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Original Article

Effects of dezocine on PAED scale and Ramsay sedation scores in patients undergoing NUSS procedure

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Abstract: Objective: To investigate the effects of dezocine on pediatric anesthesia emergence delirium (PAED) and Ramsay sedation scores in patients undergoing Nuss procedures (minimally invasive surgery for repairing pectus excavatum). Methods: Altogether, 100 patients with pectus excavatum who underwent Nuss procedures in our hospital were selected and randomly divided into group A (n=50) and group B (n=50). General anesthesia was carried out for each patient, with an anaesthetic of sufentanil for group A, and dezocine plus sufentanil for group B. The visual analogue scale (VAS) score and Ramsay sedation score were recorded at extubation (T0), 10 min after extubation (T1), 20 min after extubation (T2), 30 min after extubation (T3) and 60 min after extubation (T4) for assessment of pain intensity and sedative effect; PAED scale score was applied to observe the emergence delirium at awakening, 15 min after awakening and 30 min after awakening. Quality of recovery-15 (QoR-15) scale score was used to evaluate the quality of early rehabilitation 1 d after operation and 2 d after operation. The occurrence of adverse reactions was recorded. Results: The VAS scores at T0, T1, T2, T3 and T4 in group B were lower than those in group A, and there was statistical significance between group A and group B (P<0.001). VAS scores at T1, T2 and T3 were lower than those recorded at T0 in both groups (P<0.01), while no significant difference was noted at other time points (P>0.05). Ramsay sedation scores were increased at T0, T1, T2, T3 and T4 in group B in comparison to that in group A (all P<0.001), while the scores recorded at T4 in group A and T3 and T4 in group B were increased compared with those recorded at T0 (all P<0.01), and there was no significant difference at other time points (all P>0.05). Compared with group A, PAED scores in group B were downregulated at each time point after wakening up (all P<0.01), while QoR-15 scores in group B were increased at 1 d and 2 d after surgery (all P<0.05); there was no significant difference in adverse reactions between the two groups (all P>0.05). Conclusion: Sufentanil combined with dezocine is efficacious in general analgesia and sedation, which can reduce emergence agitation, improves the quality of rehabilitation and is relatively safe for patients undergoing minimally invasive repairing of pectus excavatum.

Keywords: Nuss procedure, dezocine, sufentanil, emergence agitation, sedation

Introduction

Pectus excavatum is a congenital malformation, which is a deformity caused by abnormal growth and development of the chest wall in children. Patients with pectus excavatum clinically present with inward depression of the sternum and a protruding abdomen [1]. Epidemiology shows that the incidence of pectus excavatum remains unknown with geographical and population differences. It is reported in Europe and the United States that the proportion of children with pectus excavatum is 1:1,000, and the incidence is higher in Asia. There is no data report in China [2]. Literature has confirmed that pectus excavatum can cause reduced thoracic space, decreased pulmonary capacity, and higher susceptibility to infection, which can progress into chronic obstructive pulmonary disease [3]. With good clinical effects, minimally invasive repair of pectus excavatum (MIRPE, also termed Nuss procedure) has been widely used in the treatment of patients with pectus excavatum in Europe and the United States [4]. During Nuss procedure, metal plate is placed on the thoracic surface and bent according to the anterior curvature of sternum. After surgery, patients will

have a stress response due to mechanical injury, resulting in pain and agitation, therefore, analgesia and sedation are of vital importance during surgery [5].

Dezocine is a commonly used anesthetic, which is an agonist of kappa and μ-receptors. With a plasma half-life of 2 min, and an elimination half-life of 4 h, it is capable of binding to proteins within the blood, leading to high drug concentration in the plasma, potent pharmacodynamic activity, and higher safety after renal excretion [6]. Dezocine is widely used in preoperative and postoperative anesthesia, which exerts a better analgesic effect than pentazocine via combining noradrenaline and serotonin to reduce reabsorption of epinephrine and serotonin, and lowering the degree of postoperative pain in patients [7]. It has been confirmed in the literature that dezocine can effectively improve postoperative agitation upon awakening in patients undergoing laparoscopic repair of indirect inguinal hernia, but few studies attach importance to the effects of emergence agitation and sedation in patients undergoing NUSS surgery [8]. The following experiments were hereby performed.

