Research Paper

Effect of Different Doses of Dexmedetomidine on Respiratory Mechanics and Analgesia in Mechanically Ventilated Centralization

HUAIJIN GU*, JIANBIN WANG, ZHE ZHU, JUN HE AND DAN QIN

Department of Critical Care Medicine, Huaibei People's Hospital, Huaibei, Anhui Province 235000, China

This study evaluated the effects of different dexmedetomidine doses on respiratory mechanics and safety indicators in intensive care unit patients undergoing centralized mechanical ventilation. Intensive care unit patients receiving mechanical ventilation from January 2016 to December 2022 were divided into dexmedetomidine-A, dexmedetomidine-B, midazolam and propofol groups. Dexmedetomidine-A received dexmedetomidine at 0.6 μg/kg/h and dexmedetomidine-B at 1.0 μg/kg/h. Respiratory mechanics and safety parameters were compared. Dexmedetomidine-A and dexmedetomidine-B groups showed no significant changes in volume, respiratory rate, minute ventilation, partial pressure of carbon dioxide in expired tidal and forced expiratory volume percentage compared to baseline (T0) at T1-T6 ($p>0.05$). In midazolam and propofol groups, significant changes were observed in volume, respiratory rate, minute ventilation at T1-T6, partial pressure of carbon dioxide in expired tidal at T1-T4 and forced expiratory volume percentage at T3-T6 compared to T0 ($p<0.05$). Differences between dexmedetomidine-A/dexmedetomidine-B and midazolam/propofol groups were statistically significant ($p<0.05$), but not between dexmedetomidine-A/dexmedetomidine-B groups ($p>0.05$). Other parameters such as partial pressure of carbon dioxide, heart rate, medication dosage, Ramsay score, Richmond agitation sedation scale score, time to achieve target Richmond agitation sedation scale, duration of ventilation and intensive care unit stay varied significantly among groups. Dexmedetomidine has less impact on respiratory mechanics compared to midazolam and propofol in intensive care unit patients undergoing centralized mechanical ventilation. Both 0.6 μg/kg/h and 1.0 μg/kg/h dexmedetomidine doses provide equivalent sedation and safety benefits.

Key words: Dose, dexmedetomidine, mechanical ventilation, respiratory mechanics, analgesia

Mechanical ventilation is one of the main modalities of treatment for Multiple Organ Dysfunction Syndrome in the Elderly (MODSE). Approximately 30 % of patients in the Intensive Care Unit (ICU) require therapeutic mechanical ventilation[1]. Although its use can provide significant benefits to ICU patients, it also carries the risk of serious complications such as Ventilator Associated Pneumonia (VAP), delirium and ICU-acquired debilitation. The occurrence of these complications not only prolongs the duration of mechanical ventilation, but also affects the recovery of neurological and physiological function, which is detrimental to the prognosis of mechanically ventilated patients in the ICU[2,3]. In 2004, the Institute for Healthcare Improvement (IHI) recommended that intensive ventilator therapy for ICU patients could reduce the risk of VAP[4]. Sedation and analgesia are essential for the treatment of mechanically ventilated patients in the ICU, with the aim of relieving pain, reducing anxiety, hypnosis and inducing amnesia[5]. The ideal sedative drug has a rapid onset of action, predictable dose-effects, short half-life, no accumulation of prototype compounds or metabolites, little inhibition of the respiratory cycle, no dependence on hepatic metabolism and is inexpensive[6]. Dexmedetomidine (Dex) is a potent alpha-2 adrenoceptor agonist that exerts local analgesic, sedative and anxiolytic effects through its high affinity for alpha-2 adrenoceptors, without inhibiting the respiratory cycle[7]. Song *et al.*[8] reported that the use of Dex in mechanically ventilated patients in the ICU not only resulted in

***Address for correspondence**
E-mail: guhuaijin76@163.com

superior sedation and reduced the incidence of delirium, but that there was a risk of complications such as hypotension and tachycardia and that the dosage of Dex in mechanically ventilated patients in the ICU was still not uniform. In view of this, this study collected data to analyze the value of different doses of dexmedetomidine in ICU mechanically ventilated patients under intensive care, using respiratory mechanics and safety as the main observation indicators, with a view to providing an experimental basis for the sedative and analgesic treatment of mechanically ventilated patients in the ICU.

MATERIALS AND METHODS

General information:

We selected patients who received mechanical ventilation bundle in the ICU from January 2016 to December 2022 as the study objects.

Inclusion criteria: Age 18-80 y old; Mean Arterial Pressure (MAP) ≥60 mmHg, Heart Rate (HR) ≥60 beats/min; patients who were mechanically ventilated in the ICU and the duration of mechanical ventilation was >24 h; duration of receiving centralized treatment was ≥3 d; body mass fluctuated within <15 % of (standard body mass=height (cm)-100); intubation of 15 % (standard body mass=height (cm)-100); intubation time <6 h and signing the study informed consent form.

