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Original Article

Bundles of care for prevention of ventilator-associated pneumonia caused by carbapenem-resistant Klebsiella pneumoniae in the ICU

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Abstract: Objective: To investigate the treatment efficacy of bundles of care for the prevention of ventilator-associated pneumonia (VAP) caused by carbapenem-resistant Klebsiella pneumoniae in the intensive care unit (ICU). Methods: A total of 102 patients undergoing mechanical ventilation in the ICU of our hospital were randomly assigned into a research group (n=51, bundles of care) and a control group (n=51, routine care). The incidence of VAP, pathogenic bacteria in the sputum, outcome and medication compliance (Morisky medication adherence scale (MMAS) score) of patients as well as the hand hygiene rate of nurses were compared between the two groups. Results: The research group showed significantly shorter time of mechanical ventilation and ICU stay, lower incidence of VAP and less ICU hospitalization costs than the control group (all P<0.05). The detection rate of pathogenic bacteria in the research group was significantly lower than that in the control group (P<0.01). Both the MMAS score and the hand hygiene rate of nurses were higher in the research group than in the control group (both P<0.01). The mortality of the research group was significantly lower than that of the control group (P<0.05). Conclusion: Bundles of care for patients undergoing mechanical ventilation in ICU can greatly shorten the time of mechanical ventilation, reduce nosocomial infection, decrease the incidence of VAP and the mortality, and is conducive to improving the hand hygiene of nurses and the medication compliance of patients.

Keywords: Bundles of care, intensive care unit, ventilator-associated pneumonia, efficacy of prevention

Introduction

Klebsiella pneumoniae is the most common isolate found in sputum and other secretions in patients with lung infection, and it is the main pathogenic bacterium in hospital-acquired pneumonia, especially respiratory infections in the intensive care unit (ICU) [1, 2]. Ventilator-associated pneumonia (VAP) is a common respiratory infection disease seen in the ICU [3]. Carbapenems antibiotic is used for the antimicrobial treatment of infection diseases caused by Klebsiella (such as VAP), but it is highly resistant to Klebsiella pneumonia due to the broad spectrum and wide application in recent years [4]. Therefore, the treatment for VAP caused by drug resistant Klebsiella pneumonia in the ICU becomes more difficult, which is not conducive to the prognosis of patients.

Bundles of care is a new nursing intervention model that has emerged in recent years. It refers to a collection of nursing interventions with evidence based treatment for patients with refractory disease, so as to provide a targeted and efficient nursing service. It is proven that the clinical intervention implemented under this nursing model are effective and can significantly improve the clinical outcome of patients [5]. Studies showed that bundles of care are highly beneficial to preventing VAP and pressure sores [6, 7]. So, we introduced bundles of care into the bedside management of patients undergoing mechanical ventilation in the ICU and proposed the hypothesis that if bundles of care can significantly reduce the incidence of VAP caused by carbapenem-resistant Klebsiella pneumoniae.

Materials and methods

General data

This study prospectively included 102 patients who underwent mechanical ventilation in the ICU of Affiliated Hospital of North Sichuan Medical College from July 2018 to January 2020. The patients were assigned into a research group (n=51) and a control group (n=51) according to a random number table. This study was reviewed and approved by the Medical Ethics Committee of Affiliated Hospital of North Sichuan Medical College, and written informed consent was obtained from all patients.

Patients were eligible if they were 30-75 years old, underwent mechanical ventilation over 48 h and signed an informed consent.

Patients were excluded if they had VAP from other causes, could not complete the examinations, had cognitive disorders or mental illness, or were participating in other clinical studies during the same period [8].

Methods

The control group was given routine ICU care. The patients were closely monitored for vital signs constantly. Physicians in charge were informed in a manner of significant changes of vital signs, including body temperature lower than 35°C or higher than 40°C, pulse less than 60 times/min or more than 140 times/min, respiratory rate more than 40 times/min or less than 8 times/min, diastolic blood pressure higher than 95 mmHg or systolic blood pressure lower than 90 mmHg [9]. Oral cleansing for patients was performed 2 times/day.

