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Efficacy of acetylcysteine combined with budesonide nebulization in the treatment of neonatal pneumonia and its effect on serum inflammatory factors and oxidative stress indicators

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Abstract: To investigate the clinical efficacy of acetylcysteine combined with budesonide nebulization in the treatment of neonatal pneumonia and its effect on serum inflammatory factors and oxidative stress indicators. 97 children with neonatal pneumonia admitted to our hospital from September 2022 to July 2024 were selected and randomly divided into a control group (n=39, receiving budesonide aerosol treatment) and an experimental group (n=38, receiving acetylcysteine combined with budesonide aerosol treatment). The clinical efficacy, inflammatory factor levels [tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), C-reactive protein (CRP)], oxidative stress indicators [superoxide dismutase (SOD), malondialdehyde (MDA) and glutathione peroxidase (GSH-Px)] and the incidence of adverse reactions during treatment were compared between the two groups. After treatment, the total effective rate in the experimental group (97.37%) was higher than that in the control group (82.05%)(P<0.05). The levels of inflammatory factors decreased significantly in both groups. After treatment, the levels of TNF-α, IL-6, and CRP in the experimental group decreased more significantly than those in the control group (P<0.05). The levels of SOD and GSH-Px in the experimental group were significantly higher than those in the control group, and the levels of MDA were significantly lower than those in the control group (P<0.05). The incidence of adverse reactions in the experimental group (7.89%) was lower than that in the control group (17.95%), but the difference was not statistically significant (P>0.05). Acetylcysteine combined with budesonide has obvious efficacy in the treatment of neonatal pneumonia. It can reduce inflammatory response, improve oxidative stress, and is safe.

Keywords: Acetylcysteine; Budesonide; Neonatal Pneumonia; Inflammatory Factors; Oxidative Stress; Aerosol Treatment

Neonatal pneumonia is a common and serious respiratory disease in the neonatal period. It is caused by infection with bacteria, viruses, fungi and other pathogens, or inhalation of amniotic fluid, intrauterine infection and other factors. Due to immature lung development and low immunity, inflammatory reactions can be quickly induced. In severe cases, it can lead to respiratory failure and endanger life [1-2].At present, the treatment of neonatal pneumonia mainly includes anti-infection, supportive treatment and measures to improve pulmonary function, such as antibiotic application, airway humidification, oxygen therapy and mechanical ventilation. Budesonide is a glucocorticoid, commonly used for aerosol treatment of respiratory diseases. It has a strong local anti-inflammatory effect, can inhibit pulmonary inflammatory response, reduce airway hyperresponsiveness, and improve ventilation function [3].Acetylcysteine is a mucolytic agent with both antioxidant and anti-inflammatory properties. It can increase pulmonary glutathione levels and scavenge reactive oxygen species free radicals, thereby reducing oxidative stress damage and promoting airway secretions excretion [4].The purpose of this study was to investigate the efficacy of acetylcysteine combined with budesonide nebulization in the treatment of neonatal pneumonia, and to analyze its impact on serum inflammatory factors and oxidative stress indicators, in order to optimize the treatment strategy of neonatal pneumonia.

1. Materials and methods

1.1 General information

Select children with neonatal pneumonia who received treatment in our hospital from September 2022 to July 2024. Inclusion criteria:① Full-term newborns with a gestational age ≥37 weeks and a birth weight ≥2.5kg;② Meet the diagnosis related to neonatal pneumonia [5], and were diagnosed with neonatal pneumonia through clinical and imaging examinations;③ The hospital stay exceeds 72 hours, which

meets the indications for aerosol treatment;④ The vital signs are stable, and there is no serious organ dysfunction or other life-threatening complications;④ No history of allergic reactions to glucocorticoids, acetylcysteine and other related drugs.Exclusion criteria:① Premature infants or low birth weight infants;② Complicated with congenital heart disease, bronchopulmonal dysplasia and other diseases that affect lung function;③ Complicated with serious infectious diseases;④ Severe liver and renal dysfunction, or other diseases that may affect drug metabolism and excretion;④ Incomplete clinical data. A total of 97 children with neonatal pneumonia were included and randomly divided into a control group (n=39, receiving budesonide aerosol treatment) and an experimental group (n=38, receiving acetylcysteine combined with budesonide aerosol treatment). There was no statistical difference between the two groups in baseline data such as age, birth weight, and gender (P>0.05)(Table 1).

