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Prevention of neonatal ventilator-associated pneumonia through oral care with the combined use of colostrum and sodium bicarbonate

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Abstract. – OBJECTIVE: This study aims to investigate the effect of oral care via the combined use of colostrum and sodium bicarbonate on the prevention of neonatal ventilator-associated pneumonia (VAP).

PATIENTS AND METHODS: In accordance with the inclusion and exclusion criteria, 120 infant patients who were hospitalized in the neonatal intensive care unit (NICU) from January to October of 2019 were selected and randomly divided into three groups (40 cases in each group), namely, colostrum combined with sodium bicarbonate nursing (experimental group), colostrum (control group I), and sodium bicarbonate (control group II) groups. The primary outcomes measured included incidence rates of VAP and oral infection, positive rate of pathogenic bacteria after sputum culture, mechanical ventilation time, and length of stay (LOS).

RESULTS: The incidence rates of VAP and oral infection and the positive rate of pathogenic bacteria after sputum culture of the experimental group, which were 6.67%, 10.00%, and 10.00%, respectively, were significantly different from those of control groups I and II ($p < 0.05$). The mechanical ventilation time of the experimental group was 156.07 ± 26.67 h, which was shortened by 9.79% and 9.43% compared with those of control groups I and II, respectively. The LOS of the experimental group was 17.6 ± 1.96 days, which was shortened by 17.74% and 17.50% compared with those of control groups I and II, respectively. The differences were statistically significant ($p< 0.05$).

CONCLUSIONS: Oral care through the combined use of colostrum and sodium bicarbonate can lower the VAP incidence rate of infant patients and shorten their mechanical ventilation time and LOS.

Key Words:

Colostrum, Sodium bicarbonate, Oral care, Neonatal ventilator-associated pneumonia.

Introduction

With the popularization of ventilators in the neonatal intensive care unit (NICU), the success rate of neonatal rescue is evidently elevated. However, ventilator-associated pneumonia (VAP) has become a major acquired infection in hospitals and the main complication of invasive mechanical ventilation[1]. VAP lengthens the mechanical ventilation time and the length of stay (LOS) of infant patients and increases the incidence rate of their complications, hospitalization expense, and mortality risk[2,3], thereby seriously affecting neonatal short- and long-term prognoses. According to previous studies[4,5], the domestic (China) and foreign VAP incidence rates are 30.0%-60.0% and 3.0%-28.3%, respectively. Thus, preventing neonatal VAP demands a prompt solution.

The oral cavity is the main path for pathogenic microorganisms to invade the human body. A large quantity of pathogenic and nonpathogenic bacteria is present in the oral cavity of a healthy person, but saliva has an autopurification effect with strong local mucosal resistance. Bacteria can be cleared by eating and gargling. Thus, the flora in the oral cavity can be kept at a relative equilibrium. Neonates have thin and tender oral mucosa with abundant blood vessels, have underdeveloped salivary glands, and produce little secretion, and their oral mucosa is dry and can easily undergo injury and local infection[6]. Under orotracheal intubation, the oral cavity is in an open state with a weakened autopurification effect and local mucosal resistance. Thus, a large quantity of bacteria can be easily reproduced in the oral cavity[7], increasing the opportunity for oral infection. El-Solh et al[8] pointed out in their study that the respiratory pathogenic bacteria of patients with hospital-acquired pneumonia are fairly comparable with those in their oral cavity. Zheng[9]

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compared sputum cultures of the deep trachea and oropharynx and found that VAP pathogenic bacteria are highly homologous to oropharyngeal bacteria in patients. Approximately 30%-70% of the tardive VAP (incubation time exceeds five days) is induced by Gram-negative bacilli, most of which are oropharyngeal bacteria[10]. Therefore, the oral care of a mechanical ventilation patient is important. Huang et al[11] and Wang et al[12] showed that local application of sanitizer to remove oropharyngeal bacteria can effectively prevent VAP or reduce the VAP incidence rate. The main oral care solutions at present include normal saline[13], chlorhexidine[14], electrolyzed oxidizing water[15], 2.0%-2.5% sodium bicarbonate solution, and breast milk[16,17], but these solutions have disadvantages[18,19]. Clinically, 2.0%-2.5% sodium bicarbonate is most frequently used as a neonatal oral care solution to prevent VAP and to inhibit fungal reproduction[19]. Guo et al[20] have combined hydrogen peroxide with sodium bicarbonate in oral care and found that this treatment can effectively eliminate neonatal oral bacterial colonization and prevent neonatal VAP, thereby shortening the mechanical ventilation time and the LOS of infant patients. However, hydrogen peroxide may irritate the oral mucosa even at low concentrations and can lead to adverse reactions, such as hypertrophy of the lingual papilla, when used for a long time.

