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Effects of dexmedetomidine combined with citrate sufentanil on the prognosis of patients with severe pneumonia and respiratory failure requiring mechanical ventilation

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Abstract: To investigate the effects of dexmedetomidine combined with citrate sufentanil on the prognosis of patients with severe pneumonia and respiratory failure requiring mechanical ventilation. 70 patients with severe pneumonia complicated with respiratory failure who were treated with mechanical ventilation were selected and divided into the combined group and the control group. The control group underwent mechanical ventilation treatment and used dexmedetomidine for sedation and analgesia, while the combined group had sufentanil analgesia in addition to the treatment of the control group. Ramsay sedation score, visual analogue scale (VAS) and pulmonary function indicators were compared between the two groups before treatment, 24h after treatment, and after extubation. After 24h treatment and extubation, the blood oxygen saturation (SpO_2), oxygenation index (OI) and arterial oxygen partial pressure (PaO_2) in the combined group were higher than those in the control group; at the same time, the serum interleukin 6 (IL-6), tumor necrosis factor α (TNF-α), and malondialdehyde (MDA) levels were lower (P<0.05). Mortality during hospitalization of the combined group was lower than the control group (P<0.05). Dexmedetomidine combined with sufentanil citrate can effectively improve sedative and analgesic effects, stress response, pulmonary function and prognosis in patients with severe respiratory failure requiring mechanical ventilation.

Keywords: Dexmedetomidine; combination; sufentanil; severe pneumonia; respiratory failure; mechanical ventilation; prognosis.

INTRODUCTION

The clinical condition of severe pneumonia is critical, the fatality rate is high, and the curative effect and prognosis are poor; in the treatment of severe pneumonia with respiratory failure, mechanical ventilation is a common rescue method (Ocal *et al*., 2016; Uvizl *et al.*, 2018). Mechanical ventilation can quickly improve the patient's lung ventilation function and relieve hypoxia and dyspnea, which is effective in the treatment of severe pneumonia with respiratory failure clinically (Tsuruta *et al*., 2014). However, mechanical ventilation intubation can irritate the patient's mouth, throat and trachea mucous membranes, causing anxiety, restlessness, pain and delirium, thereby affecting the smooth progress and therapeutic effect of mechanical ventilation treatment (Walter *et al.*, 2018). Sufentanil is safe and effective in clinical analgesia, while dexmedetomidine is a clinical anesthetic drug with good sedative and analgesic effects (Keating *et al.*, 2015; Lee *et al.*, 2019). Therefore, dexmedetomidine and sufentanil might have good results in mechanical ventilation for severe pneumonia combined with respiratory failure. Therefore, the effects of dexmedetomidine and sufentanil citrate on the condition and prognosis of patients with severe respiratory failure requiring mechanical ventilation were investigated. The results were as follows.

MATERIALS AND METHODS

A total of 70 patients with severe pneumonia combined with respiratory failure admitted to our hospital from July 2016 to June 2019 were selected as the study object. Inclusion criteria: all the patients met the clinical diagnostic criteria for severe pneumonia and respiratory failure (Guo *et al.*, 2019). The patients had indications of mechanical ventilation, and there was no gender or age limitation. Exclusion criteria: Patients with combined psychological failure or other diseases that may affect their respiratory function and prognosis, patients with allergy to related drugs and patients transferred out of treatment. All the patients met the inclusion criteria and no patients were excluded. Finally, 70 patients with severe pneumonia combined with respiratory failure were included and planned to be treated with mechanical ventilation. The patients were divided into a combined group (n=35) and a control group (n=35) by the envelope method. This experiment met ethical standards and was approved by the ethics committee of Yiwu Central Hospital. All included patients were informed and signed the informed consents. There was no statistically significant difference in baseline data such as gender, age, body mass index (BMI), and blood oxygen saturation (SpO_2) between the two groups (P>0.05), which were comparable, as shown in table 1.