Table1 Comparison of baseline data between the two groups [±s,n(%)]

Index	Control Group (n=39)	Experimental Group (n=38)	χ2/t Values	P Value
Age (days)	16.29±2.31	16.32±2.44	0.055	0.956
Gender			0.639	0.424
Male	21(53.85)	17(44.74)		
Female	18(46.15)	21(55.26)		
Weight (kg)	3.49±0.26	3.51±0.35	0.285	0.776
Disease Duration (days)	4.19±1.04	4.23±1.12	0.162	0.871
Apgar Score (5 min) (days)	9.52±0.22	9.43±0.31	1.472	0.145

1.2 Treatment methods

The children in the control group received routine supportive treatment, including keeping the respiratory tract unobstructed, oxygen therapy, maintaining water and electrolyte balance, and anti-infective treatment. On this basis, they were given budesonide (Health Yuan Pharmaceutical Group Co., Ltd., Sinopharm Approval H20203343, 2ml: 0.5 mg) nebulized inhalation. A PARIBOYSX medical nebulizer was used to ensure that the diameter of the drug particles was controlled at 3 - 5μm and the concentration of the drug solution was 0.5 mg/2mL, 2mL each time, twice a day, for 7 consecutive days. During aerosol treatment, the child is in a supine or lateral position, and the aerosol mask is placed close to the face to ensure adequate inhalation of the drug.

The children in the experimental group received nebulized inhalation of acetylcysteine (Renhe Yikang Group Co., Ltd., Sinopharm Approval No. H20223650, 3ml: 0.3 g) based on the control group. The concentration of the drug solution was 100mg/2mL, 1.5 mL each time, twice a day, and was used in combination with nebulized budesonide for 7 consecutive days.

1.3 Observation indicator

(1)Clinical efficacy. Effective: The child's symptoms such as shortness of breath, wheezing, and coughing were significantly relieved or disappeared, and the auscultation wet rales in the lungs were significantly reduced or disappeared. Imaging showed that the lung lesions were completely absorbed, and the level of inflammatory factors was significantly reduced or close to the normal range; Effective: The clinical symptoms were partially relieved, coughing and wheezing were reduced, and the auscultation rales in the lungs were reduced but still existed. Imaging showed that the shadow of inflammation in the lungs was absorbed by 50% to 75%, and the level of inflammatory factors decreased compared with before but did not return to normal; Invalid: Clinical symptoms have not been significantly improved or even worsened [6]. The total effective rate of treatment is the sum of the percentages of effective and effective.

(2)Inflammatory factor levels. All children received 2mL venous blood samples in the morning before treatment and after the seventh day of treatment. After serum was separated, TNF-α, IL-6, and CRP levels were measured by enzyme-linked immunosorbent assay. The kit was purchased from R& D Systems.

(3)Oxidative stress level. The blood collection method was the same as above. After separating the serum, the levels of superoxide

dismutase (SOD), malondialdehyde (MDA) and glutathione peroxidase (GSH-Px) were measured by colorimetric method. The kit was purchased from Nanjing Jiancheng Institute of Bioengineering.

(4)Adverse reactions. The occurrence of adverse reactions such as worsening dyspnea, bronchospasm, laryngeal edema, and vomiting during treatment was recorded.

1.4 Statistical methods

Statistical analysis was performed using SPSS25.0. Measurement data such as inflammatory factors that conform to normal distribution were tested. Independent t tests were used for inter-group comparisons, and paired t-test within group was expressed as ($\overline{x} + s$). Statistical data such as gender and clinical efficacy were tested using χ 2, and the data were expressed as n (%). P <0.05 was used as the difference was statistically significant.

2. Results

2.1 Clinical efficacy

The total effective rate of treatment in the observation group (97.37% vs 82.05%) was significantly higher than that in the control group (P<0.05)(Table 2).

Table2 Comparison of clinical efficacy in group 2 [n (%)]

Group	Markedly Effective	Effective	Invalid	Total Effective Rate
Control Group (n=39)	15(38.46)	17(43.59)	7(17.95)	32(82.05)
Experimental Group (n=38)	23(60.53)	14(36.84)	1(2.63)	37(97.37)
χ2				4.850
P				0.028

2.2 Inflammatory factors level

After treatment, the levels of inflammatory factors decreased in both groups, and the decrease in TNF-α, IL-6, and CRP in the experimental group was greater than that in the control group (P<0.05)(Table 3).

Table3 Comparison of inflammatory factor levels in group 2 children ($\overline{x} + s$)

Group	TNF-α(pg/mL)		IL-6(pg/mL)		CRP(mg/L)	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Control Group (n=39)	35.21±4.86	25.43±3.76 a	50.82±6.74	34.87±5.92 a	5.18±1.12	2.47±0.72 a
Experimental Group (n=38)	35.57±5.14	20.32±3.21 a	51.12±7.05	27.41±4.88 a	5.24±1.23	2.02±0.65 a
t	0.316	6.406	0.191	6.025	0.224	2.876
P	0.753	<0.001	0.849	<0.001	0.823	0.005

Note: Compared with the same group before treatment, a P<0.05.

2.3 Oxidative stress level

After treatment, the levels of SOD and GSH-Px in the experimental group were significantly increased, and the level of MDA decreased significantly, which was statistically significant compared with the control group (P<0.05)(Table 4).