Exclusion criteria: Severe craniocerebral injury, cranial hypertension, combined cerebrovascular sequelae, persistent epilepsy; combined cognitive impairment unable to communicate; allergic to sedative and analgesic drugs; pregnant or lactating women; hemodynamically unstable; child liver function class C; combined with severe bradycardia; acute phase of myocardial infarction; grade II or III atrioventricular block; patients with missing clinical data or discharged from hospital on non-medical advice. According to the inclusion and exclusion criteria, 138 patients receiving mechanical ventilation in ICU were finally selected for this study, then divided them into Dexmedetomidine-A (Dex-A) group (n=40), Dexmedetomidine-B (Dex-B) group (n=38), Midazolam (Mid) group (n=30) and Propofol (Pro) group (n=30) according to the anesthesia method. The four groups were assessed for gender, age, weight, Body Mass Index (BMI), Acute Physiology and Chronic Health Evaluation II (APACHE II), cause of ICU admission sepsis, severe pneumonia, Multiple Organ Dysfunction Syndrome (MODS), Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD), multiple injuries, American Society of Anesthesiologists (ASA) and the New York Heart Association (NYHA) cardiac function classification were not statistically significant ($p<0.05$) as shown in Table 1.

TABLE 1: COMPARISON OF GENERAL INFORMATION OF THE FOUR GROUPS

General information	Group Dex-A	Group Dex-B	Mid group	Pro group	F/χ^2	p
Age (cases, %)					8.08	0.232
<60 y old	15 (37.50)	13 (34.21)	14 (46.67)	17 (56.67)		
60-69 y old	24 (60.00)	23 (60.53)	13 (43.33)	10 (33.33)		
≥70 y old	1 (2.50)	2 (5.26)	3 (10.00)	3 (10.00)		
Gender (cases, %)					1.091	0.779
Male	22 (55.00)	23 (60.53)	17 (56.67)	20 (66.67)		
Female Body weight ($\bar{x}\pm s$, kg)	63.35±5.77	60.32±7.48	62.87±6.33	61.85±7.33	1.659	0.179
BMI ($\bar{x}\pm s$, m^2)	22.69±2.75	21.06±2.87	22.05±3.25	22.57±3.01	2.356	0.075
APACHE II ($\bar{x}\pm s$)	17.88±5.14	19.52±6.09	18.69±5.42	18.01±6.33	0.637	0.592
Cause of ICU admission (cases, %)					5.385	0.944
Sepsis	10 (25.00)	12 (31.58)	8 (26.67)	8 (26.67)		
Severe pneumonia	7 (17.50)	6 (15.79)	8 (26.67)	9 (30.00)		

MODS	8 (20.00)	7 (18.42)	4 (13.33)	3 (10.00)		
AECOPD	6 (15.00)	7 (18.42)	4 (13.33)	3 (10.00)		
Multiple injuries	9 (22.50)	6 (15.79)	6 (20.00)	7 (23.33)		
ASA classification (cases, %)					0.779	0.854
II	22 (55.00)	18 (47.37)	17 (56.67)	15 (50.00)		
III	18 (45.00)	20 (52.63)	13 (43.33)	15 (50.00)		
NHYA classification (cases, %)					2.146	0.543
I	16 (40.00)	20 (52.63)	11 (36.67)	14 (46.67)		
II	24 (60.00)	18 (47.37)	19 (63.33)	16 (53.33)		

Methods:

All four groups were treated with invasive mechanical ventilation. The mode of ventilation treatment was synchronized intermittent command ventilation or bi-level positive airway pressure ventilation, routine blood gas analysis monitoring, routine treatment with symptomatic management, standardized anti-infection, energy supply, airway care and centralization; 0.05-1.0 μg/kg/min fentanyl was applied for continuous pumping analgesia.

The Dex-A group was infused with Dex at a constant rate at a dose of 0.6 μg/kg/h (Jiangsu Huatai Chenguang Pharmaceutical Co. Ltd. H20193382) until the target Richmond Agitation Sedation Scale (RASS) is reached (0-2 points daytime, 1-3 points nighttime); in group Dex-B, Dex is infused at a constant rate of 1.0 μg/kg/h until the target RASS is reached; during continuous pumping of Dex in both groups, the Dex dose was titrated downward every 30 min to the target RASS at a dose of 0.2 μg/kg/h during daytime if the RASS was ≤-3, and upward every 30 min at a dose of 0.2 μg/kg/h if the RASS was >1; if RASS>-1 or <-3 at night, Dex dosage was also adjusted upward or downward every 30 min by 0.2 μg/kg/h. For the Mid group, Mid (HEXAL AG, H20160339) was pumped intravenously at 2-3 mg with a maintenance dose of 0.05 mg/kg/h; for the Pro group, Pro was pumped intravenously at 1 mg/kg with a maintenance dose of 0.5-4.0 mg/kg/h, both groups adjusted the dose of the drug at a frequency of 4 h/time to achieve the target RASS; during sedation in all four groups, if MAP was <60 mmHg, norepinephrine was given at 0.05 mg/kg/h. Patients in the four groups stopped sedative and analgesic drugs at 7:00 a.m. daily and underwent a wake-up test to evaluate three items; call to open eyes, eye tracking and command to shake hands, and if the sedation target was not reached, the drug dose was adjusted until the target was reached and then underwent a wake-up test. After complete awakening, the dose of fentanyl (Eurocept BV, H20150125) was increased if the pain Visual Analogue Scale/Score (VAS) was >4, and the ventilator was disconnected if the disconnected condition was met.

