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Original Article

Clinical research on postoperative analgesia effect of using dezocine before suturing skin in patients with internal fixation of spine

Xueping Wen[1*], Ying Huang[3,4*], Yuanli Chen[3,4*], Shangping Fang[5], Suzhen Wu[2]

[1]Department of Orthopedics, Ningxiang People's Hospital of Hunan Province, Ningxiang, Hunan, China; [2]Department of Anesthesiology, Ningxiang People's Hospital of Hunan Province, Ningxiang, Hunan, China; [3]Jiangsu Province Key Laboratory of Anesthesiology, Xuzhou Medical College, China; [4]Jiangsu Province Key Laboratory of Anesthesia and Analgesia Application Technology, China; [5]Department of Anesthesiology, Changzheng Hospital, The Second Military Medical University, China. [*]Equal contributors.

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Abstract: Objective: To discuss the effect of using different doses of dezocine before suturing skin on the postoperative pain of patients, and to evaluate the analgesia effect and the optimal dose of dezocine in inter-fixation of spine. Methods: 80 cases of patients underwent inter-fixation of spine were selected and randomly divided into four groups (n = 20): Group D1 (dezocine 0.1 mg/kg),Group D2 (dezocine 0.15 mg/kg), Group D3 (dezocine 0.20 mg/kg) and control group (Group C) (normal saline 5 ml). Group D1, D2 and D3 were intravenously injected of different dosage of dezocine 5 min before suturing skin, while Group C were intravenously injected with 5 ml saline, The four groups used postoperative sufentanil PCIA for analgesia. We observed and recorded blood pressure (BP), heart rate (HR), respiratory rate (RR) and pulse oxygen saturation of patients at entering PACU (T0), extubation (T1), 2 min post-extubation (T2), 5 min post-extubation (T3) and 10 min post-extubation (T4). In addition, we also recorded surgery time, wake up time, extubation time, cough score, agitation score, Ramsay score and postoperative VAS score, postoperative sufentanil dosage and adverse reactions of four groups of patients. Results: (1) The VAS scores within postoperative 24 h and the postoperative Sufentanil dosage of Group D1, D2 and D3 were lower than Group C, while Group D2, D3 was lower than Group D1 ($P<0.05$); (2) The wake up time and extubation time of Group D1, D2 and C were shorter than Group D3, the difference were statistically significant ($P<0.05$); Ramsay scores in postoperative 2 h of Group D1, D2, and Group C were shorter than Group D3, and the difference were statistically significant ($P<0.05$). (3) The cases of dizziness and drowsiness of Group D1, D2 and Group C were less than Group D3, and the difference were statistically significant ($P<0.05$). Conclusions: (1) The postoperative analgesia effect of using dezocine at 5min before suturing skin is positivein inter-fixation of spine. (2) The application of dezocine in inter-fixation of spine can significantly reduce the stress reaction during wakening period, improve postoperative analgesia satisfaction and reduce postoperative sufentanil dosage. (3) The most optimal dose of dezocine is 0.15 mg/kg with least adverse reactions.

Keywords: dezocine, inter-fixation of spine, postoperative analgesia

Introduction

In addition to respiration, pulse, blood pressure and body temperature, pain has been considered as "the fifth vital sign" [1]. In the environment of modern medical paradigm shift, exploring an ideal analgesia way to reduce the postoperative pain, as well as to reduce the impact on body brought by surgical trauma, and to improve the comfort degree of patients has been a pursuing goal for medical staff [2]. In order to improve postoperative analgesia effect and reduce the occurrence of adverse reactions, it is advocated to use a balanced or multimodes analgesia way, which is to administrate drugs at different time, and by different ways or combine use of different drugs etc. to act on different phase and different target of pathophysiological mechanisms, to overcome the shortage and reduce pain, side effects and impact on body caused by single medication, as well as to further maintain a relatively stable internal environment [3]. We proposed to apply different doses of dezocine at 5 min before

suturing skin to study its effect of postoperative analgesia. However, the analgesic efficacy of dezocine can be enhanced with the dose increasing, and this will cause excessive sedation and even respiratory depression and other adverse reactions [4]. Therefore, the research on the best dose of dezocine is particularly important. This study selected 80 cases of patients undergoing selective inter-fixation of spine [5] in our hospital from January 2015 to October 2015 as research subjects; the patients were infused with different doses of dezocine as well as normal saline at 5 minutes before skin closure, to evaluate the analgesic effect of dezocine and the most optimal dosage in inter-fixation surgery, so as to provide a reliable basis for the post-operative analgesia in spinal inter-fixation [5].