The research group was given bundles of care for VAP proposed by American IHI in 2009 and the study of Jam et al. [6, 10]. Bundles of care for VAP were developed with the following measures. Firstly, we established the bundles of care management group, who were regularly trained by the specialized infection-control personnel and ICU part-time infection-control nurses in the Affiliated Hospital of North Sichuan Medical College. The training included knowledge about susceptible factors for VAP, a seven-step handwashing method and standardized operations for airway care. The bundles of care were implemented under the supervision and guidance of the head nurse. Secondly, hand hygiene guidelines were followed. The seven-step handwashing method was strictly applied before the contact with patients, before the aseptic operation, as well as after the contact with the patient's blood, body fluids or surrounding environment. Thirdly, the bed head was raised 30-45° (for patients without contraindications) to prevent reflux of stomach content which may increase the risk of bacteria entering the lungs. Routine suction of subglottic secretions was performed for patients who were on mechanical ventilation for over 72 h. Oral cleansing for patients, especially for VAP high-risk patients was highly recommended. The patients were regularly turned over, pated on the back or treated for pressure sore prevention with the use of an applicator, and measures were taken for the prevention of peptic ulcers. Fourthly, strict and effective oral hygiene care was performed for the protection of the airway and the prevention of VAP for patients with endotracheal intubation. Besides, oral care was performed with sterile mouthwash every 6-8 hours. Fifthly, the condensate water in the ventilator pipeline was strictly managed by timely dumping out the condensate water (when over 1/2 of the capacity). Sixthly, the assessment for test shutdown and extubation was performed once a day, so as to shorten the ventilation time as much as possible. Seventhly, an ICU clinical pharmacist group was established to be responsible for standardizing the use of antimicrobial drugs, evaluating the use of antimicrobial drugs in the ICU regularly and correcting the problems (if any) according to feedback, so that the unreasonable use of antimicrobial drug was minimized. Lastly, the examination for chest (X-ray), body temperature, blood tests and lower respiratory tract bacteria were carried out according to the conditions of each patient. Timely treatment for VAP was conducted as needed.

Outcome measures

There were 2 sets of main outcome measures. First, the time of mechanical ventilation, incidence of VAP, time of ICU stay, and the ICU hospitalization costs were compared between the two groups [11]. Second, the pathogenic bacteria in the sputum was compared between the two groups by collecting patients' lower respira-

Table 1. Baseline data of two groups (n, $\bar{x}$ ± sd)

	Research group (n=51)	Control group (n=51)	χ^2/t	P
Sex			0.982	0.322
Male	27	22		
Female	24	29		
Age (years)	59.8±4.4	61.2±5.8	1.373	0.173
APACHE II score (points)	17.60±3.20	17.13±2.95	0.771	0.442
Primary disease			0.784	0.440
Cerebral hemorrhage	12	10		
Severe craniocerebral injury	7	9		
Cerebral thrombosis	8	10		
Diabetic hyperosmolar coma	5	6		
Diabetic ketoacidosis	5	3		
Acute organophosphorus pesticide poisoning	4	3		
Acute COPD exacerbation	6	7		
Others	4	3		

Note: APACHE: acute physiology and chronic health evaluation; COPD: chronic obstructive pulmonary disease.

Table 2. Comparison of clinical indicators ($\bar{x}$ ± sd)

Group	Time of mechanical ventilation (d)	Incidence of VAP (%)	Time of ICU stay (d)	ICU hospitalization cost (10,000 yuan)
Research group (n=51)	8.8±2.1	5 (9.80)	12.1±3.2	3.97±0.70
Control group (n=51)	12.2±2.8	13 (25.49)	15.8±4.2	5.12±0.78
χ^2/t	6.937	4.317	5.004	7.836
P	<0.001	0.038	<0.001	<0.001

Note: VAP: ventilator-associated pneumonia; ICU: intensive care unit.

tory tract secretions and sending the specimens to the microbiology laboratory immediately. The identification of pathogenic bacteria was performed with an automatic microorganism identification and drug sensitivity analyzer (bioMerieux, France; model: VITEK 2 Compact) [12].