Several studies have proven that breast milk contains abundant cytokines and immune agents, e.g., IgA, IgM, TGF-β, TNF-α, IL-1, IL-6, and IL-8, which are always under dynamic equilibrium *in vivo*, thereby strengthening the resistance of pathogenic microorganisms; exerting a protective effect on bacteriostasis, sterilization, antivirus, anti-inflammation, immunoregulation, and anti-infection; and playing a significant role in neonatal growth and development[21]. Colostrum is early-stage breast milk generated due to tight junctions and the opening of mammary epithelial cells, and many early immune factors can be transferred from the mother's blood into the colostrum via alternative cellular pathways. Therefore, colostrum contains secretory immunoglobulin A (sIgA), anti-inflammatory cytokines, growth factors, lactoferrin, antioxidants, and other protective ingredients at high concentrations[22]. In 2009, Rodriguez et al[23] expounded neonatal oropharyngeal colostrum administration from a theoretical perspective and pointed out that colostrum can provide a wide range of protection for neonates with very low birth weight. In 2010, Rodriguez et al[24] verified the safety of colostrum. In 2013, Thibeau and Boudreaux[25] reported the effect of oropharyngeal colostrum administration on neonates with very low birth weight who received mechanical ventilation via a ventilator and found that the positive rates of respiratory secretion culture and blood culture in the oropharyngeal colostrum administration group were evidently decreased in comparison with those in the control group. Zhang et al[26] revealed that breast milk (i.e., colostrum, transitional milk, and mature milk) for oral care can effectively prevent neonatal VAP and shorten mechanical ventilation and LOS, but many shortcomings remain, such as insufficient sample sizes and uncertain curative effects. According to research suggestions, a set of comprehensive oral hygiene care should be carried out for patients with high VAP risk[27]. This study aims to discuss the preventive effect of the combined use of colostrum and 2.5% sodium bicarbonate for oral care on neonatal VAP.

Patients and Methods

Study Object

According to the inclusion and exclusion criteria (Table I), 120 infant patients who were hospitalized in the NICU from January to October of 2019 were selected after obtaining informed consent from their guardians, and the random grouping method was used to divide the patients into three groups (40 cases in each group), namely, colostrum combined with sodium bicarbonate nursing (experimental group), colostrum (control group I) and sodium bicarbonate (control group II) groups. This study was reviewed and approved by the Ethics Committee in our hospital.

Operation Steps

In order to test the efficacy of combining colostrum and sodium bicarbonate in preventing VAP, the experimental group received oral care with colostrum and 2.5% sodium. Only colostrum was applied in control group I, and the control group II was treated with 2.5% sodium bicarbonate alone. All three treatments were carried out every 6 h. All staff participating in this project were allowed to perform treatment only after they became qualified after strict and scientific training. Before oral care, oral secretions were cleared by gentle vacuum aspiration. Operators were instructed to (1) wash hands; (2) collect colostrum and prepare 2.5% sodium bicarbonate solution

Table I. Inclusion and exclusion criteria of the grouped cases.

Inclusion criteria
1. NICU-hospitalized patients (gestational age = 37-42 weeks), **2.** Patients needing mechanical ventilation due to diseases, **3.** Patients without respiratory infection before orotracheal intubation, **4.** Mechanical ventilation time ≥ two days through preliminary evaluation, and **5.** Patients neither receiving a large quantity of adrenocortical hormone or immunosuppressant within 48 h before orotracheal intubation nor diagnosed with immunodeficiency disease.
Exclusion criteria
1. Guardians of the study subjects refused to participate. **2.** Patients with the following symptoms during hospitalization: pulmonary inflammation before mechanical ventilation and chest radiograph showed new or progressive pulmonary infiltration, **3.** Patients who quit the study midway, and **4.** Patients who died in the treatment process.

and cotton swab; (3) wear gloves; (4) dip cotton swabs in the 2.5% sodium bicarbonate solution first to collect 0.1 mL of the solution and wipe the oral cavity in accordance with regular oral nursing steps (this step was bypassed in the control group I); and (5) 3-5 min later, dip cotton swabs in colostrum and perform oral care (this step was bypassed in the control group II). Colostrum (0.1 mL) was used each time, and the wiping step was repeated until the oral cavity was cleaned.

Primary Measurement Index

The clinical manifestation including the VAP incidence rate, detection result of positive pathogenic bacteria in endotracheal sputum culture, oral infection, mechanical ventilation time, LOS, and hospitalization expense of the three groups were compared.