Material and methods

Grouping

This study was approved by the ethics committee of our hospital, and the informed consent was obtained from all patients. 80 cases of patients, who were scheduled for spinal interfixation surgery in our hospital, were chosen for this study, including 43 cases of male and 37 cases of female with ASA levels of I-II, the patients aged from 25-60 years old and BMI ranged from 16 to 25. The patients were randomly divided into 4 groups (n=20 in each group) according to random number table. Group D1 (dezocine 0.1 mg/kg), Group D2 (dezocine 0.15 mg/kg), Group D3 group (dezocine 0.20 mg/kg), and Group C (normal saline 5 ml). Each group was infused at 5 minutes before skin was sutured. The included patients were excluded from respiratory dysfunction, severe liver and renal function damage, cardiovascular and cerebrovascular disease history, and analgesic drugs application history for long term.

Methods of anesthesia and analgesia

Tracheal intubation was used on patients after induction of anesthesia with midazolam 0.04 mg/kg, fentanyl 5 μg/kg, vecuronium bromide 0.1 mg/kg and propofol 1 mg/kg [6]. After intubation, pump infusion of propofol, remifentanil and cisatracurium to maintain anesthesia. During the operation, when the anesthesia was shallow, fentanyl was added; the total amount of fentanyl should not exceed 10 μg/kg; maintain the stability of hemodynamics. Stop adding fentanyl in 1.5 h before the end of the operation, and do not use muscle relaxants in 30 minutes before the end of surgery. Group D1, D2 and D3 were intravenously injected of dezocine 0.1 mg/kg, 0.15 mg/kg and 0.20 mg/kg respectively at 5 minutes before suturing skin, while Group C was intravenously injected of 5ml normal saline. All patients underwent sufentanil PCIA for analgesia after operation.

Observation index

The blood pressure, heart rate, breathing rate and pulse oxygen saturation of patients were recorded at entering PACU (T0), extubation (T1), 2minutes after extubation (T2), 5minutes after extubation (T3) and 10 minutes after extubation (T4).

The operation time, wake up time, extubation time and Ramsay sedation score, cough score and agitation score of all patients were observed and recorded [8].

The VAS score at postoperative 2 h (P1), 6 h (P2), 12 h (P3) and 24 h (P4), and the incidence of adverse reactions as well as postoperative dosage of sufentanil were recorded.

Coughing score: 1 point, no cough or only cough at extubation; 2 points, regular spontaneous breathing and cough while catheter was in trachea; 3 points, cough or choke under un-spontaneous breathing [9].

Agitation score: 0 point, peaceful cooperation; 1 point, mild irritation, physical activity under sputum suction stimulation, intermittent moan; 2 points, agitate without stimulation, sustained groan; 3 points, continuous struggle and shout, extra-force were required to press limbs [10].

Pain score: VAS score method was adopted (0 point for pain free, 10 points for unbearable pain, patients self-evaluated according to their own pain) [7].

Sedation score: Ramsay sedation score method was adopted (stage 1 for agitated or restless; stage 2 for co-operative, oriented and tranquil; stage 3 for response to instructions; stage 4 for brisk response to loud auditory stimulus; stage 5 for sluggish response to loud auditory stimulus; and stage 6 for no response) [11].

Table 1. General situation in four groups of patients before anesthesia

Group	Cases	Gender (male/female)	Age (year)	ASA (I/II)	BMI (kg/m^2)	SBP (mmHg)	HR (time/min)
D1	20	13/7	43.9±11.8	11/9	21.5±1.4	115.9±9.3	74.8±6.3
D2	20	11/9	42.8±12.7	10/10	22.1±1.7	116.8±8.8	75.5±6.4
D3	20	10/10	42.5±12.5	13/7	21.7±1.3	115.9±9.6	74.9±6.2
C	20	8/12	43.5±12.3	8/12	19.9±1.5	116.6±9.5	75.8±5.9

Table 2. Comparison of SBP in four groups of patients during recovery period (x±s)