There were 3 secondary outcome measures. First, the hand hygiene rate of nurses was compared, hand hygiene rate = times of handwashing according to the "seven-step handwashing method"/total times of handwashing *100%. Second, the outcomes (death or survival) of two groups were compared. Last, the medication compliance was evaluated with the use of the Morisky medication adherence scale (MMAS). The closer the score was to 8 points, the better the medication compliance [13].

Statistical analysis

SPSS 20.0 software was used for data processing. Count data were expressed as (n, %) and compared with χ^2 test. Measurement data meeting a normal distribution were expressed as mean ± standard deviation ($\bar{x}$ ± sd) and compared between groups using an independent sample t test. P<0.05 was considered to be statistically significant.

Results

Baseline data

There was no statistical difference in age, sex, acute physiology and chronic health evaluation (APACHE) II score as well as primary diseases between the two groups of patients (all P> 0.05), so that the two groups were comparable. See **Table 1**.

Comparison of clinical indicators

The research group had significantly shorter time of mechanical ventilation and ICU stay, lower incidence of VAP and less ICU hospitalization costs than the control group (all P<0.05). See **Table 2**.

Table 3. The detection rate of pathogenic bacteria in sputum (n, %)

Pathogenic bacteria	Research group (n=51)		Control group (n=51)		χ^2/t	P
	Strains	Proportion	Strains	Proportion		
G^+						
Staphylococcus aureus	2	3.92	3	5.88	/	/
Streptococcus pneumoniae	1	1.96	2	3.92	/	/
Subtotal	3	5.88	5	9.80	/	/
G^-						
Klebsiella pneumoniae	6	11.76	10	19.61	/	/
Acinetobacter baumannii	6	11.76	9	17.65	/	/
Pseudomonas aeruginosa	4	7.84	8	15.69	/	/
Escherichia coli	4	7.84	4	7.84	/	/
Subtotal	20	39.22	31	60.78	/	/
Fungus	0	0.00	1	1.96	/	/
In total	23	45.10	37	72.55	7.933	0.005

Table 4. Comparison of hand hygiene rate of nurses

Group	Number of nurses	Total number of handwashing (n)	Times of handwashing according to the "seven-step hand-washing method" (n)	Hand hygiene rate (%)
Research group (n=51)	5	75	63	84.00
Control group (n=51)	5	66	37	56.06
χ^2/t	/	/	/	13.288
P	/	/	/	<0.001

Table 5. Comparison of morality during hospitalization

Group	Death (n)	Survival (n)	Mortality (%)
Research group (n=51)	3	48	5.88
Control group (n=51)	10	41	19.61
χ^2	/	/	4.320
P	/	/	0.038

Detection of the pathogenic bacteria in sputum

A total of 23 patients (45.10%) were detected to have pathogenic bacteria in the research group. G^+ and G^- accounted for 5.88% and 39.22%, respectively. A total of 37 patients (72.55%) were detected to have pathogenic bacteria in the control group. G^+, G^- and fungi accounted for 9.80%, 60.78% and 1.96%, respectively. The detection rate of pathogenic bacteria was significantly lower in the research group than in the control group (P<0.01). See **Table 3**.

Hand hygiene rate of nurses

Five nurses in each group were randomly selected for the examination of hand hygiene. The total times of handwashing of nurses was 75 in the research group and 66 in the control group. Also, the hand hygiene rate of nurses was found to be significantly higher in the research group than in the control group (P<0.001). See **Table 4**.

Comparison of outcomes

The mortality in the research group was significantly lower than that of the control group during the ICU stay (χ^2=4.320, P=0.038). See **Table 5**.

Comparison of medication compliance

The MMAS score of the research group (5.86±1.21) was significantly higher than that of the control group (5.20±1.10; t=2.882, P=0.005), as shown in **Figure 1**.

