

## Original Article

# An investigation on delirium and hemodynamics influenced by dexmedetomidine for sedating elderly patients in mechanical ventilation

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**Abstract:** Objective: This study aims to investigate the influence on delirium and hemodynamics by dexmedetomidine for sedating elderly patients with mechanical ventilation in intensive care unit (ICU). Methods: A total of 80 patients in ICU were recruited in this study from February 2015 to January 2016, and randomly divided into two groups (40 patients in each group). Treatment with dexmedetomidine was carried out in the investigation group, while midazolam were used in the control group. All patients received fentanyl. A comparison was made on the anti-delirium effect and the influence on hemodynamics between the two groups of elderly patients in mechanical ventilation during sedation. Results: Statistical significance was observed in variation of hemodynamic parameters including central venous pressure, heart rate, respiratory rate, and blood oxygen saturation (all  $P < 0.05$ ). No delirium occurred in the investigation group, when compared with 4 subjects experiencing delirium symptom in the control group. However, there was no significant difference between the two groups ( $P > 0.05$ ). The difference for the incidence rate of adverse reaction between the investigation and control group was not statistically significant (both  $P > 0.05$ ). The total dose of fentanyl in the investigation group was lower than that in the control group, with a significant difference ( $P < 0.05$ ). Conclusion: Dexmedetomidine has an anti-delirium effect, a minor influence on hemodynamics, and lower dosage demand for fentanyl. It is worth promoting in future clinical practice.

**Keywords:** Dexmedetomidine, delirium, sedation, mechanical ventilation, elderly patients

## Introduction

Along with economic development, improvement of living standards and prolongation of human average life span, Chinese society has entered into an aged era, with an increase year after year in both number and percentage of elderly patients. The most common diseases of elderly patients in the intensive care unit (ICU) are respiratory diseases such as COPD and pulmonary infections, which need mechanical ventilation and sedation. Poor compliance to sedation and analgesia existing in elderly patients was observed, because of the variance in pharmacokinetic and pharmacodynamic parameters influenced by degenerative and biological/pathological changes of histocytes as well as deteriorated function of systemic organs during the aging process. A causal link has been reported between the high incidence of delirium and analgesic/sedative regimen commonly used [1-3]. Therefore, the choice of an appro-

prate sedative has great importance on both security and early rehabilitation after operation in elderly patients to ensure not only the induction of cooperative sleep of a patient but also so that they can be awakened. Also sedation provides the convenience to observe the disease situation and evaluate neurological functions and safety, with minimized interference with biological functions and hemodynamics. The sedation chosen for elderly patients in the ICU is important, because it is an essential issue to find new approaches and drugs to improve safety in sedated elderly patients. Dexmedetomidine, a novel  $\alpha$ -2 adrenoceptor agonist, is characterized by a good sedative and analgesic effect [4-6].

In this study, we selected 80 elderly patients who were admitted into ICU from February 2015 to January 2016 in our hospital. We then investigated the influence on delirium and hemodynamics by dexmedetomidine.

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**Table 1.** Comparison of baseline characteristics between two groups

Variable	Case	Male/ female	Age (year)	Weight (kg)	APACHII scores
Investigation Group	40	28/12	73.38±8.59	60.35±8.01	21.35±4.11
Control group	40	24/16	73.83±7.96	61.58±7.66	23.51±5.47
t/ $\chi^2$		0.879	0.243	0.699	0.293
P		0.348	0.809	0.487	0.582

## Materials and methods

### General data

Eighty patients were recruited in this study who were admitted into ICU in our hospital from February 2015 to January 2016. The patients were randomly divided into the investigation group and the control group (40 patients in each group). The inclusion criteria were (A) more than 60 years old; (B) needed mechanical ventilation treatment; (C) the duration of intubation was more than 24 h; (D) the patients and their families actively cooperated. The exclusion criteria were (A) accompanied by multiple organ dysfunction syndrome in heart, lung, liver or kidney; (B) allergic to anesthetics (midazolam and dexmedetomidine) mentioned in this study; (C) had central nervous system disease, coma, shock, and bradycardia. All family members of the patients recruited in this study submitted written informed consent, and this study was approved from the Hospital Ethics Committee of Fuling Center Hospital of Chongqing City.