Index	Group	T0	T1	T2	T3	T4
SBP (mmHg)	D1	126.34±5.17$^{*,\Delta}$	130.55±5.77$^{\#,\Delta,*}$	136.99±5.13$^{\#,\Delta,*}$	139.01±4.27$^{\Delta,*}$	127.88±5.57$^{\#,\Delta,*}$
	D2	117.33±9.60$^{\#}$	114.21±11.07$^{\#}$	125.68±10.23$^{\#}$	121.26±10.89$^{\#}$	114.87±10.01$^{\#}$
	D3	116.21±6.28$^{\#}$	113.59±7.88$^{\#}$	123.76±7.67$^{\#}$	116.98±8.87$^{\#}$	114.01±7.67$^{\#}$
	C	128.31±7.22$^{*,\Delta}$	135.09±7.37$^{*,\Delta}$	139.99±7.07$^{*,\Delta}$	141.98±5.07$^{*,\Delta}$	135.34±5.77$^{*,\Delta}$

Note: #: *P*<0.05, *vs.* Group C; *: *P*<0.05, *vs.* Group D2; Δ: *P*<0.05, *vs.* Group D3.

Table 3. Comparison of HR in four groups of patients during recovery period (x±s)

Index	Group	T0	T1	T2	T3	T4
HR (beats per minute)	D1	76.5±2.99$^{\Delta,*}$	82.18±5.76$^{\#,\Delta,*}$	87.66±5176$^{\Delta,*}$	83.09±5.06$^{\#,\Delta,*}$	78.01±4.36$^{\#,\Delta,*}$
	D2	69.78±7.66$^{\#}$	68.75±6.96$^{\#}$	78.68±7.06$^{\#}$	73.98±7.75$^{\#}$	71.02±6.96$^{\#}$
	D3	67.98±5.16$^{\#}$	67.66±4.66$^{\#}$	77.59±3.69$^{\#}$	74.01±4.76$^{\#}$	69.97±5076$^{\#}$
	C	79.08±4.86$^{\Delta,*}$	89.08±7.86$^{\Delta,*}$	89.99±7.07$^{\Delta,*}$	87.25±5.36$^{\Delta,*}$	81.11±4.69$^{\Delta,*}$

Note: #: *P*<0.05, *vs.* Group C; *: *P*<0.05, *vs.* Group D2; Δ: *P*<0.05, *vs.* Group D3.

Statistical analysis

All measurement data were expressed by mean ± standard deviation (x ± s), and SPSS l3.0 was used for statistical analysis. The measurement data were analyzed by repeated measures. The count data were analyzed by X^2, and the rank sum test was used for analgesia satisfaction. The difference was statistically significant when *P*<0.05.

Results

General conditions in four groups of patients before anesthesia

There was no significant difference (*P*>0.05) in gender, age, ASA, BMI, SBP and HR among the four groups (n=20). (See **Table 1**).

Systolic blood pressure, heart rate, respiratory rate and pulse oxygen saturation in four groups of patients during recovery period

Comparison of SBP in four groups of patients during recovery period: Compared with Group C, patients in Group D1 had a lower SBP at T1, T2 and T4, and patients in Group D2 and D3 had a lower SBP at T0-T4, the differences were statistically significant (*P*<0.05); compared with Group D2 and Group D3, patients in Group D1 and Group C had a higher SBP at T0-T4, the differences were statistically significant (*P*< 0.05); there was no significant difference (*P*> 0.05) at T0-T4 between group D2 and group D3, see **Table 2**.

Changes of HR in four groups of patients during recovery period: Compared with Group C, patients of Group D1 had a lower HR at T1, T3 and T4, and patients of Group D2, D3 had a lower HR at T0-T4, the differences were statistically significant (*P*<0.05); compared with Group D2 and D3, patients of Group D1 and Group C had a higher HR at T0-T4, the differences were statistically significant (*P*<0.05); there was no significant difference (*P*>0.05) at T0-T4 between Group D2 and Group D3, as shown in **Table 3**.