Table4 Comparison of oxidative stress levels in children in groups 2 ($\bar{x} + s$)

Group	SOD(U/mL)		MDA(nmol/mL)		GSH-Px(U/L)	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Control Group (n=39)	101.13±13.52	122.36±10.78 a	5.14±0.83	4.59±0.76 a	123.44±18.62	183.08±19.47 a
Experimental Group (n=38)	100.38±14.29	137.80±9.84 a	5.20±0.89	3.18±0.64 a	122.47±20.13	215.86±21.72 a
t	0.237	6.559	0.306	8.795	0.220	6.977
P	0.814	<0.001	0.760	<0.001	0.827	<0.001

Note: Compared with the same group before treatment, a P<0.05.

2.4 Adverse reactions

During treatment, the incidence of adverse reactions in the experimental group (7.89% vs. 17.95%) was lower than that in the control group (P>0.05)(Table 5).

Table5 2 Adverse comparison of children in groups [n (%)]

Group	Aggravated Dyspnea	Bronchospasm	Laryngeal Edema	Vomiting	Total Incidence
Control Group (n=39)	3(7.69)	1(2.56)	1(2.56)	2(5.13)	7(17.95)
Experimental Group (n=38)	1(2.63)	1(2.63)	0	1(2.63)	3(7.89)
$\chi 2$					1.722
P					0.189

3. Discussion

Neonatal pneumonia is a common infectious disease in the neonatal period. Its pathological mechanism involves many aspects such as inflammatory response, oxidative stress damage and increased airway secretions. In recent years, the application of aerosol therapy in the management of neonatal lung diseases has gradually increased. Among them, budesonide, as a glucocorticoid, can effectively inhibit inflammatory reactions and reduce airway hyperresponsiveness; acetylcysteine not only has mucolytic effect, but also has certain antioxidant and anti-inflammatory capabilities. Therefore, exploring the effect of combined atomization therapy with the two is of great significance to improving the treatment strategy of neonatal pneumonia.

The results of this study show that the clinical efficacy of the experimental group is better than that of the control group, suggesting that acetylcysteine combined with budesonide can more effectively relieve the symptoms of neonatal pneumonia. Studies have shown that acetylcysteine nebulization therapy plays an important role in improving sputum viscosity and airway patency in patients with chronic airway diseases [7-8]. Wang et al.[8] also showed that combined aerosol therapy can promote the improvement of symptoms in patients with respiratory diseases more than glucocorticoid alone treatment, which is consistent with the results of this study. TNF-α and IL-6 are pro-inflammatory cytokines that can induce an inflammatory cascade and aggravate lung tissue damage during the course of pneumonia, while CRP levels can reflect the body's inflammatory state. The results of this study showed that the levels of TNF-α, IL-6 and CRP in the experimental group were all reduced, and the decrease was greater than that in the control group, indicating that the combination treatment can more effectively inhibit the inflammatory response related to neonatal pneumonia. This study suggests that the application of acetylcysteine may reduce inflammatory damage in the lungs by increasing glutathione levels and reducing reactive oxygen-induced inflammatory reactions. This result is similar to the study by Chen et al.[6]. Acetylcysteine has a significant role in reducing the level of inflammatory factors in patients with acute lung injury and reduces lung tissue damage by resisting oxidative stress.

SOD and GSH-Px are important endogenous antioxidant enzymes in the body, which can reduce free radical damage to lung tissue, while MDA is the end product of lipid peroxidation, and its level reflects the degree of cellular oxidative damage. This study found that the levels of SOD and GSH-Px in the experimental group increased, and the level of MDA decreased significantly, both better than the control

group, indicating that the application of acetylcysteine can effectively increase the level of antioxidant enzymes and reduce MDA production, thereby reducing the level of oxidative stress. Chen et al.[9] pointed out that acetylcysteine can improve the function of alveolar epithelial cells by inhibiting ROS production and reducing lipid peroxidation damage. This mechanism can also partially explain the significant improvement in oxidative stress levels in the experimental group in this study. This study found that the incidence of adverse reactions in the experimental group was lower than that in the control group. Although the difference was not statistically significant, it still suggested that the combination therapy has good safety. Aerosolized glucocorticoids may cause laryngeal irritation or bronchospasm, while aerosolized acetylcysteine may temporarily increase airway secretions by diluting sputum, thereby inducing coughing or choking [10]. However, moderate use of acetylcysteine not only does not increase serious adverse reactions, but can improve airway wetness, reduce mucus blockages, and enhance airway barrier function by reducing oxidative stress levels, thereby reducing drug-related adverse reactions and improving aerosol treatment. Safety [11].

In summary, acetylcysteine combined with budesonide nebulized treatment can significantly improve the clinical efficacy of neonatal pneumonia, reduce the level of inflammatory factors, improve oxidative stress, and at the same time have good safety. This study provides new clinical basis for optimal treatment of neonatal pneumonia. In the future, multi-center, large-sample randomized controlled studies can be further carried out to further verify its long-term efficacy and safety.

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