### Treatment methods

After admission into the ICU, patients in the control group underwent a bolus infusion with a loading dose (0.05 mg/kg) of midazolam, followed by a sustained pumping at rate of 0.05-0.10 mg/(kg·h). The patients in the investigation group underwent pumping of dexmedetomidine with a loading dose of 1 µg/kg (completed within 20 minutes), then followed by a sustained sedation/analgesia with 0.2-0.7 µg/kg of dexmedetomidine. All patients received a loading dose (0.4 µg/kg) of fentanyl, followed by sustained pumping at a rate of 0.5-1.0 µg/(kg·h). According to the Ramsay scores, the dose of drugs was adjusted.

### Outcome measures

The central venous pressure (CVP), heart rate, absolute change of blood pressure, respiratory

rate, and blood oxygen saturation from 24 hours after sedation to pre-admission were compared between two groups. The incidence rates of delirium and adverse reaction such as hypotension and bradycardia were compared between

two groups at 24 hours after the sedation. The total doses of fentanyl were compared between two groups.

### Statistical analysis

All statistical data were processed using SPSS software, version 19.0. Measurement data with normal distribution are described as mean  $\pm$  standard deviation ( $\bar{x} \pm sd$ ). The measurement data was conducted with t test. The count data was expressed by percentage, and compared with  $\chi^2$  test.  $P < 0.05$  indicates statistically significant difference.

## Results

### Comparison of baseline data between two groups

The patients in the control group and the investigation group differed insignificantly in age, sex, weight, and other characteristics at baseline data (all  $P > 0.05$ , **Table 1**).

### Comparison of hemodynamics indexes between two groups

Compared with the control group, the absolute changes of central venous pressure, heart rate, respiratory rate and blood oxygen saturation were significantly decreased. There was statistically significant difference between two groups (all  $P < 0.05$ ). There was no significant difference in term of blood pressure between two groups (both  $P > 0.05$ , **Table 2**).

### Comparison of delirium between two groups

There was no patient with delirium in the investigation group. The incidence rate of delirium in the investigation group was lower than that in the control group, but there was no significant difference between two groups ( $P > 0.05$ , **Table 3**).

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**Table 2.** Comparison of absolute changes for hemodynamics indexes between two groups

Variable	Case	Systolic Pressure (mmHg)	Diastolic Pressure (mmHg)	CVP (cmH <sub>2</sub> O)	Heart rate (beats/min)	Respiratory Rate (times/min)	Blood Oxygen saturation (%)
Investigation Group	40	37.72±15.31	25.41±8.42	2.43±1.11	29.43±13.82	7.38±3.44	4.63±1.44
Control group	40	35.13±13.42	26.92±8.24	3.03±1.10	37.51±10.84	13.20±4.20	12.71±2.62
t/χ <sup>2</sup>		0.801	0.798	2.435	2.951	6.791	5.807
P		0.426	0.429	0.017	0.004	<0.001	<0.001

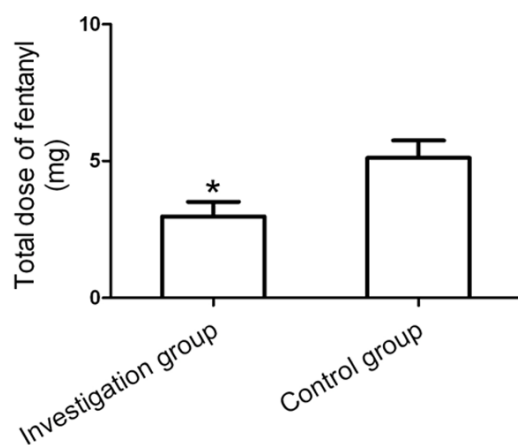
Note: CVP, central venous pressure.