Changes of RR in four groups of patients during recovery period: There was no significant difference between Group D1 and Group C at T0-T4

Table 4. Comparison of RR in four groups of patients during recovery period (x±s)

Index	Group	T0	T1	T2	T3	T4
RR (beats per minute)	D1	12.31±0.54	12.54±0.81$^{\#,\Delta}$	12.56±0.76$^{\Delta}$	12.02±0.01$^{\Delta}$	12.00±0.00$^{\Delta}$
	D2	12.12±0.44	12.21±0.47$^{\#,\Delta}$	12.18±0.49$^{\#,\Delta}$	12.28±0.62$^{\Delta}$	12.28±0.67$^{\Delta}$
	D3	12.01±0.01$^{\#}$	10.88±0.96$^{\#,*}$	10.85±0.81$^{\#,*}$	10.91±0.82$^{\#,*}$	10.88±0.85$^{\#,*}$
	C	12.36±0.60	12.68±0.79$^{\Delta}$	12.62±0.72$^{\Delta}$	12.25±0.49$^{\Delta}$	12.21±0.47$^{\Delta}$

Note: #: *P*<0.05, *vs.* Group C; *: *P*<0.05, *vs.* Group D2; Δ: *P*<0.05, *vs.* Group D3.

Table 5. Comparison of SPO2 in four groups of patients during recovery period (x±s)

Index	Group	T0	T1	T2	T3	T4
SPO_2	D1	99.71±0.64	99.74±0.63	99.76±0.56$^{*,\Delta}$	99.69±0.66$^{*,\Delta}$	99.71±0.56$^{*,\Delta}$
	D2	99.88±0.36	99.86±0.44	99.88±0.42$^{\Delta}$	99.58±0.74$^{\Delta}$	99.68±0.67$^{\Delta}$
	D3	99.90±0.41	99.96±0.16	95.89±0.91$^{\#,*}$	95.91±1.06$^{\#,*}$	95.88±0.95$^{\#,*}$
	C	99.62±0.66	99.58±0.72	99.59±0.71$^{\Delta}$	99.55±0.76$^{\Delta}$	99.41±0.79$^{\Delta}$

Note: #: *P*<0.05, *vs.* Group C; *: *P*<0.05, *vs.* Group D2; Δ: *P*<0.05, *vs.* Group D3.

Table 6. Comparison of VAS scores in four groups of patients (x±s)

Groups	P1	P2	P3	P4
D1	2.89±1.0$^{\#,*,\Delta}$	2.58±0.63$^{\#,*,\Delta}$	2.36±0.48$^{\#,*,\Delta}$	2.23±0.51$^{\#,*,\Delta}$
D2	0.99±0.62$^{\#}$	0.81±0.61$^{\#}$	0.81±0.60$^{\#}$	0.79±0.58$^{\#}$
D3	0.78±0.42$^{\#}$	0.68±0.51$^{\#}$	0.64±0.50$^{\#}$	0.59±0.52$^{\#}$
C	5.31±0.81$^{*,\Delta}$	4.35±0.79$^{*,\Delta}$	4.41±0.71$^{*,\Delta}$	4.21±0.63$^{*,\Delta}$

Note: #: *P*<0.05, *vs.* Group C; *: *P*<0.05, *vs.* Group D2; Δ: *P* <0.05, *vs.* Group D3.

(*P*>0.05), while the difference between Group D2 and Group C was statistically significant at T1 and T2 (*P*<0.05). Meanwhile Group D3 was statistically significant at T1-T4. Compared with Group D3, patients of Group D1 had a higher RR at T0-T4, and the patients of Group D2 also had a higher RR at T1-T4, the differences were statistically significant (*P*<0.05); there was no significant difference (*P*>0.05) between Group D1 and Group D2. Patients of Group D3 had a significant lower RR at T1-T4 than the other three groups, the difference was statistically significant (*P*<0.05), see **Table 4**.

Changes of SPO2 in four groups of patients during recovery period: There was no significant difference between Group D1, D2 and Group C at T0-T4 (*P*>0.05); the difference between Group D3 and Group C at T2-T4 had statistical significance (*P*<0.05); Compared with Group D2, there was no significant difference in Group C and Group D1 at each time point (*P*>0.05); the SPO2 in patients of Group D3 was significantly lower than the other three groups at T2-T4, the difference was statistically significant (*P*<0.05). See **Table 5**.

Postoperative pain in four groups of patients

Comparison of post-operative VAS score among four groups of patients: The postoperative VAS scores of Group D1, D2, D3 were lower than Group C at P1-P4, the difference were statistically significant (*P*<0.05); comparing with Group D2, Group C and Group D1 had significantly higher VAS scores at P1-P4, which is similar with comparing to Group D3 (both *P*<0.05); there was no significant difference at each point between group D2 and group D3 (*P*>0.05) (see **Table 6**).