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Treatment

(1) Patients in the control group were routinely treated with mechanical ventilation and were continuously monitored by intensive care before intubation. The monitoring indicators included ECG, invasive radial arterial blood pressure, pulse blood pressure saturation, heart rate (HR), respiratory rate and mean arterial pressure (MAP). Propofol was injected at 1mg/kg after intubation according to the monitor display data, and 1g/kg dexmedetomidine was continuously pumped for 10min. The BIS was detected below 60, the laryngoscope was inserted rapidly after satisfactory sedation, and the strengthened endotracheal catheter was inserted under the direct vision of the laryngoscope. The catheter was observed to be in the right position and then the ventilator was used for mechanical ventilation. The mode was auxiliary/control mode (A/C) or synchronous intermittent instruction + pressure mode (SIMV+PSV), FiO_2 was 0.5~0.8, positive end-expiratory pressure (PEEP) was 4~5cmH_2O and tidal volume was 6~8ml/kg. Relevant parameters were adjusted according to the change in arterial partial oxygen pressure (PaO_2) and PaO_2 was maintained at 6.7~10.8kPa. (2) The combined group was given sufentanil to relieve pain in addition to the treatment of the control group and the monitoring method was the same as that of the control group. Propofol injection of 1mg/kg and sufentanil citrate injection of 1g/kg were administered after intubation according to the monitoring data, and dexmedetomidine injection of 1g/kg was continuously pumped for 10min. BIS was lower than 60 and intubation and mechanical ventilation were performed. The specific parameters were set as the control group.

Observation indicators and detection methods

Before treatment, 24h after treatment and after extubation, the Ramsay sedation score, visual analogue scale (VAS), incidence of adverse reactions and in-hospital mortality of both groups were measured and compared. Meanwhile, the following indicators were measured and compared: (1) hemodynamic indicators, including HR, MAP, and SpO_2; (2) pulmonary function indicators, including PaO_2 and arterial partial carbon dioxide pressure ($PaCO_2$); (3) stress response indicators, including serum interleukin-6 (IL-6), tumor necrosis factor (TNF-α), and malondialdehyde (MDA). Statistics of VAS score, Ramsay sedation score, hemodynamic indicators, incidence of adverse reactions and in-hospital mortality were performed by the responsible nurses. The detection of pulmonary function indicators was performed by the trained personnel through the American GEM Premier4000 automatic blood and gas analyzer according to the guidance of the instrument manual. The oxygen index (OI) was calculated according to the equation "$OI = PaO_2/ FiO_2$". 5ml venous blood sample was drawn from each patient and immediately placed in an anticoagulation tube containing heparin sodium before treatment, 24h after treatment, and after extubation. After shaken and mixed, the sample was placed for 20min and centrifuged at a speed of 3500r/min and a centrifugal radius of 3cm for 5min. After stratification, the upper serum was taken and refrigerated at -20°C. All relevant tests were completed within 24h after sampling. Half an hour before detection, the samples were taken out and dissolved at room temperature (20°C). Serum IL-6, TNF-α, and MDA levels were detected by double-antibody sandwich enzyme-linked immunosorbent assay. The American BIO-RAD Model 550 enzyme marker and its mating kit were used for the test. The operation was conducted in strict accordance with the instructions of the instrument and the kit by laboratory physicians with more than 3 years of testing experience to ensure the accuracy of the test results.

STATISTICAL ANALYSIS

The SPSS22.0 software was used; the enumeration data were compared between groups by the chi-square test; the measurement data were compared between groups by the two-independent sample t-test and the prognosis of the two groups was analyzed by Kaplan Meyer survival curve. $P<0.05$ was considered statistically significant.

RESULTS

Comparison of Ramsay sedation score and VAS score before and after treatment in the combined group and the control group

The comparison of baseline data between the two groups is shown in table 1. Before the experiment, there was no significant difference in gender, age, BMI, and SpO_2 between the two groups. There was no significant difference in the VAS score between the two groups before treatment ($P>0.05$). Compared with the control group, in the combined group, the proportion of patients with Ramsay sedation score of 2~3 points after 24h of treatment and extubation was higher, and the VAS score decreased during the same period ($P<0.05$). The VAS score of the combined group and the control group

Table 1: Comparison of baseline data between the two groups

Group	Number of cases	Sex (man/woman)	Age (years old)	BMI (kg/m^2)	SpO_2 (%)
The combined group	35	17/18	61.03±8.39	23.27±3.56	91.44±0.97
The control group	35	18/17	61.06±8.31	23.65±3.73	91.28±0.91
Statistical magnitude		χ^2=0.057	t=0.015	t=0.436	t=0.712
P		>0.05	>0.05	>0.05	>0.05

decreased after 24h of treatment and extubation (P<0.05) compared with that before treatment, as shown in table 2.