1. Neonatal VAP diagnostic criteria: (1) Infant patients with signs of pulmonary inflammation 48 h after mechanical ventilation, and chest radiograph showing new or progressive pulmonary infiltration; (2) body temperature > 37.5°C; purulent secretions aspirated out of respiratory tract; moist rale that could be heard from their lungs, and increasing peripheral white blood cells (> 10×10^9 per L); (3) chest radiograph showing infiltration shade in the lungs; (4) pathogenic bacteria cultured from tracheal secretions; and (5) patients already experiencing pulmonary infection should undergo sputum culture 48 h before and after mechanical ventilation. VAP could be diagnosed when a difference in pathogenic bacteria was found.

2. Collection method of sputum culture: the endotracheal sputum was collected from all cases for bacterial culture when VAP signs (conforming to any of VAP diagnostic criteria) were found 48 h after mechanical ventilation. If the mechanical ventilation time exceeded 72 h, sputum culture was carried out every two days or regularly as required.

3. Diagnostic criteria for oral infection: erythema, edema, erosion, ulceration, and thrush appearing in the oral mucosa.

1. Quality control: the specimens were collected by well-trained nurses who worked for five years in the NICU. The nurses washed hands strictly before collecting the specimens, and a disposable sterile sputum suction catheter was inserted through the endotracheal tube to collect secretions from the lower respiratory tract for bacterial culture. The specimens were collected and preserved in strict accordance with sterile operating procedures and sent to the laboratory within 30 min after collection.

Statistical Analysis

The statistical analysis was implemented via SPSS 21.0 (IBM, Armonk, NY, USA) software. Measurement data were described using the mean ± standard deviation, and enumeration data were expressed using case number and percentage. The Chi-square test was adopted for the incidence rates of VAP and oral infection and the positive rate of sputum culture (incidence rate of respiratory tract infection). The independent-samples *t*-test was carried out for the mechanical ventilation time, LOS, and hospitalization expense of the three groups, and the test level was $p = 0.05$.

Table II. Comparison of the NICU treatment time of infant patients in the three groups.

	Experimental group	Control group I	Control group II
LOS (days, mean ± SD)	17.60 ± 1.96	19.43 ± 1.73	21.33 ± 1.85
t	NA	-3.85	-7.59
p	NA	5.47×10^{-5}	9.18×10^{-9}
Mechanical ventilation time (h, mean ± SD)	156.03 ± 26.67	172.97 ± 36.95	189.70 ± 28.10
t	NA	-2.04	-4.76
p	NA	0.013	3.48×10^{-5}

t and *p*-values are the statistical analysis results of the control groups I and II in comparison with the experimental group.

Results

LOS and Mechanical Ventilation Time of the Infant Patients

The three groups were compared on the basis of LOS and mechanical ventilation time (Table II and Figure 1). The average LOS of the experimental group was significantly shorter than those in control groups I and II (all $p < 0.01$). The *p*-value of the mechanical ventilation time between the experimental group and control group I was 0.08, indicating that the difference was not significant. The *p*-value between the experimental group and the control group II was 0.004, indicating a significant difference.

Incidence Rates of VAP, Respiratory Infection, and Oral Infection

The results are shown in Table III. The incidence rates of VAP and respiratory infection in the experimental group were significantly lower than those in control group II ($p < 0.05$). The incidence rate of oral infection in the experimental group was also lower than those in control groups I and II, but the difference was not statistically significant ($p > 0.05$).

Discussion

VAP, a common hospital-acquired infection in the NICU, markedly increases the treatment time and the expense of infant patients and elevates their fatality rate. Oral care, the simplest and most effective preventive method for VAP in infant patients, keeps the oral cavity clean and prevents oral infection. The common oral care solutions at present include normal saline, 2.0%-2.5% sodium bicarbonate, chlorhexidine, and breast milk. This study reveals that in comparison with the independent use of colostrum or 2.5% sodium bicarbonate solution, their combined use for the oral care of infant patients under mechanical ventilation can lower the incidence