Observation indicators:

Including gender, age, weight, BMI, APACHE II, reason for ICU admission (medical illness, emergency surgery and emergency admission), mode of ICU transfer (emergency admission, ward transfer) and proportion of Cardiac Resynchronization Therapy (CRT).

Respiratory mechanics indexes: Adopt Datex-Ultima respiratory mechanics detector, para flow method to detect respiratory mechanics index, the mask should be closely fitted with the patient's face during the examination, autonomous breathing mode, adjust the inhalation oxygen concentration to 100 %, oxygen flow rate 0.5 l/min, and basic filling of the air storage bag. The patient's Tidal Volume (V_T), Minute Ventilation (MV), Respiratory Rate (RR), Partial Pressure of Carbon dioxide in Expired Tidal ($P_{ET}CO_2$), Forced Expiratory Volume (FEV1) as a percentage of the expected value (FEV1 %), Pressure-Volume (PV) loop, and Flow-Volume (FV) loop were continuously monitored; the above indicators were the respiratory mechanics collected at the time points pre-dose (T0), 5 min after administration (T1), 10 min (T2), 15 min (T3), 20 min (T4), 25 min (T5) and 30 min (T6).

Safety indicators: In blood gas and circulatory indicators; collect Partial Pressure of Carbon dioxide ($PaCO_2$), arterial blood oxygen partial pressure (PaO_2), pH, MAP and HR levels at the time point pre-dose (T0), 5 min after administration (T1), 15 min (T3) and 30 min (T6). Drug dosage of fentanyl, norepinephrine and Pro was counted in the four groups. Sedative and analgesic effects and days of mechanical ventilation and ICU stay adopted the Ramsay score and RASS score to evaluate the sedative effects, and the time to achieve the target RASS, days of mechanical ventilation and ICU stay were recorded. Occurrence of adverse effects and adverse events; delirium, hypotension (MAP <65 mmHg), bradycardia (HR <55 bpm), unscheduled extubating and restraint belt usage were counted in the four groups.

Statistical methods:

The statistical analysis software was Statistical Package for the Social Sciences (SPSS) 23.0. The measurement data were subjected to normal distribution and Chi-square (χ^2) test and data not conforming to normal distribution were transformed into normal distribution and described by ($\bar{x}\pm s$). Respiratory mechanics and blood gas, and circulation indexes were compared by repeated measures Analysis of Variance (ANOVA), two-by-two comparisons were made by Least Significant Difference (LSD)-t test, and the rest of the measurement data were subjected to independent samples t-test; the count data were described by cases (%), χ^2 test or continuous correction χ^2 test; $p<0.05$ was considered a statistically significant difference.

RESULTS AND DISCUSSION

Compared with T0, V_T, RR and MV at time points T1 to T6, P_{ET} CO_2 at time points T1 to T4 and FEV1 % at time points T3 to T6 were significantly increased or decreased in Mid and Pro groups ($p<0.05$), but V_T, RR, MV, P_{ET} CO_2 and FEV1 % at time points T1 to T6 were not significantly changed in Dex-A and Dex-B groups ($p>0.05$). And the difference was statistically significant ($p<0.05$) when compared with the corresponding time points in Mid and Pro groups; however, the difference between groups in Dex-A and Dex-B groups for the above indicators was not statistically significant ($p>0.05$) as shown in fig. 1 and fig. 2, and Table 2.

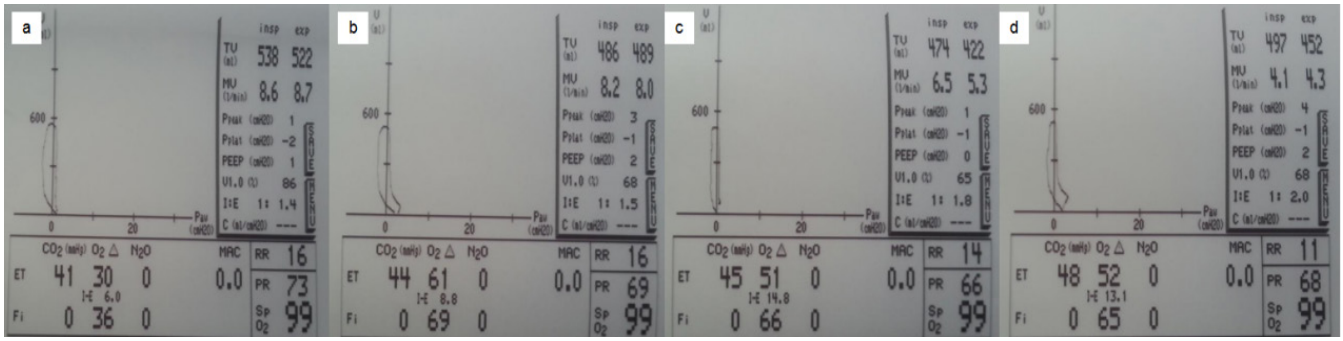

Fig. 1: 50 y old male weighing 63 kg; (a): T0 time point, respiratory mechanics parameters (PaO_2 , RR, V_T , MV, P_{ET} CO_2 , FEV1, PV ring) were within normal limits; (b): T1 time point, MV and FEV1 % decreased after administration of 0.6 µg/kg/h Dex 5 min later, PV ring normal; (c): T3 time point, RR, MV, FEV1 % decreased after administration of 0.6 µg/kg/h Dex 15 min later, PV ring area decreased, PaO_2 normal and (d): T6 time point, after administration of 0.6 µg/kg/h Dex for 30 min, RR, MV continued to decrease, P_{ET} CO_2 increased to 48 mmHg, PV ring area decreased, PaO_2 normal