Materials and methods

General data

A total of 100 patients who received Nuss procedure in our hospital from January 2018 to June 2020 were selected as the study subjects. Patients were included if they (1) Were aged 6 to 12 years old; (2) Met the indications for Nuss procedure including: a. Haller index of greater than 3.25 measured from CT image [9]. b. Respiratory dysfunction; c. Heart valve prolapses; d. Mental disorders; e. Strong willingness for the correction of pectus excavatum, and with two or more indications for Nuss procedure; (3) Participated voluntarily in this study. Patients were excluded if they: (1) Didn't meet one of the following indications for Nuss procedure including: a. Haller index of less than 3.0; b. A need for thoracotomy; c. Severe thoracic depression and asymmetry; d. Complicated pectus excavatum; e. Severe rachiocamposis; (2) Had skin infection; (3) Withdraw from the study for objective or subjective reasons; (4) Showed poor compliance; (5) Were involved in other projects. This study was approved by hospital's Ethics Committee.

The patients were randomly divided into group A and group B, with 50 cases in each group. General anesthesia was performed, with sufentanil for group A, and dezocine combined with sufentanil injection for group B. Patients and their families of both groups were fully aware of this experiment and signed the informed consent.

Methods

Before surgery, patients in both groups were intravenously injected with penehyclidine hydrochloride injection (Chongqing Pharscin Pharmaceutical, China) at a dose of 0.01 mg/kg to reduce respiratory gland secretion, and electrocardiogram (ECG), blood pressure, heart rate and body temperature were monitored using aVS01 multi-parameter vital sign Monitor (Guangzhou Xicoo Medical Technology Co., Ltd., China). The depth of anesthesia was monitored using the Narcotrend 'depth of anesthesia' monitor (Germany), and electrolytic balance was maintained by intravenous injection of multiple electrolyte injection (Huaren Pharmaceutical Co., Ltd., China) at a dose of 2 mg/kg. All patients were instructed to refrain from food for 8 h and water for 4 h. Surgery was performed under general anesthesia with endotracheal intubation. Patients in group A successively received intravenous injection of propofol (Hebei Yipin Pharmaceutical Co., Ltd., China) at a dose of 1 to 2 mg/kg, sufentanil (Zhejiang Hailisheng Pharmaceutical Co., Ltd., China) at a dose of 0.3 μg/kg, and rocuronium (North China Pharmaceutical Co., Ltd., China). Patients in group B received 0.1 mg/kg of dezocine injection (Nanjing Yoko Bio-Pharma Co., Ltd., China) intravenously based on the treatment in group A. Patients in both groups were injected intravenously at a dose of 10 mL for 10 min. Surgical disinfection was performed after the patient fell asleep. The blood pressure and heart rate were maintained at a fluctuation by no more than 20% during the operation. Intravenously injection of propofol was carried out at a dose of 2 mg/kg if patients moved during the operation. Atropine (Wuhan Yuqing Jiaheng Pharmaceutical Co., Ltd., China) was injected intravenously at a dose of 0.01 mg/kg if there was a drop in patients' heart rate, and

received intravenous injection, and balloon-assisted ventilation was given if respiratory depression occurred.

Outcome measures

VAS score: The visual analogue scale (VAS) scores were measured at extubation (T0), 10 min after extubation (T1), 20 min after extubation (T2), 30 min after extubation (T3) and 60 min after extubation (T4). Scores were on a scale of 0-10, with a score of 1 point indicating no pain; a score of greater than 1 but less than or equal to 3 points indicating mild pain; a score of greater than 3 but less than or equal to 6 points indicating moderate pain or intolerance; a score of greater than 6 but less than 10 points indicating severe pain and severely affected sleep [10].

Ramsay sedation score: The sedation scoring was performed at extubation (T0), 10 min after extubation (T1), 20 min after extubation (T2), 30 min after extubation (T3) and 60 min after extubation (T4). Previously published literature was referred to during evaluation: with scores of 1, 2, 3, 4, 5, and 6 points representing irritability, consciousness and cooperative, deeper sleep and more agile response, lighter sleep, faster awakening time, sound sleep, slow response and deeper sleep, and no response, respectively. A score of 2 to 4 points was considered as proper sedation and 5 to 6 points as excessive sedation [10].