Discussion

Each nursing measure implemented during the bundles of care is an evidence-based measure to improve patients' prognosis and outcomes, and the clinical efficacy of the bundles is significantly better than that of each measure alone

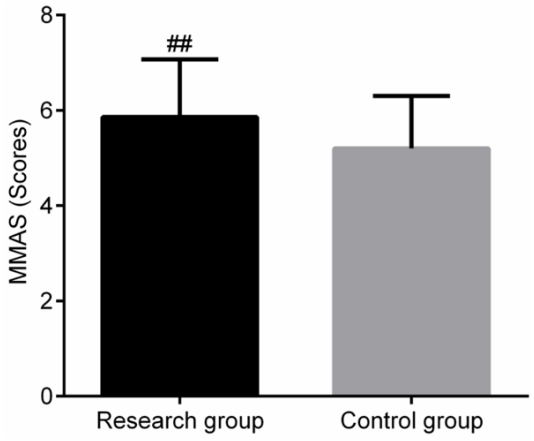

Figure 1. Comparison of MMAS scores between the two groups. Compared with the control group, ##P<0.01. MMAS: Morisky medication adherence scale.

[14]. This study found that the research group had shorter time of mechanical ventilation and ICU stay, as well as lower incidence of VAP, suggesting bundles of care for patients undergoing mechanical ventilation in the ICU can greatly reduce the time of mechanical ventilation and the incidence of VAP, which is consistent with the study of Tian et al., who found that bundles of care for ICU bedside care can significant reduce the incidence of VAP and the mortality of patients in the ICU, as well as improve the prognosis of patients [8]. In this study, the mortality in the research group was found to be lower than that in the control group (5.88% vs. 19.61%), suggesting that bundles of care for patients undergoing mechanical ventilation in the ICU can significantly reduce the mortality caused by VAP and improve the prognosis, which is also in line with the study of Tian et al. [8]. The favorable results in this study possibly came from the strict implantation of bundles of care for the prevention VAP. We applied subglottic secretion suction, oral care, prevention of peptic ulcers and pressure sores, assessment of extubation and standardized use of antimicrobial drugs for the bedside care of patients undergoing mechanical ventilation in ICU [15, 16]. The measures were conducive to shortening the mechanical ventilation time, which significantly decrease the incidence of VAP, thereby improving the prognosis and reducing the medical expenses.

This study found that G^- and G^+ are the main pathogenic bacteria that cause nosocomial infection in patients undergoing mechanical ventilation in ICU. G^- mainly included Klebsiella pneumoniae, Acinetobacter Baumannii, pseudomonas aeruginosa and Escherichia Coli. G^+ mainly included staphylococcus aureus, streptococcus pneumoniae. Fungi infections were relatively few. Our results are similar to those of Luyt et al. [17]. Statistical analysis showed that the detection rate of pathogenic bacteria in the research group was significantly lower than that in the control group (45.10% vs. 72.55%), suggesting that bundles of care for patients undergoing mechanical ventilation in the ICU can significantly reduce the nosocomial infection, which is similar to the findings of Bukhari et al. [18]. The possible reason is that we implemented hand hygiene, aseptic management and daily (morning and evening) aseptic cleansing for ventilator tube in the present study according to the prevention protocol for VAP proposed by the US Centers for Disease Control. These interventions can greatly reduce the incidence of nosocomial infection [19]. However, the detection rate of fungi in this study did not show a significant difference between the two groups, possibly because the low infection rate of fungi, and the limited sample size of this study.

According to the prevention protocol for VAP proposed by the US Centers for Disease Control, this study applied hand hygiene management. We found that the hand hygiene rate of nurses was significantly higher in the research group than that in the control group, suggesting that bundles of care are conducive to improving the hand hygiene rate of nurses. Insufficient hand hygiene rate of nurses can be an important risk factor for nosocomial infection [20]. Therefore, improving the hand hygiene rate of nurses can be considered as an important measure to reduce the nosocomial infection of patients in ICU. It was found that the MMAS score of the research group was significantly higher than that of the control group, suggesting that bundles of care for patients undergoing mechanical ventilation in the ICU can significantly improve medication compliance in patients, which is consistent with the research of Bateman et al. [21]. However, this study is a single-center study with a limited sample size, and we did not follow up the quality of life of the surviving patients after discharge, which needs to be studied in the future.

In summary, bundles of care for patients undergoing mechanical ventilation in the ICU can greatly shorten the time of mechanical ventilation, reduce the nosocomial infection, the incidence of VAP and the mortality, as well as improve the medication compliance of patients and the hand hygiene rate of nurses, so it is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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