Comparison of postoperative Sufentanil dosage among four groups of patients: The postoperative PCIA Sufentanil dosage of Group D1, D2, D3 at P1-P4 were lower than Group C, the differences were statistically significant (*P*< 0.05); Group D2, D3 were lower than Group D1 at P1-P4, and the differences were statistically significant (*P*<0.05); The differencebetween Group D2 and Group D3 was not statistically significant (*P*>0.05), (see **Table 7**).

Sedation between four groups of patients

Surgery time, wake up time and extubation time of four groups of patients: There was no significant difference in surgery time among

Table 7. Postoperative dosage of sufentani in four groups of patients (μg) (x±s)

Groups	P1	P2	P3	P4
D1	4.2±0.9$^{\#,*,\Delta}$	11.1±2.4$^{\#,*,\Delta}$	19.1±4.0$^{\#,*,\Delta}$	34.1±7.0$^{\#,*,\Delta}$
D2	3.2±1.3$^{\#}$	8.6±2.2$^{\#}$	16.4±5.3$^{\#}$	29.9±6.5$^{\#}$
D3	3.0±1.1$^{\#}$	8.2±2.2$^{\#}$	16.1±6.2$^{\#}$	29.6±6.8$^{\#}$
C	5.0±1.7$^{*,\Delta}$	16.2±4.1$^{*,\Delta}$	29.3±5.8$^{*,\Delta}$	46.1±6.9$^{*,\Delta}$

Note: #: *P*<0.05, *vs.* Group C; *: *P*<0.05, *vs.* Group D2; Δ: *P*<0.05, *vs.* Group D3.

Table 8. Comparison of operation time, recovery time and extubation time among the four groups

Groups	Operation time (min)	Wake up time (min)	Extubation time (min)
D1	160.2±10.5	7.2±1.0$^{\Delta}$	12.9±1.1$^{\Delta}$
D2	158.6±11.3	6.9±1.1$^{\Delta}$	13.2±1.3$^{\Delta}$
D3	159.9±10.7	9.0±1.3	16.5±1.4
C	161.1±9.7	7.0±1.2$^{\Delta}$	12.7±0.9$^{\Delta}$

Note: Δ: *P*<0.05, *vs.* Group D3.

Table 9. Ramsay sedation score, cough score and agitation score in four groups of patients

Groups	Ramsay sedation score (points)	Cough score (points)	Agitation score (points)
D1	1.29±0.50$^{*,\Delta}$	2.58±0.49$^{*,\Delta}$	2.29±0.64$^{*,\Delta}$
D2	2.31±0.51$^{\#}$	1.03±0.02$^{\#}$	0.09±0.20$^{\#}$
D3	3.28±0.80$^{\#,*}$	1.01±0.00$^{\#}$	0.05±0.19$^{\#}$
C	1.02±0.01$^{*,\Delta}$	2.79±0.40$^{*,\Delta}$	2.56±0.62$^{*,\Delta}$

Note: #: *P*<0.05, *vs.* Group C; *: *P*<0.05, *vs.* Group D2; Δ: *P*<0.05, *vs.* Group D3.

four groups of patients (*P*>0.05); As for wake up time and extubation time, Group D3 was significantly longer than Group D1, D2 and C, the differences were statistically significant (*P*<0.05); there was no significant difference among Group D1, D2 and C (*P*>0.05), (see **Table 8**).

Ramsay sedation score, cough score and agitation score of four groups of patients while awakening: (1) Sedation score: Group D2 and D3 had a better sedation score than Group D1 and Group C, while Group D2 was better than Group D3, the differences were statistically significant (P<0.05). (2) Cough score: there was no significant difference between Group D1 and Group C, (P>0.05); Group D2 and D3 had a lower cough score than Group D1 and Group C, the differences were statistically significant (P<0.05); the difference between Group D2 and Group D3 was not statistically significant (P>0.05). (3) Agitation score: the difference between Group D1 and Group C was not statistically significant (P>0.05); compared with Group D1 and Group C, the agitation scores of group D2, D3 was significantly lower (P<0.05); the difference between group D2 and group D3 was not statistically significant (P>0.05). (See **Table 9**).