Pediatric anesthesia emergence delirium (PAED) scale score: The PAED scores of the two groups at awakening, 15 min after awakening and 30 min after awakening were observed and assessed from five dimensions including abilities to follow instructions, communicating with medical staff, and perceiving surroundings, the degree of restlessness and crying and purposeful behaviors, with four points for each dimension, 5 dimensions for a total of 20 points, and higher score indicated more severe emergence delirium [11].

QoR-15 scale score: QoR-15 scoring was performed at 1 d and 2 d after operation [12]. Quality of recovery-15 (QoR-15) scale contains 5 dimensions, including independence, emotion, psychological support, physical comfort and pain, with 0 to 10 points in each dimension, and a higher score indicating better recovery quality of patients.

Adverse reactions: The incidence of adverse reactions was observed and recorded during anesthesia and awakening in the two groups, including nausea, vomiting, respiratory depression, restlessness and chills. Incidence of adverse reactions = number of cases/total number of cases *100%.

Statistical analysis

SPSS 23.0 software was used for statistical analysis. The scores of analgesia, sedation, emergence agitation and recovery in the two groups were expressed by ($\bar{x} \pm sd$), and examined using t test. An independent sample t test was used for comparison between the groups, and paired sample t test was used for comparison within the group. The incidence of adverse reactions was expressed by (n, %), and examined by χ^2 test. $P<0.05$ indicated that the difference was statistically significant.

Results

Comparison of general data between the two groups

There was no significant difference between group A and group B regarding sex, mean age, mean body weight, pleural fluid withdrawal, Haller index, American Society of Anesthesiologists (ASA) score, scoliosis and incidence of cardiopulmonary abnormalities (all $P>0.05$). See **Table 1**.

Comparison of VAS scores at different time points after extubation

The VAS scores at T0, T1, T2, T3 and T4 in group B were significantly lower than those in group A (all $P<0.001$). Compared with those recorded at T0, the VAS scores at T1, T2 and T3 in the two groups were decreased (all $P<0.01$), and no significant difference was noted at other time points (all $P>0.05$). See **Table 2**.

Comparison of Ramsay sedation score after extubation between the two groups

Compared with group A, Ramsay sedation scores increased at T0, T1, T2, T3 and T4 ($P<0.001$). Compared with those recorded at

Table 1. General data

Group	Group A (n=50)	Group B (n=50)	χ^2/t	P
Gender			0.332	0.847
Male	42	44		
Female	8	6		
Mean age (years)	8.6±1.9	8.3±2.1	0.749	0.456
Mean weight (kg)	30.50±7.51	31.13±6.82	0.419	0.676
Pleural fluid withdrawal (mL)	49.55±19.85	48.63±20.17	0.230	0.819
Haller index	4.0±0.9	3.9±0.7	0.620	0.537
ASA score			0.372	0.830
Class I	28	31		
Class II	22	19		
Scoliosis (n)			0.060	0.970
Yes	10	11		
No	40	39		
Cardiopulmonary abnormalities (n)			0.096	0.953
Yes	18	16		
No	32	34		

Note: ASA: American society of anesthesiologists.

T0, Ramsay sedation scores increased at T4 in group A, and increased at T3 and T4 in group B (all P<0.01). No difference was found at other time points (all P>0.05). See **Table 3**.

Comparison of PAED scale score between the two groups

Compared with group A, the pediatric anesthesia emergence delirium (PAED) scale score decreased at awakening, 15 min after awakening, and 30 min after awakening in group B (all P<0.01). See **Table 4**.

QoR-15 scores of the two groups 1 d and 2 d after operation

The Quality of recovery-15 (QoR-15) scores at 1 day and 2 days after surgery in both groups were increased compared with those in group A, and the QoR-15 scores at 1 day and 2 days after surgery in group B were increased (all P<0.05), as shown in **Figure 1**.

Comparison of the incidence of adverse reactions between the two groups

Certain degree of adverse reactions was observed in both groups. No excessive sedation occurred in group A. No chills and agitation occurred in group B. There was no significant difference in the incidence of adverse reactions between the two groups (P>0.05). See **Table 5**.

Discussion

The purpose of treating patients with pectus excavatum is to repair chest deformity, improve physical appearance and respiratory circulation. Nuss surgery is a common method for the treatment of pectus excavatum. Unlike the conventional invasive thoracotomy approach, it preserves the sternum and ribs, allowing better deformity correction effect and low recurrence rate. However, literature confirms that the Nuss procedure can cause certain damage to skin tissue and postoperative pain, further affecting the patient's respiratory and cardiovascular system function [13]. Therefore, intraoperative anesthesia plays an important role in reducing postoperative pain for patients.