Comparison of hemodynamic indicators before and after treatment between the combined group and the control group

There was no significant difference in HR, MAP, SpO_2, and other hemodynamic indicators between the two groups before and after treatment (P>0.05). Compared with before treatment, HR and MAP in the combined group and the control group decreased after treatment for 24h and extubation, while SpO_2 increased during the same period (P<0.05), as shown in table 3.

Comparison of pulmonary function indicators before and after the combined group and the control group

There was no significant difference in pulmonary function between the two groups before treatment (P>0.05).

Table 2: Comparison of Ramsay sedation score and VAS score before and after treatment in the combined group and the control group

Group	Number of cases	Before treatment		Treatment for 24h		After extubation	
		Ramsay 2~3 points [case (%)]	VAS (point)	Ramsay 2~3 points [case (%)]	VAS (point)	Ramsay 2~3 points [case (%)]	VAS (point)
The combined group	35	None	4.77±1.35	26(74.29)	3.86±0.94[a]	30(85.71)	2.60±0.81[a]
The control group	35	None	4.91±1.15	15(42.86)	4.31±0.83[b]	16(45.71)	3.14±0.73[b]
Statistical magnitude		None	t=0.467	χ^2=7.124	t=2.123	χ^2=12.428	t=2.930
P		None	>0.05	<0.05	<0.05	<0.05	<0.05

Table 3: Comparison of hemodynamic indicators before and after the treatment in the combined group and the control group

Time	Group	HR (times/min)	MAP (mmHg)	SpO_2 (%)
Before treatment	The combined group (n=35)	103.06±5.41	108.71±5.64	91.44±0.97
	The control group (n=35)	103.00±5.53	108.44±4.65	91.28±0.91
	t	0.046	0.219	0.712
	P	>0.05	>0.05	>0.05
Treatment for 24h	The combined group (n=35)	74.57±2.65[a]	77.44±6.03[a]	96.69±0.73[a]
	The control group (n=35)	74.51±3.19[b]	77. 36±3.03[b]	96.87±0.82[b]
	t	0.086	0.070	0.970
	P	>0.05	>0.05	>0.05
After extubation	The combined group (n=35)	74.77±2.98[a]	80.51±4.23[a]	98.52±0.68[a]
	The control group (n=35)	74.97±2.58[b]	80.79±5.23[b]	98.64±0.52[b]
	t	0.300	0.246	0.829
	P	>0.05	>0.05	>0.05

Table 4: Comparison of pulmonary function indicators before and after the treatment in the combined group and the control group

Time	Group	OI (mmHg)	PaO_2 (mmHg)	$PaCO_2$ (mmHg)
Before treatment	The combined group (n=35)	152.07±17.51	55.55±2.69	59.42±4.18
	The control group (n=35)	152.09±14.45	55.39±3.13	59.54±3.34
	t	0.005	0.229	0.133
	P	>0.05	>0.05	>0.05
Treatment for 24h	The combined group (n=35)	351.41±30.36	84.95±3.27	42.02±2.69
	The control group (n=35)	322.26±30.03	70.48±4.09	50.66±2.40
	t	4.039	16.348	14.179
	P	<0.05	<0.05	<0.05
After extubation	The combined group (n=35)	363.97±28.38	81.95±2.77	42.42±1.99
	The control group (n=35)	331.77±28.23	69.00±3.50	50.86±2.19
	t	4.759	17.164	16.874
	P	＜0.05	＜0.05	＜0.05

Note: compared with the same group before medication, [a]P<0.05, [b]P<0.05.

Compared with the control group, in the combined group, the OI and PaO_2 increased after 24h of treatment and extubation, while $PaCO_2$ decreased during the same period (P<0.05). Compared with before administration, OI and PaO_2 in the combined group and the control group increased after 24h of treatment and extubation, while $PaCO_2$ decreased during the same period (P<0.05), as shown in table 4.