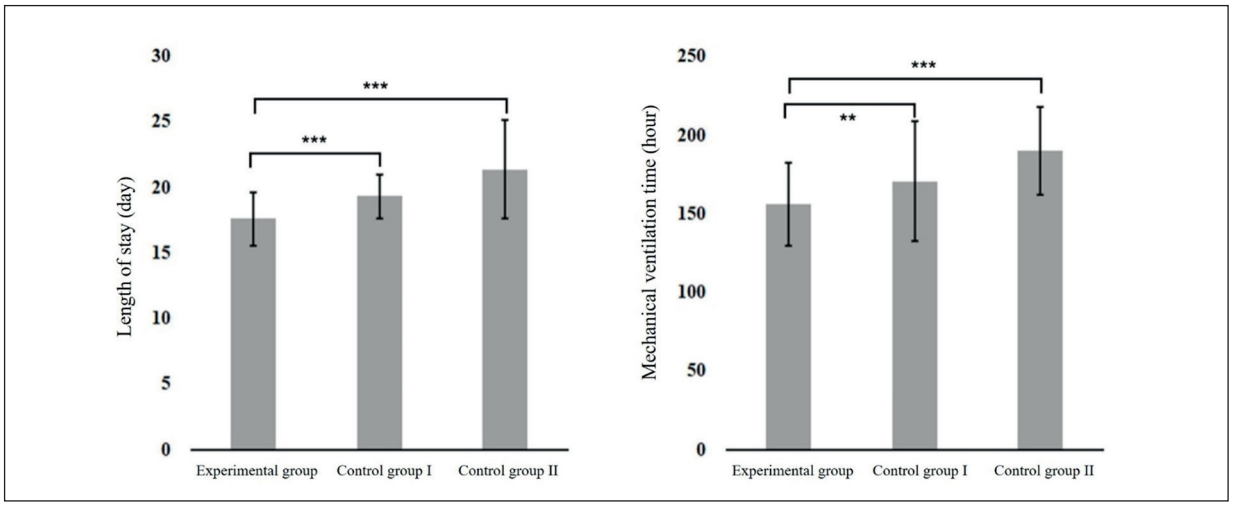

Figure 1. NICU treatment time of the infant patients in the three groups. *: $p > 0.05$; **: $0.05 > p > 0.01$; ***: $p < 0.01$.

Table III. Incidence rates of VAP, respiratory infection, and oral infection of the infant patients in the three groups.

	Experimental group	Control group I	Control group II
VAP			
Case number (percentage)	2 (6.67%)	6 (20.00%)	8 (26.67%)
χ^2	NA	2.31	4.32
p	NA	0.13	0.04
Positive rate of pathogenic bacteria in sputum culture			
Case number (percentage)	3 (10.00%)	8 (26.67%)	10 (33.33%)
χ^2	NA	2.78	4.81
p	NA	0.10	0.03
Oral infection			
Case number (percentage)	3 (10.00%)	5 (16.67%)	6 (20.00%)
χ^2	NA	0.58	1.18
p	NA	0.45	0.28

χ^2 and *p*-values are statistical analysis results of the control groups I and II in comparison with the experimental group.

rates of VAP and oral infection and shorten their mechanical ventilation time and LOS. In addition to high safety, economic efficiency and effectiveness, high parent compliance is another remarkable advantage of the combined use of colostrum and 2.5% sodium bicarbonate for oral care. Mobilizing the mother's initiative in looking after hospitalized infant patients and relieving the anxiety of their family members can improve the doctor-patient relationship and improve the satisfaction of patients.

The effect of the independent use of colostrum for oral care is superior to that of the independent use of 2.5% sodium bicarbonate, and the effect of their combined use is better than the effect of their respective independent use, indicating that colostrum and sodium bicarbonate have different oral care mechanisms and can be mutually complementary. The main function of sodium bicarbonate is to change the pH of the oral environment, maintain a weak alkaline environment, and repress the growth of some of the acidophilic environmental microorganisms. Furthermore, unlike normal saline, the sodium bicarbonate solution cannot easily form a local hypertonic environment, which can cause dehydration and shrinkage of oral epithelial cells and mucosal bleeding, indicating its superior safety in neonatal oral care[27]. Colostrum contains probiotics and all kinds of immune ingredients from mothers. Compared to transitional (4-10 days after delivery) and mature (11 days-9 months after delivery) milk, colostrum has higher concentrations of secretory immunoglobulin A (slgA), anti-inflammatory cytokines, growth factors, lactoferrin, antioxidants, and other protective ingredients[27] and has stronger immune effects. Hence, the combined use of colostrum and 2.5% sodium bicarbonate can exert the "1 + 1 > 2" (multiplying) effect.

Our study reveals that the incidence rates of VAP and respiratory infection in the experimental group declined in comparison with those in control groups I and II. However, the Chi-square test results show that the difference between the experimental group and control group I is not statistically significant but that between the experimental group and control group II is statistically significant, thereby proving that the probiotics and immune ingredients contained in colostrum play an important role in oral care. Regarding the incidence rate of oral infection, the differences in the experimental group from those of the control groups I and II were not statistically significant. In this study, the diagnostic criteria for oral infection were erythema, edema, erosion, ulceration, and thrush in the oral mucosa. In addition to microbial infection, oral mucosal injury and dehydration during the mechanical ventilation process may lead to similar clinical manifestations and cause a certain proportion of misjudgments (false positives). Additionally, some of the infant patients included in the study may be the result of these misjudgments. Increased sample size and a more objective diagnostic method for oral infection (e.g., microculture, macrogenomic sequencing) will contribute to further study of the relationship between oral care and the incidence rate of oral infection in neonatal mechanical ventilation treatment.

Conflict of Interest
The Authors declare that they have no conflict of interests.

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