This study confirmed that anesthesia with sufentanil plus dezocine lowered pain after extubation in patients with Nuss procedure, and this combined anesthesia had a better postoperative analgesic effect. At present, there are a wide variety of clinical anesthetic drugs, and adjuvant drugs are commonly used in clinical practice to improve sedative effect while reducing adverse reactions [14]. Sufentanil is an opioid analgesic that demonstrates a high affinity for μ receptor. Its analgesic effect is 7 to 10 times that of fentanyl, ensuring oxygen supply of myocardium, while stabilizing hemodynamics [15]. The use of sufentanil with high affinity for μ receptor for general anesthesia during Nuss surgery has a regulatory effect, which exerts an inhibitory effect on sympathetic and vasomotor centers, thereby reducing post-extubation pain. Sufentanil is more effective than fentanyl in binding to plasma proteins and exerts a stronger analgesic effect to maintain the stability of various systems and relieve

Table 2. Comparison of VAS scores at different times after extubation

Group	n	T0	T1	T2	T3	T4
Group A	50	4.50±0.81	2.85±0.51$^{\#\#}$	3.56±0.62$^{\#\#}$	3.84±0.59$^{\#\#}$	3.62±0.43
Group B	50	3.10±0.66***	1.32±0.42$^{***,\#\#}$	2.03±0.38$^{***,\#\#}$	2.14±0.44$^{***,\#\#}$	2.33±0.37***
t		9.475	16.380	14.880	16.330	16.080
P value		<0.001	<0.001	<0.001	<0.001	<0.001

Note: VAS: visual analog scale. Compared with group A, ***P<0.001; compared with T0, $^{\#\#}$P<0.01.

Table 3. Comparison of Ramsay sedation score after extubation between the two groups

Group	n	T0	T1	T2	T3	T4
Group A	50	1.35±0.20	1.69±0.29	1.86±0.30	1.93±0.28	2.30±0.35$^{\#\#}$
Group B	50	2.33±0.23***	2.87±0.33***	3.06±0.25***	3.44±0.29$^{***,\#\#}$	3.52±0.26$^{***,\#\#}$
t		22.740	18.990	21.730	26.490	19.790
P value		<0.001	<0.001	<0.001	<0.001	<0.001

Note: Compared with group A, ***P<0.001; compared with T0, $^{\#\#}$P<0.01.

Table 4. Comparison of PAED scores between the two groups

Group	n	At awakening	15 min after awakening	30 min after awakening
Group A	50	6.30±1.15	7.56±1.54	6.82±1.55
Group B	50	5.10±1.33**	6.40±1.37**	5.41±1.37**
t		4.826	3.979	4.820
P value		0.001	0.001	0.001

Note: PAED: pediatric anesthesia emergence delirium scale score. Compared with group A, **P<0.01.

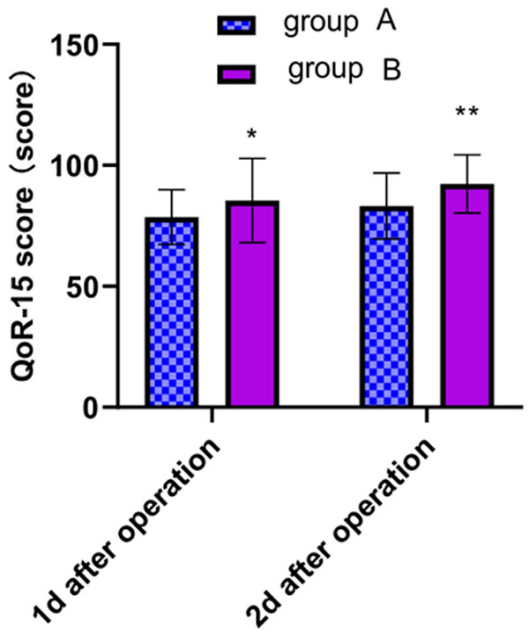

Figure 1. QoR-15 scores of the two groups 1 d and 2 d after operation. QoR-15: Quality of recovery-15 score. Compared with group A, *P<0.05, **P<0.01.

stress in children [16]. Dezocine injection is a μ-receptor agonist as well as a k-receptor antagonist. It has an analgesic effect comparable to that of morphine, but has a lower possibility to cause addiction and works faster [17]. The main mechanism of action is that by raising the threshold of nerve action potentials, delaying the transmission of nerve impulses, and the elevation of action potentials, dezocine can block the generation and conduction of nerve impulses and has the effects of both anesthesia sedation [18]. Z-G et al. confirmed that dezocine can effectively improve post-extubation pain in patients undergoing surgery, mainly through anesthesia of μ receptors in the brain and spine [19]. Such results are similar to that of our study.