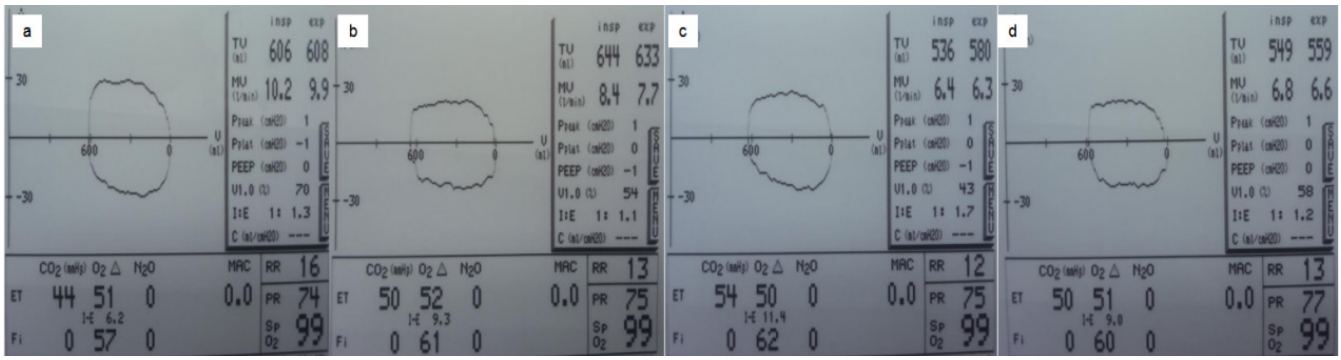

Fig. 2: 49 y old male weighing 61 kg; (a): T0 time point, respiratory mechanics parameters (PaO_2, RR, V_T, MV, P_{ET} CO_2, FEV1, FV ring) were normal; (b): T1 time point, after administration of 1.0 µg/kg/h Dex 5 min, P_{ET} CO_2 increased, MV, FEV1 % decreased, FV ring narrowed; (c): T3 time point, after administration of 1.0 µg g/kg/h Dex 15 min, RR, MV, FEV1 % decreased, FV ring area decreased, PaO_2 normal and (d): T6 time point, RR, MV, FEV1 % decreased, FV ring area decreased, PaO_2 normal after 1.0 µg/kg/h Dex given for 30 min

TABLE 2: COMPARISON OF RESPIRATORY MECHANICS INDICATORS BETWEEN BOTH GROUPS

Respiratory mechanics	Group	T0	T1	T2	T3	T4	T5	T6
V_T (ml)	Dex-A	517.48±44.25	516.49±32.33[2,3]	514.45±46.01[2,3]	513.27±46.88[2,3]	515.48±33.05[2,3]	512.49±36.37[2,3]	516.88±26.49[2,3]
	Dex-B	515.27±56.33	528.45±57.26[2,3]	519.84±55.692,3	510.47±65.32[2,3]	524.48±55.31[2,3]	518.49±53.97[2,3]	526.66±54.87[2,3]
	Mid	514.97±32.55	497.52±32.81[1]	486.45±33.091	476.48±32.67[1]	476.45±32.11[1]	482.94±33.09[1]	483.47±31.39[1]
	Pro	516.33±40.62	500.85±33.66[1]	490.33±45.311	480.22±30.88[1]	482.45±40.521	483.66±29.711	490.52±33.611
$F_{intergroup, time, interaction}$				37.812, 1.166, 1.503				
$P_{intergroup, time, interaction}$				<0.001, 0.558, 0.471				
RR (times/min)	Dex-A	17.24±0.78	16.75±0.42	17.09±0.88[2,3]	17.15±0.42[2,3]	16.88±0.39[2,3]	16.71±0.69[2,3]	17.09±0.52[2,3]
	Dex-B	17.35±0.85	17.24±0.85[2,3]	17.36±0.96[2,3]	17.27±0.65[2,3]	17.12±0.88[2,3]	17.36±0.69[2,3]	17.25±0.81[2,3]
	Mid	17.49±0.72	16.80±0.54[1]	15.79±0.66[1]	15.57±0.52[1]	15.87±0.56[1]	16.33±0.52[1]	16.57±0.48[1]
	Pro	17.50±0.66	16.77±0.62[1]	15.80±0.57[1]	15.63±0.44[1]	15.90±0.30[1]	16.21±0.47[1]	16.63±0.39[1]
$F_{intergroup, time, interaction}$				63.116, 11.854, 18.667				
$P_{intergroup, time, interaction}$				<0.001, <0.001, <0.001				
MV (L)	Dex-A	8.87±0.79	8.69±0.42[2,3]	8.82±0.79[2,3]	8.82±0.81[2,3]	8.73±0.54[2,3]	8.65±0.47[2,3]	8.78±0.36[2,3]
	Dex-B	8.85±0.92	9.14±1.03[2,3]	9.00±1.17[2,3]	8.82±1.09[2,3]	8.92±0.87[2,3]	9.00±0.84[2,3]	9.12±0.85[2,3]
	Mid	8.82±0.54	8.36±0.42[1]	7.69±0.48[1]	7.36±0.42[1]	7.55±0.47[1]	7.82±0.48[1]	8.01±0.56[1]