Comparison of stress response indicators before and after treatment in the combined group and the control group

Before treatment, there was no significant difference in the stress response indicators between the two groups (P>0.05). Compared with the control group, in the combined group, serum IL-6, TNF-α, and MDA levels decreased after 24h of treatment and extubation (P<0.05). Serum IL-6, TNF-α, and MDA levels in the combined group and the control group after 24h of treatment and extubation were all reduced (P<0.05), as shown in table 5.

Comparison of prognosis between the combined group and the control group

In the combined group, 0 patients died and 35 survived during hospitalization. The mortality rate during hospitalization was 0.00% (0/35) and the survival rate was 100.00% (35/35). In the control group, there were 6 cases of death and 29 cases of survival during hospitalization. The mortality rate during hospitalization was 17.14% (6/35) and the survival rate was 82.86% (29/35). The combined group had lower mortality and a higher survival rate than the control group (2=4.557, P<0.05), as shown in fig. 1.

Comparison of the incidence of adverse reactions between the combined group and the control group

There was no statistically significant difference in the incidence of adverse reactions between the combined group and the control group (P>0.05), as shown in table 6.

DISCUSSION

Symptoms of severe pneumonia often include hypoxemia, acid-base imbalance, electrolyte disorder, and edema of lung tissue, which can lead to a significant decline in pulmonary function, rapid disease progression, difficulty in treatment, high mortality and poor efficacy and prognosis (Mizgerd *et al.*, 2017; Mizgerd *et al., 2017*; Zhou *et al*., 2020; Reyes *et al*., 2017). In recent years, with the deepening of people's understanding to severe pneumonia, the diagnostic criteria for severe pneumonia are becoming more and more perfect (Kreiniz *et al*., 2018; Russell *et al*., 2019). Severe pneumonia can be diagnosed and treated at an early stage. The emergence of new treatment methods has improved the efficacy and prognosis of severe pneumonia; however, there are still some controversy about the diagnosis and treatment of

Table 5: Comparison of stress response indicators before and after treatment in the combined group and the control group

Time	Group	IL-6 (pg/ml)	TNF-α (pg/ml)	MDA (nmol/L)
Before treatment	The combined group (n=35)	32.54±2.80	25.15±2.66	6.73±0.87
	The control group (n=35)	32.26±4.22	25.20±2.99	6.69±0.93
	t	0.327	0.074	0.186
	P	>0.05	>0.05	>0.05
Treatment for 24h	The combined group (n=35)	18.46±1.93	10.55±0.75	2.51±0.48
	The control group (n=35)	23.43±2.88	18.64±2.46	4.29±0.46
	t	8.481	18.610	15.840
	P	<0.05	<0.05	<0.05
After extubation	The combined group (n=35)	18.92±2.35	11.17±0.67	2.64±0.38
	The control group (n=35)	23.79±2.88	18.93±2.30	4.38±0.45
	t	7.751	19.164	17.478
	P	<0.05	<0.05	<0.05

Note: compared with the same group before medication, [a]P<0.05, [b]P<0.05.

Table 6: Comparison of the incidence of adverse reactions between the combined group and the control group

Group	The number of cases	Nausea	Emesis	Pruritus	Delirium	Hypotension	The total incidence
The combined group	35	3 (8.57)	1 (2.86)	2 (5.71)	1 (2.86)	2 (5.71)	8 (22.86)
The control group	35	2 (5.71)	2 (5.71)	3 (8.57)	2 (5.71)	2 (5.71)	9 (25.71)
χ^2		0.000	0.000	0.000	0.000	0.265	0.078
P		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

severe pneumonia and its prognosis is still poor (Wu *et al*., 2017; Omer *et al*., 2018; Xie *et al*., 2019; Yang *et al*., 2019). Therefore, the prognosis of severe pneumonia was analyzed through experiments. The results showed that the mortality rate of severe pneumonia patients receiving routine treatment was more than 15%, the fatality rate was high and the prognosis was poor. Improving the treatment level of severe pneumonia and the prognosis of patients was still an important issue to be solved urgently.