This study showed that in patients undergoing Nuss operation, general anesthesia using sufentanil and dezocine can improve the effect of sedation and reduce emergence agitation score. Emergence agitation may occur in some patients during recovery from anesthesia for Nuss surgery and is a common clinical complication. Research on the mechanism of this complication suggest that it is associated with abnormalities in subcortical neural circuits [4]. Epidural anesthesia can reduce the dosage of anesthetic drugs, shorten the awakening time, reduce the postoperative stress response, inhibit catecholamine release, and improve the prognosis. Sufentanil can reduce the surgical stress response and exert an inhibitory effect on the sympathetic-adrenal medullary system and the hypothalamic-pituitary-adrenal cortex

Table 5. Comparison of incidence of adverse reactions between the two groups (n, %)

Group	n	Nausea and vomiting	Tachycardia	Respiratory depression	Restlessness and chills
Group A	50	3 (6.00)	2 (4.00)	3 (6.00)	2 (4.00)
Group B	50	5 (10.00)	3 (6.00)	4 (8.00)	0 (0.00)
χ^2/Z		0.481	0.195	0.138	0.050
P value		0.786	0.907	0.933	0.224

axis, with a better sedative effect [20]. Dezocine can significantly reduce the incidence of emergence agitation. It is demonstrated by pharmacokinetics studies that intravenous injection of dezocine is associated with rapid onset of therapeutic effect and can prevent physical and psychological stress to a certain extent by stabilizing hemodynamics during extubation, which is helpful for postoperative rehabilitation [21]. Li H et al. stated that dezocine can significantly improve post-extubation sedation and reduce excessive sedation while reducing emergence agitation in patients undergoing thoracic surgery [22].

In this study, the recovery of patients at 1 day and 2 days after surgery was observed by using the QoR-15 scale, and the QoR-15 score in group B was higher than that in group A, indicating that sufentanil combined with dezocine can promote early rehabilitation of patients by reducing the stress response during extubation. It is confirmed through international clinical evaluation that QoR-15 scale scoring system is both effective and reliable, and is more popular among patients, which is worthy of application [23]. Dezocine can accelerate the rehabilitation of patients by improving postoperative pain and inflammatory indicators and reducing immunosuppression. The mechanism of antioxidative stress of dezocine may be due to the inhibition of Toll-like receptor 4 (TLR4)/nuclear transcription factor κB (NF-κB) signaling by reducing the inflammatory response, which is consistent with the findings of Li Shufen et al. [24].

This study confirmed that there was no difference in adverse reactions between the two groups. Sufentanil, as a potent anesthetic with high lipid solubility and opioid receptor affinity, has little impact on the heart and respiratory system while rapidly exerting anesthetic effects, without histamine release [25]. Since dezocine is a partial μ-receptor agonist and has no significant effect on μ2 receptors during analgesia, it has lower probability to bring about respiratory depression and excessive sedation [26]. Xu Y et al. reported that general anesthesia using dezocine alone produced fewer adverse reactions and higher safety in patients undergoing Nuss surgery [27]. This is consistent with the findings of Ma Fang et al. [28].

However, this experiment has certain limitations. A small sample size of the experiment cannot comprehensively reflect the profile of patients injected with dezocine after Nuss operation. The use of anesthetics drugs and rehabilitation from it is a complex physiological process, and the lack of detection of biochemical indicators may have an impact on the experimental results. Therefore, in future studies, we will strengthen the cooperation with other relevant research units, increase the sample size, and enrich the experiments, with the purpose of providing a reference for the selection of anesthetic drugs in patients undergoing Nuss surgery.

In summary, for patients undergoing minimally invasive repair of pectus excavatum, the use of sufentanil combined with dezocine in general anesthesia has better analgesic and sedative effects, reduces recovery agitation, improves the quality of rehabilitation, and is safer.

Disclosure of conflict of interest

None.

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