	Pro	8.80±0.47	8.22±0.53[1]	7.70±0.40[1]	7.29±0.38[1]	7.49±0.43[1]	7.80±0.47[1]	8.10±0.60[1]
$F_{intergroup, time, interaction}$				100.352, 6.338, 7.481				
$P_{intergroup, time, interaction}$				<0.001, <0.001, <0.001				
P_{ET} CO_2 (mmHg)	Dex-A	37.15±1.36	37.84±1.69	37.77±1.54	37.11±1.92	37.36±1.48[2,3]	37.19±1.45	37.12±1.84
	Dex-B	37.47±1.65	37.77±1.72	37.15±1.54	37.08±1.82[2,3]	37.77±1.79[2,3]	37.25±1.98	37.42±2.35
	Mid	37.54±2.08	36.35±2.121	36.14±2.191	39.38±2.16[1]	38.57±2.49[1]	37.66±1.98	37.84±2.07
	Pro	37.44±1.99	36.85±1.971	36.30±2.001	39.40±1.98[1]	38.66±2.57[1]	37.71±2.09	37.90±1.99
$F_{intergroup, time, interaction}$				0.229, 1.636, 7.011				
$P_{intergroup, time, interaction}$				0.891, 0.441, <0.001				
FEV1% (%)	Dex-A	73.44±5.27	74.15±5.57	74.19±5.36	73.57±5.09[2,3]	73.74±5.92[2,3]	74.09±4.98[2,3]	73.57±5.14[2,3]
	Dex-B	75.45±6.15	75.68±6.44[2,3]	74.82±5.63	74.61±6.82[2,3]	74.82±5.66[2,3]	74.52±5.34[2,3]	75.25±4.98[2,3]
	Mid	73.29±6.48	72.27±6.67	70.48±5.82	65.33±7.24[1]	65.17±6.35[1]	66.47±5.63[1]	67.25±6.32[1]
	Pro	73.40±5.99	72.30±5.87	70.77±6.01	65.02±7.13	65.18±7.33	66.80±5.39	67.01±6.00
$F_{intergroup, time, interaction}$				56.312, 4.011, 3.666				
$P_{intergroup, time, interaction}$				<0.001, <0.001, <0.001				

Note: Compared to T0 time point 1p<0.05; compared to Mid group [2]p<0.05; compared to Pro group [3]p<0.05 and compared to Dex-B group [4]p<0.05

Compared with T0, no significant changes were seen in $PaCO_2$, HR in Dex-A group and Dex-B group, MAP at T3 and T6 time point in Dex-A group and T6 time point in Dex-B group, $PaCO_2$ at T1, T3 and T6 time point in Mid group and Pro group, HR at T1, T3 and T6 time point and MAP at T3 and T6 time point were statistically significant compared with T0 time ($p<0.05$); $PaCO_2$ at T1, T3 and T6 time points, MAP at T3 and T6 time point and HR at T1, T3 and T6 time point in Dex-A and Dex-B groups were statistically significant ($p<0.05$) compared with Mid and Pro groups, but there was no statistically significant difference between groups in Dex-A and Dex-B for the above indexes ($p>0.05$) as shown in Table 3.

Fentanyl and norepinephrine dosages were significantly lower in the Dex-A and Dex-B groups than in the Mid and Pro groups ($p<0.05$), and the difference between the Dex-A and Dex-B comparisons was not statistically significant ($p>0.05$) as shown in Table 4.

The Ramsay score and RASS score in the Dex-A and Dex-B groups were significantly lower than those in the Mid and Pro groups, and the time to reach the target RASS, the number of days of mechanical ventilation and the length of ICU stay were significantly shorter than those in the Mid and Pro groups ($p<0.05$), but there was no statistically significant difference between the groups in the Dex-A and Dex-B groups for the above indicators ($p>0.05$) as shown in Table 5.

The proportion of bradycardia in the Dex-B group was significantly lower than in the Dex-A, Mid and Pro groups, and the proportion of unplanned extubating in the Dex-A group was significantly lower than in the Mid and Pro groups ($p<0.05$) as shown in Table 6.