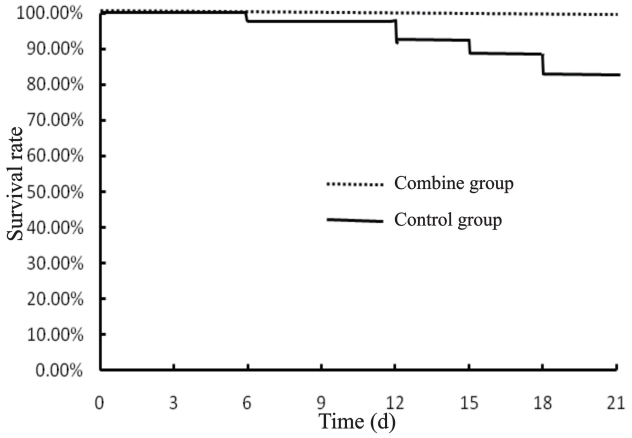

Fig. 1: Kaplan Meyer survival curves of the prognosis of the combined and the control groups

Severe pneumonia causes dysfunction in pulmonary gas exchange, which leads to severe hypoxia and carbon dioxide retention; consequently, a series of physiological-biochemical disorders, respiratory failure and respiratory failure-related complications will occur. The main treatment of respiratory failure is to relieve hypoxia; in addition, respiratory support treatment and the correction of hypoxemia are the key to the treatment of respiratory failure (de Prost *et al*., 2014). Mechanical ventilation is the most effective means to correct hypoxemia, which often requires endotracheal intubation to establish an artificial airway. However, intubation significantly affects the nervous system, cardiovascular system, and hemodynamics of patients, resulting in anxiety, restlessness, pain, delirium, and other stress reactions that affect the smooth progress of mechanical ventilation treatment (Piraino *et al.*, 2017). Adequate sedative analgesia helps reduce the occurrence of various stress responses during mechanical ventilation. Dexmedetomidine has a good analgesic effect; its combination with opioids has a good synergy effect, which has excellent applications in mechanical ventilation (Yamamura *et al.*, 2017). Sufentanil is a commonly used analgesic drug with strong analgesic efficacy, stable efficacy, good pharmacodynamics and pharmacokinetics. It has been used in clinical analgesia for a long time with few side effects. It has a good effect in mechanical ventilation analgesia, and the analgesic and sedative effects were better when combined with dexmedetomidine (Kawazoe *et al.*, 2017). Therefore, the combination of dexmedetomidine and sufentanil for mechanical ventilation might achieve a good analgesic sedation effect.

To explore the effects of dexmedetomidine-sufentanil citrate combination on patients with severe pneumonia and respiratory failure requiring mechanical ventilation, changes in sedative analgesia effects, hemodynamic indicators, pulmonary function indicators, and stress response indicators of patients before treatment, 24h after treatment and after extubation were observed and compared. Also, the prognosis and safety of the treatment were observed. Make tube drawing after treatment for 24 hours, Ramsay Sedation score 2-3, SpO_2, OI and PaO_2 in the combined group were higher than those in the control group; meantime, VAS score, $PaCO_2$, IL-6, TNF-α and MDA levels in arterial blood decreased, and the difference between the two groups was statistically significant ($P<0.05$). The results showed that dexmedetomidine combined with sufentanil citrate had good sedative and analgesic effects on patients with severe respiratory failure requiring mechanical ventilation. The HR, blood pressure, stress-related states such as oxidative stress and inflammatory response, and symptoms of hypoxemia and carbon dioxide retention in patients were improved and relieved significantly. The therapeutic effect of mechanical ventilation was good, the control of hemodynamic indicators was good and adverse reactions was few. So, dexmedetomidine combined with sufentanil citrate was safe and effective in treating patients with severe respiratory failure requiring mechanical ventilation.

CONCLUSION

The results showed that dexmedetomidine combined with sufentanil had a good sedative and analgesic effect on patients with severe respiratory failure requiring mechanical ventilation, which was safe and conducive to the control of stress response, as well as the improvement of pulmonary function and prognosis. Their combined application in clinic was helpful to improve the treatment, condition, and prognosis of severe pneumonia respiratory failure. Although this study has achieved certain results, there are still some deficiencies. For example, the research data included is not enough, which may be affected by some accidental factors. Therefore, the research data will be added to obtain more convincing and representative research results.

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