**Table 3.** Comparison of delirium between two groups

Variable	Case	Incidence of delirium (n, %)	
		Yes	No
Investigation Group	40	0 (0)	40 (100)
Control group	40	4 (10)	36 (90)
χ <sup>2</sup>		5.756	
P		0.116	

**Table 4.** The comparison of adverse reaction between two groups (n, %)

Variable	Case	Hypotension	Bradycardia
Investigation Group	40	1 (2.5)	0 (0)
Control group	40	6 (15.0)	3 (7.5)
χ <sup>2</sup>		4.305	4.276
P		0.108	0.241



**Figure 1.** Comparison for total dose of fentanyl between two groups. Compared with control group, \*P<0.001.

### Comparison of adverse reaction between two groups

The incidence rates of adverse reaction in the investigation group were lower than those in

the control group. There was no significant difference between two groups (both P>0.05, **Table 4**).

### Comparison of fentanyl dose between two groups

The total dose of fentanyl in the investigation group was 2.98±0.53 mg. Whereas the total dose of fentanyl in the control group was 5.12±0.63 mg. The statistical difference was significant between two groups (t=12.356, P<0.001, **Figure 1**).

### Discussion

Mechanical ventilation is an important part of the treatment for ICU elderly patients [7, 8]. However, mechanical ventilation is an invasive procedure and it could induce pain, anxiety, irritability and other reactions, and make the patient's stress response extremely intense. In severe cases, it leads human-machine against and unstable hemodynamics [9, 10]. Therefore, it takes effective and reasonable sedation measures, which can assist treatment to improve the invasiveness of elderly patients with mechanical ventilation. Thus, it has great significance for clinical study.

The two agents, midazolam and fentanyl, are most frequently used among all classical analgesic/sedatives. They are characterized in low onset of their effects in ICU patients [11, 12]. In the elderly patients in mechanical ventilation particularly, they can more easily induce hemodynamic disorders and even cause cardiac arrest in severe cases. Moreover, delayed anaesthesia meant the increased expense for the aged [13]. Dexmedetomidine hydrochloride, a novel sedative/analgesic agent is widely applied to ICU. It is a dextroisomer of medetomidine and belongs to imidazole derivatives. Its competitive effect is generated through activation of a subtype of the central A<sub>2</sub> adrenergic

receptor. Through acting upon  $\alpha$ 2A receptor in nucleus ceruleus in brain stem, dexmedetomidine hydrochloride has the effects of sedation, analgesia, hypnotism, and anti-anxiety. Its analgesic effect correlates to dorsal/intermediate horns of spinal cord, inhibiting the central up-going transmission of trauma-related signals [14, 15].

In this study, we analyzed mainly on sedative effects and found that anti-delirium effect and the hemodynamic variations that dexmedetomidine induced in elderly patients in ICU in mechanical ventilation. It had no obvious advantages in comparison with the control group, as far as blood pressure was concerned. In respects of heart rate, CVP, respiratory rate and blood oxygen saturation, significant differences were observed between the investigation group and the control group (all  $P < 0.05$ ). This result was in accordance with previous studies [16, 17]. Moreover, some studies reported that dexmedetomidine could effectively inhibit incidence of delirium [18]. However in this study, as for the delirium control, no significant difference was revealed between two groups ( $P > 0.05$ ), and it may due to the small sample size. Among 40 patients in each of the groups, 4 experienced delirium in the control group in contrast to no incidence of delirium in the investigation group. The results suggest a very low possibility for dexmedetomidine to induce delirium.

One study reported that when dexmedetomidine was used alone, the analgesic effect is weak, and it is thus combined with fentanyl or other opioid analgesics. When it used, the dosage can be reduced, and the analgesic effect can be enhanced [19]. In this study, the result revealed that elderly patients from the investigation group received lower fentanyl doses compared with those in the control group. Moreover, this study showed that no significant difference for adverse effects such as hypotension and bradycardia were observed between the investigation group and the control group. The results suggest that dexmedetomidine has a low incidence rate of adverse effects and is safe. This result was the similar as that in the study by Tripathi et al. [20].

In conclusion, elderly patients with easy analgesia and stabilized hemodynamics in mechanical ventilation in ICU were treated with dexme-

detomidine. The results indicate that it is an ideal analgesic/sedative agent, and unlikely to induce respiratory inhibition but capable of reducing delirium. It can be used in further clinical application and popularization.

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### Disclosure of conflict of interest

None.

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