TABLE 3: COMPARISON OF SAFETY INDICATORS BETWEEN THE FOUR GROUPS

Blood gas, circulation indicators	Group	T0	T1	T3	T6
$PaCO_2$ (mmHg)	Dex-A	39.24±1.45	39.35±2.34[2,3]	39.17±1.48[2,3]	40.04±1.52[2,3]
	Dex-B	39.11±4.35	38.42±2.17[2,3]	39.08±1.38[2,3]	39.65±2.08[2,3]
	Mid	39.08±2.27	41.85±1.96	43.36±2.271	42.35±2.481
	Pro	39.12±2.30	41.77±2.03	43.40±1.971	42.44±2.351
$F_{intergroup, time, interaction}$			24.317, 9.885, 12.033		
$P_{intergroup, time, interaction}$			<0.001, <0.001, <0.001		
PaO_2 (mmHg)	Dex-A	227.35±29.28	229.27±21.68	225.75±29.33	227.35±33.46
	Dex-B	236.47±32.71	229.57±30.33	227.28±29.46	235.69±31.22
	Mid	232.47±31.16	238.65±33.37	234.71±32.08	235.57±33.94
	Pro	232.40±29.87	237.00±30.31	234.52±30.66	236.47±31.55
$F_{intergroup, time, interaction}$			1.203, 1.772, 1.817		
$P_{intergroup, time, interaction}$			0.230, 0.078, 0.071		
pH	Dex-A	7.39±0.03	7.38±0.02	7.39±0.07	7.39±0.04
	Dex-B	7.40±0.02	7.39±0.03	7.38±0.04	7.39±0.04
	Mid	7.40±0.05	7.39±0.08	7.36±0.05	7.37±0.02
	Pro	7.39±0.04	7.40±0.07	7.37±0.06	7.38±0.03
$F_{intergroup, time, interaction}$			1.302, 0.771, 1.665		
$P_{intergroup, time, interaction}$			0.194, 0.441, 0.097		
MAP (mmHg)	Dex-A	87.12±3.52	86.17±2.46	83.55±3.09[1,2,3]	78.57±5.18[1,2,3]

	Dex-B	86.52±6.17	89.77±5.42	88.05±4.76[1]	90.08±4.95[1,2,3]
	Mid	87.56±5.82	88.87±8.54	95.16±8.57[1]	80.78±8.66[1]
	Pro	87.60±5.77	88.73±8.60	95.27±8.60[1]	79.94±10.12[1]
$F_{intergroup, time, interaction}$			35.812, 8.665, 9.317		
$P_{intergroup, time, interaction}$			<0.001, <0.001, <0.001		
HR (bpm)	Dex-A	75.58±6.80	76.74±7.13[2,3]	77.13±7.20[2,3]	79.15±4.47[2,3]
	Dex-B	77.25±6.28	77.09±5.62[2,3]	77.37±7.54[2,3]	78.57±5.36[2,3]
	Mid	76.58±7.22	69.35±7.27[1]	52.11±3.76[1]	59.35±2.40[1]
	Pro	76.60±6.98	70.01±7.45[1]	52.09±4.13[1]	59.40±2.13[1]
$F_{intergroup, time, interaction}$			125.718, 15.663, 20.227		
$P_{intergroup, time, interaction}$			<0.001, <0.001, <0.001		

Note: Compared to T0 time point, [1]p<0.05; compared to Mid group, [2]p<0.05 and compared to Pro group, [3]p<0.05

TABLE 4: COMPARISON OF CUMULATIVE DOSES OF SEDATIVE, ANALGESIC AND ANTIHYPERTENSIVE DRUGS IN THE FOUR GROUPS

Group	Example	Fentanyl (mg)	Norepinephrine (mg)	Propofol (mg)
Dex-A	40	0.54±0.20[1,2]	3.35±2.27[1,2]	34.15±6.77
Dex-B	38	0.59±0.37[1,2]	3.71±1.85[1,2]	32.39±6.58
Mid	30	1.13±0.49	8.95±1.87	31.08±8.57
Pro	30	1.20±0.33	8.77±2.21	30.88±9.22
F		32.959	775.778	1.356
p		0.000	0.000	0.259

Note: Compared with Mid group, [1]p<0.05 and compared with Pro group, [2]p<0.05

TABLE 5: COMPARISON OF SEDATION AND ANALGESIA EFFECTS AND DAYS OF MECHANICAL VENTILATION AND ICU LENGTH OF STAY IN THE FOUR GROUPS

Group	Example	Ramsay score (points)	RASS score (points)	Time to reach target RASS (min)	Number of days of mechanical ventilation (d)	Length of ICU stay (d)
Dex-A	40	3.61±0.54[1,2]	-1.32±0.70[1,2]	28.87±6.54[1,2]	6.82±2.84[1,2]	11.36±2.77[1,2]
Dex-B	38	3.40±0.47[1,2]	-1.33±0.69[1,2]	32.45±5.18[1,2]	6.79±3.09[1,2]	11.35±3.59[1,2]
Mid	30	3.96±0.71	-1.98±1.35	36.45±5.72	8.57±3.02	14.15±4.08
Pro	30	3.88±0.90	-2.00±1.17	35.97±6.01	8.60±2.22	13.94±3.88
F		5.207	5.186	12.614	4.463	6.482
p		0.002	0.002	0.000	0.005	0.000

Note: Compared to Mid group, [1]p<0.05; compared to Pro group, [2]p<0.05 and compared to Dex-B group, [3]p<0.05

TABLE 6: COMPARISON OF THE INCIDENCE OF ADVERSE REACTIONS AND ADVERSE EVENTS IN THE FOUR GROUPS

Group	Example	Delirium (cases)	Hypotension (cases)	Bradycardia (cases)	Unplanned extubation (cases)	Binding band usage rate (examples)
Dex-A	40	6 (15.00)	18 (45.00)	15 (37.50)[3]	0[1,2]	21 (52.50)
Dex-B	38	8 (21.05)	9 (23.68)	5 (13.16)[1,2]	2 (5.26)	19 (50.00)
Mid	30	9 (30.00)	14 (46.67)	12 (40.00)	5 (16.67)	19 (63.33)
Pro	30	10 (33.33)	13 (43.33)	13 (43.33)	4 (13.33)	18 (60.00)
χ^2		3.991	5.323	9.294	8.113	1.600
p		0.262	0.150	0.026	0.021	0.659

