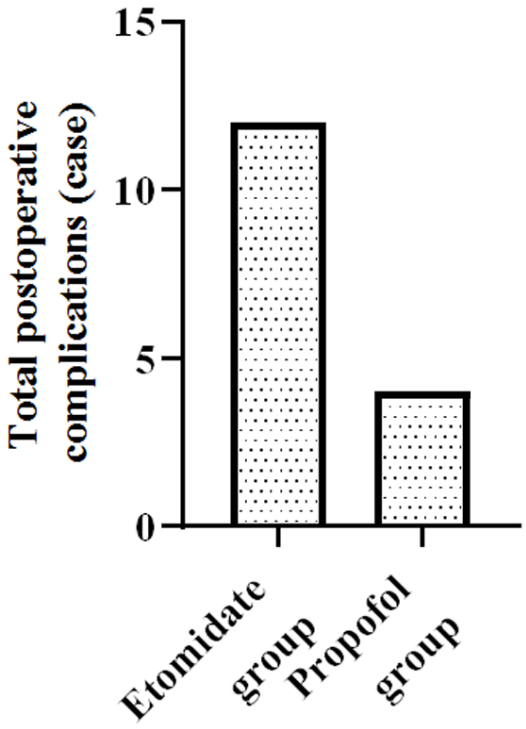

Figure 3. Total postoperative complications. Note: The number of cases was 48 in the etomidate group and 42 in the propofol group.

caused by urinary duct irritation, surgical incision pain, muscle relaxant residue, CO_2 retention, etc. At present, the mechanism of etomidate-induced myoclonus is not completely clear, but it may be related to the inhibition of spinal cord and cerebral cortex by etomidate, leading to the disinhibition of subcortical structure. Studies have shown that etomidate could compete with endogenous dopamine for dopamine receptors after reaching the substantia nigra and striatum in the brain, and the resulting competitive inhibition could reduce endogenous dopamine and cause myoclonus in patients [22]. The results of this study also showed that etomidate caused more nausea and Emesis symptoms than propofol, so we suggest that patients using etomidate should be routinely given antiemetic drugs.

Advantages and limitations

This study found that for spinal surgery anesthesia in elderly patients, the application of etomidate induction and maintenance could help the stability of hemodynamics in patients, so that patients obtained greater clinical benefits. Etomidate has clinical application value and a positive role in the anesthesia of clinical spinal surgery. However, there are some shortcomings in this study. Firstly, this is a retrospective study, and there was no prospective controlled experiments to verify the reliability of the results of this study. Secondly, this is a single-center study with limited patient sample, so the effect of etomidate induction in spinal anesthesia should be studied in extended external samples. Lastly, in terms of the design of the study, there were no more point-in-time evaluations of outcome measurements and no postoperative recovery evaluations. Therefore, future studies should be extended to prospective multi-centers, multi-time points and postoperative evaluations, so as to further confirm the conclusions of this study.

Conclusion

To sum up, compared to propofol, etomidate combined with BIS feedback closed-loop target-controlled infusion in spinal surgery anesthesia for elderly patients can keep hemodynamics in a stable state, without affecting postoperative resuscitation, showing high safety, so it is worthy of clinical application.

Disclosure of conflict of interest

None.

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References

[1] Arsh A, Darain H, Iqbal M, Rahman MU, Ullah I and Khalid S. Effectiveness of manual therapy to the cervical spine with and without manual therapy to the upper thoracic spine in the management of non-specific neck pain; a randomized controlled trial. J Pak Med Assoc 2020; 70: 399-403.

[2] Soncrant C, Neily J, Sum-Ping SJT, Wallace AW, Mariano ER, Leissner KB, Mills PD, Mazzia L and Paull DE. Sharing lessons learned to prevent adverse events in anesthesiology nationwide. J Patient Saf 2021; 17: e343-e349.

[3] Zheng H, Zhu Y, Chen K and Shen X. The effect of etomidate or propofol on brainstem function during anesthesia induction: a bispectral index-guided study. Drug Des Devel Ther 2019; 13: 1941-1946.