Postoperative adverse reactions in four groups of patients

The cases of dizziness and somnolence in Group C, D1 and D2 were less than Group D3, and the differences were statistically significant (*P*<0.05); four groups showed no significant difference in other adverse reactions (*P* >0.05), (See **Table 10**).

Discussion

Postoperative pain is a common clinical problem. Patients underwent inter–fixation of spine usually have large trauma and suffers severe postoperative pain; unsatisfactory control of postoperative pain will not only stimulate the patients that causes psychological disorders such as insomnia and anxiety etc. but also worsen the disorders of neuroendocrine system, it's not conducive to the early rehabilitation of patients. There are a variety of postoperative analgesic drugs, the commonly used drugs are fentanyl, morphine [12], sufentanil, tramadol and flurbiprofen etc. however, the timing of administration of these drugs is still inaccurate, and there are varying degrees of adverse reactions, such as respiratory depression, addiction etc. [13]. Dezocine is a novel opioid analgesics that belongs to the synthetic hybrid opioid receptor agonist - antagonists; it mainly excites K receptors and antagonize μ receptor; it has fewer typical μ receptor-dependent complications, such as nausea, vomiting etc. and not easy to produce irritation or anxiety [14]. The onset time, analgesic intensity and duration of action of Dezocine is comparable with morphine [14], but with less impact on blood pressure and cardiac function [15], and it has less drug addiction than morphine [16, 17]. However, when dezocine dosage reaches a certain level, the analgesia effect will stop to increase, on the contrary, the incidence of side effects will rise [18]. Dezocine is widely used in

Table 10. Comparison of postoperative adverse reactions in four groups of patients

Groups	Number	Nausea	Vomit	Dizziness	Itching	Drowsiness
D1	20	2	1	1^{Δ}	1	1^{Δ}
D2	20	1	0	1^{Δ}	0	1^{Δ}
D3	20	1	1	4	0	4
C	20	2	1	0^{Δ}	0	0^{Δ}

Note: Δ: $P<0.05$, *vs.* Group D3.

acute pain control in clinic, such as surgery or trauma related acute pain control, but it is rarely researched in the field of preemptive analgesia effect and the best dose [19].

Cuifeng Huang et al. [20] found that the preventive application of dezocine can reduce postoperative pain and the dosage of analgesic drugs after operation. The results of this study showed that injection of different doses of dezocine at 5 minutes before suturing skin can reach a certain analgesic and sedative effect on patients who underwent spinal fixation, and can reduce the pain response to surgery, which is consistent with the findings of Liu Ping et al. Although 0.1 mg/kg dezocine (Group D1) has certain analgesic effect, the VAS score and PCIA sufentanil dosage of group D1 was still significantly higher than Group D2 (0.15 mg/kg) and Group D3 (0.2 mg/kg), as shown by **Tables 6** and **7**.

As shown by **Tables 8** and **9**, the recovery time and extubation time of Group D3 were longer than those of Group D1, D2 and C, in the meanwhile, the postoperative sedation score of Group D3 was not as good as Group D2. From **Table 10**, we can see the incidence of dizziness and drowsiness in Group D3 were higher than those of the other three groups, indicating that after 3-4 h metabolism, the injected dezocine (0.2 mg/kg) before suturing skin still existed *in vivo* with a comparatively high blood drug concentration, as a result, there were the occurrence of excessive sedation [21, 22], this may be related to the long duration of dezocine to reach the effective blood concentration and the long terminal half-life [23, 24]. So, appropriate dose of dezocine should be used for preventive analgesia.

To sum up, the injection of dezocine (0.15 mg/kg and 0.2 mg/kg) at 5 min before suturing skin for preventive analgesia in inter-fixation of spine, can significantly reduce the postoperative pain and the dosage of postoperative PCIA sufentanil, as well as effectively inhibit the stress response during recovery; but 0.2 mg/kg dezocine is prone to result in excessive sedation, therefore, 0.15 mg/kg is considered as the optimal dose of dezocine to reach suitable effect of analgesia and, sedation.

Disclosure of conflict of interest

None.

Address correspondences to: Dr. Suzhen Wu, Department of Anesthesiology, Ningxiang People's Hospital of Hunan Province, 209 Yihuan Road, Yutan Town, Ningxiang 410600, Changsha, Hunan, China. Tel: 13907484463; Fax: 0731-87808558; E-mail: wusuzhen951074@163.com

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