Note: Compared to Mid group, [1]p<0.05; compared to Pro group, [2]p<0.05 and compared to Dex-B group, [3]p<0.05

Due to their condition, mechanically ventilated patients in the ICU often require prolonged analgesic sedation to keep them in a state of cooperative sleep that allows them to awaken and complete their commanded movements, to facilitate clinical observation and neurological assessment, and to ensure safety[9]. Appropriate sedation therapy not only promotes physiological recovery, shortens the duration of mechanical ventilation and has a soothing effect on the patient's psychological state; too shallow or too deep sedation not only leads to a series of adverse effects such as hemodynamic instability, but also is not conducive to observing the patient's state of consciousness and checking sensorimotor reflexes and even prolongs the duration of mechanical ventilation, ICU stay and total hospital stay[10,11]. Therefore, the choice of sedative drugs, drug dosage is crucial. The 2013 Society of Critical Care Medicine (SCCM) guidelines on analgesia, sedation and delirium recommend that adult ICU patients should be sedated as lightly as possible and that Pro or Dex, is recommended regardless of the duration of sedation, benzodiazepines are no longer recommended. Yang *et al.*[12] also reported that Dex sedation in mechanically ventilated patients in the ICU significantly reduced other cardiovascular adverse events and reduced 28 d mortality with a good safety profile. Dex doses of 0.6 μg/kg/h and 1.0 μg/kg/h are currently used clinically, but the most appropriate dose to achieve sedation remains to be investigated.

The significance of respiratory mechanics testing is to identify mechanical changes in the respiratory system from an engineering point of view and is also an important indicator for clinical evaluation of lung function and respiratory function of patients during anesthesia[13]. Previous studies have reported[14,15] that Dex has a slight respiratory depressant effect, with some patients experiencing a slight decrease in MV and a slight increase in $PaCO_2$ after Dex sedation, but there are relatively few reports investigating the effects of different doses of Dex on respiratory mechanics. In contrast, the study showed that no significant changes were observed in V_T, RR, MV, $P_{ET}CO_2$ and FEV1 % at T1 to T6 time points in the Dex-A and Dex-B groups compared with T0; however, V_T, RR and MV at T1 to T6 time points in the Mid and Pro groups, $P_{ET}CO_2$ at T1 to T4 time points and FEV1 % at T3 to T6 time points were significantly increased or decreased, and the differences were statistically significant when comparing the corresponding time points of Dex-A group and Dex-B group; while the differences between the groups of Dex-A group and Dex-B group for the above indicators were not statistically significant. This shows that the effect of Dex on respiratory mechanics is undoubtedly less than that of Mid and Pro, but the effect of a dose of 1.0 μg/kg/h on respiratory mechanics is not significantly different from that of 0.6 μg/kg/h.

As for the safety indicators, this study showed that compared with T0, no significant changes were seen in $PaCO_2$, HR in Dex-A group and Dex-B group, MAP at T3, T6 time point in Dex-A group and T6 time point in Dex-B group, $PaCO_2$ at T1, T3, T6 time point in Mid group and Pro group, HR at T1, T3, T6 time point and MAP at T3, T6 time point, the differences were statistically significant when comparing T0 time; $PaCO_2$ at T1, T3, T6 time points, MAP at T1, T3, T6 and HR at T1, T3, T6 time points in Dex-A and Dex-B groups were statistically significant when comparing with Mid and Pro groups, but the differences between groups of the above indicators in Dex-A and Dex-B groups were not statistically significant. This shows that the use of Dex undoubtedly has a smaller effect on blood gas and circulatory indexes than the application of Mid and Pro, and the effect of the 1.0 μg/kg/h dose on blood gas and circulatory indexes was not

significantly different from the 0.6 μg/kg/h dose.

This study also showed that there was no statistically significant difference between the four groups in terms of propofol dosage, but the dosage of fentanyl and norepinephrine in the Dex-A and Dex-B groups was significantly lower than that in the Mid and Pro groups; and the Ramsay score and RASS score in the Dex-A and Dex-B groups were significantly lower than those in the Mid and Pro groups, and the target RASS time, days of mechanical ventilation and ICU. The time to reach the target RASS, days of mechanical ventilation, and ICU length of stay were significantly shorter than those in the Mid and Pro groups, suggesting that Dex used for mechanical ventilation in the ICU could achieve better sedation more quickly and reach the target RASS time, days of mechanical ventilation, and ICU length of stay. This differs somewhat from the findings reported by Wu *et al.*[16], which showed that Dex shortened the number of days of mechanical ventilation and ICU length of stay compared to Mid and Pro, but the sedation effect was comparable. The main reason for the difference in the study may be related to individual differences in sample size, but it also shows that there is still room for further investigation into the value of Dex in mechanically ventilated patients in the ICU. At the same time, based on the conclusion that the differences between the Dex-A and Dex-B groups in this study were not statistically significant, it can be seen that both the 0.6 μg/kg/h dose and the 1.0 μg/kg/h dose of Dex achieved satisfactory sedation, with comparable effects on the time to achieve the target RASS, the number of days of mechanical ventilation and the length of stay in the ICU.