[4] Yamada N, Shiba J, Kikuchi H, Yamada T, Taga N and Takeuchi M. Bispectral index™ variation during living donor liver transplantation in a child with hepatic encephalopathy: a case report. JA Clin Rep 2021; 7: 66.
[5] Doi M, Hirata N, Suzuki T, Morisaki H, Morimatsu H and Sakamoto A. Safety and efficacy of remimazolam in induction and maintenance of general anesthesia in high-risk surgical patients (ASA class III): results of a multicenter, randomized, double-blind, parallel-group comparative trial. J Anesth 2020; 34: 491-501.
[6] Südfeld S, Brechnitz S, Wagner JY, Reese PC, Pinnschmidt HO, Reuter DA and Saugel B. Post-induction hypotension and early intraoperative hypotension associated with general anaesthesia. Br J Anaesth 2017; 119: 57-64.
[7] Araújo NMS, Dias LP, Costa HPS, Sousa DOB, Vasconcelos IM, de Morais GA and Oliveira JTA. CITI, a Kunitz trypsin inhibitor purified from Cassia leiandra Benth. seeds, exerts a candidicidal effect on Candida albicans by inducing oxidative stress and necrosis. Biochim Biophys Acta Biomembr 2019; 1861: 183032.
[8] Vecchione M, Ghezzi V, Alessandri G, Dentale F and Corr PJ. BIS and BAS sensitivities at different levels of personality description: a latent-variable approach with self- and informant-ratings. J Pers Assess 2021; 103: 246-257.
[9] Li Z, Cai J, Li J, Xu X and Zheng L. Comparative evaluation of the bispectral index (BIS) and BISpro during propofol anaesthesia. J Int Med Res 2021; 49: 3000605211001705.
[10] Liang Z, Cheng L, Shao S, Jin X, Yu T, Sleigh JW and Li X. Information integration and mesoscopic cortical connectivity during propofol anesthesia. Anesthesiology 2020; 132: 504-524.
[11] Şimşek HO, Kocatürk Ö, Demetoğlu U and Gürsoytrak B. Propofol based total intravenous anesthesia versus sevoflurane based inhalation anesthesia: the postoperative characteristics in oral and maxillofacial surgery. J Craniomaxillofac Surg 2020; 48: 880-884.
[12] Berndt N, Rösner J, Haq RU, Kann O, Kovács R, Holzhütter HG, Spies C and Liotta A. Possible neurotoxicity of the anesthetic propofol: evidence for the inhibition of complex II of the respiratory chain in area CA3 of rat hippocampal slices. Arch Toxicol 2018; 92: 3191-3205.
[13] Messina AG, Wang M, Ward MJ, Wilker CC, Smith BB, Vezina DP and Pace NL. Anaesthetic interventions for prevention of awareness during surgery. Cochrane Database Syst Rev 2016; 10: CD007272.
[14] Pich J. Anaesthetic interventions for prevention of awareness during surgery. J Perioper Pract 2019; 29: 38-39.
[15] Song JC, Lu ZJ, Jiao YF, Yang B, Gao H, Zhang J and Yu WF. Etomidate anesthesia during ERCP caused more stable haemodynamic responses compared with propofol: a randomized clinical trial. Int J Med Sci 2015; 12: 559-565.
[16] Meyancı Köksal G, Erbabacan E, Tunalı Y, Karaören G, Vehid S and Öz H. The effect of single dose etomidate during emergency intubation on hemodynamics and adrenal cortex. Ulus Travma Acil Cerrahi Derg 2015; 21: 358-365.
[17] Goettel N, Bharadwaj S, Venkatraghavan L, Mehta J, Bernstein M and Manninen PH. Dexmedetomidine vs propofol-remifentanil conscious sedation for awake craniotomy: a prospective randomized controlled trial. Br J Anaesth 2016; 116: 811-821.
[18] Subramaniam B, Shankar P, Shaefi S, Mueller A, O'Gara B, Banner-Goodspeed V, Gallagher J, Gasangwa D, Patxot M, Packiasabapathy S, Mathur P, Eikermann M, Talmor D and Marcantonio ER. Effect of intravenous acetaminophen vs placebo combined with propofol or dexmedetomidine on postoperative delirium among older patients following cardiac surgery: the DEXACET randomized clinical trial. JAMA 2019; 321: 686-696.
[19] Smischney NJ, Hoskote SS, Gallo de Moraes A, Racedo Africano CJ, Carrera PM, Tedja R, Pannu JK, Hassebroek EC, Reddy DR, Hinds RF and Thakur L. Ketamine/propofol admixture (ketofol) at induction in the critically ill against etomidate (KEEP PACE trial): study protocol for a randomized controlled trial. Trials 2015; 16: 177.
[20] Gyulaházi J, Varga K, Iglói E, Redl P, Kormos J and Fülesdi B. The effect of preoperative suggestions on perioperative dreams and dream recalls after administration of different general anesthetic combinations: a randomized trial in maxillofacial surgery. BMC Anesthesiol 2015; 15: 11.
[21] Matchett G, Gasanova I, Riccio CA, Nasir D, Sunna MC, Bravenec BJ, Azizad O, Farrell B, Minhajuddin A, Stewart JW, Liang LW, Moon TS, Fox PE, Ebeling CG, Smith MN, Trousdale D and Ogunnaike BO; EvK Clinical Trial Collaborators. Etomidate versus ketamine for emergency endotracheal intubation: a randomized clinical trial. Intensive Care Med 2022; 48: 78-91.
[22] Gupta M and Gupta P. Nalbuphine pretreatment for prevention of etomidate induced myoclonus: a prospective, randomized and double-blind study. J Anaesthesiol Clin Pharmacol 2018; 34: 200-204.