This study also showed no statistically significant differences in group delirium, hypotension, and restraint band usage, but the rates of bradycardia and unplanned extubating were lower in the Dex-A and Dex-B groups than in the Mid and Pro groups, which differs from the findings reported by Yang *et al.*[17], who reported that Dex reduced the incidence of delirium in patients with acute phase aortic coarctation. In the present study, although the difference in the incidence of delirium between the three groups was not statistically significant, the incidence of delirium in the Dex-A and Dex-B groups was still lower than that in the Mid and Pro groups and based on this trend, the author believes that an increase in the sample size may make the difference significant. However, this also shows that Dex has a good safety profile and the safety profile of the 0.6 μg/kg/h dose and the 1.0 μg/kg/h dose is also equivalent.

In summary, Dex at a dose of 0.6 μg/kg/h or 1.0 μg/kg/h has less effect on respiratory mechanics, blood gas parameters and circulatory parameters than Mid and Pro in ICU mechanically ventilated cluster patients, has a more significant sedative effect and reduces the dose of fentanyl and norepinephrine, shortens the time to target RASS, the number of days of mechanical ventilation, the length of ICU stay, and with better safety.

Conflict of interests:

The authors declared no conflict of interests.

REFERENCES

1. Zhou D, Yang QM, Tang JG. A study on the effectiveness of a comfortable shallow sedation protocol based on the eCASH concept in mechanically ventilated patients. J Nurs Train 2020;35(11):1033-6.
2. Liu HJ, Shi P, Li SS. Analysis of the current status and risk factors of intensive care acquired debilitation in mechanically ventilated patients. J Chin Med 2020;37(6):36-9.
3. Cheng J, Xi MX, Zhou CY. Evaluation of eCASH strategy to prevent delirium in mechanically ventilated patients in ICU. J Nurs Sci 2019;34(20):27-30.
4. Wang YL, Wang YZ, Wang JJ. Study on the application of cluster analgesic sedation nursing intervention in mechanically ventilated patients in ICU. Chin Nurs Res 2018;32(22):3643-6.
5. Liu KF, Zhang ZP, Yang JS. Bedside ultrasound combined with sedation agitation score to guide the timing of extubation in mechanically ventilated elderly ICU patients. Chin J Gerontol 2020;40(12):2595-8.
6. Luo YN, Wang XY, Wang XC. ESCAPE strategy in the management of delirium in mechanically ventilated patients. Chin Nurs Res 2019;34(19):37-40.
7. Li Q, Zhu X, Me GQ. Evaluation of the sedative effect and safety of dexmedetomidine in combination with midazolam in patients with short duration mechanical ventilation in ICU. Chin J Minim Invasive Surg 2019;19(6):534-7.
8. Song RX, Li JY, Dong CM. Clinical application study of dexmedetomidine in ICU mechanical ventilation centralized treatment. Chin Crit Care Med 2015;(10):836-40.
9. Kaier K, Heister T, Motschall E, Hehn P, Bluhmki T, Wolkewitz M. Impact of mechanical ventilation on the daily costs of ICU care: A systematic review and meta regression. Epidemiol Infect 2019;147:e314.
10. Wilson ME, Barwise A, Heise KJ, Loftsgard TO, Dziadzko M, Cheville A, *et al.* Long-term return to functional baseline after mechanical ventilation in the ICU. Crit Care Med 2018;46(4):562-9.
11. Radosevich MA, Wanta BT, Meyer TJ, Weber VW, Brown DR, Smischney NJ, *et al.* Implementation of a goal-directed mechanical ventilation order set driven by respiratory therapists improves compliance with best practices for mechanical ventilation. J Intens Care Med 2019;34(7):550-6.

12. Yang MQ, Zhou J, Cao JW. Safety evaluation of dexmedetomidine sedation in ICU mechanically ventilated patients. Chin Crit Care Med 2016;28(9):839-44.
13. Fernandes FC, Ferreira HC, Cagido VR, Carvalho GM, Pereira LS, Faffe DS, *et al.* Effects of dexmedetomidine on respiratory mechanics and control of breathing in normal rats. Respir Physiol Neurobiol 2006;154(3):342-50.
14. Pu D, Ye WG, Wang TL. Effect of dexmedetomidine on oxygenation and respiratory mechanics during one-lung ventilation in elderly patients. J Clin Anesthesiol 2018;34(7):631-4.
15. Ma GG, Zheng JL, Xue Y. Feasibility study of dexmedetomidine for salvage sedation in patients intolerant to noninvasive ventilation after cardiac surgery. Chin J Emerg Med 2017;26(4):420-5.
16. Wu X, Tao F, Wu XD. Comparison of sedation effect of dexmedetomidine and Mid group for mechanically ventilated patients in ICU. Chin Pharm J 2016;27(24):3343-5.
17. Yang JJ, Xie L, Gui PG. Comparison of dexmedetomidine and midazolam group sedation-assisted treatment of acute stage aortic coarctation. J Pract Med 2016;32(24):4105-7.

This article was originally published in a special issue, "Drug Development in Biomedical and Pharmaceutical Sciences" Indian J Pharm Sci 2023:85(5) Spl Issue "81-91"