Research Article

Evaluation of the Efficacy of Budesonide Combined with Pulmonary Surfactants on the Neonatal Respiratory Distress Syndrome by Pulmonary Ultrasonography

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Objective. This study aimed to investigate the value of lung ultrasound images in evaluating the efficacy of budesonide combined with pulmonary surfactant (PS) in the treatment of neonatal respiratory distress syndrome (NRDS) in premature infants. **Methods.** 76 NRDS premature infants admitted to the hospital were randomly divided into experimental group and control group, with 38 children in each group. The premature infants in control group underwent PS, and those in experimental group underwent budesonide combined with PS. After treatment, lung ultrasound imaging was used to evaluate the curative effect, and X-ray results were used as a reference. The changes in clinical signs of two groups were detected, and the pulmonary ultrasound was used to evaluate the clinical efficacy of two groups. The changes in the lung ultrasound score (LUS) and arterial blood gas (ABG) indexes of two groups were compared before and after treatment. **Results.** LUS and improvement of patients of experimental group were obviously higher than those of the control group after treatment. LUS of experimental group was 12.1 ± 3.7 , and that of control group was 18.2 ± 2.3 , respectively. The differences were statistically significant ($P < 0.05$). The arterial partial oxygen pressure (PaO_2) and oxygenation index ($\text{PaO}_2/\text{FiO}_2$) levels of two groups of patients increased dramatically after treatment. PaO_2 and $\text{PaO}_2/\text{FiO}_2$ levels of experimental group were 65.59 ± 12.46 mmHg and 112.57 ± 19.3 mmHg, and those of control group were 45.12 ± 11.21 mmHg and 101.28 ± 21.36 mmHg, respectively. However, arterial partial pressure of carbon dioxide (PaCO_2) level was significantly decreased in two groups after treatment. PaCO_2 level of experimental group was 40.24 ± 8.92 mmHg, and that of control group was 41.22 ± 9.24 mmHg, respectively ($P < 0.05$). The diagnostic accuracy of lung ultrasound images in two groups was 95.3% and 96.2%, respectively. **Conclusion.** Pulmonary ultrasonography showed a high diagnostic accuracy in evaluating the efficacy of budesonide combined with PS in the treatment of NRDS in premature infants. It can evaluate the cardiopulmonary function of premature infants with NRDS and effectively improve the respiratory status of premature infants. In conclusion, this study provided some reference value for upgrading the clinical treatment of NRDS in premature infants.

1. Introduction

Neonatal respiratory distress syndrome (NRDS) is a common respiratory disease of premature infants, mainly manifested as expiratory moans, dyspnea, and other symptoms [1]. At present, the principle of clinical treatment of NRDS is to restore the normal breathing of children as soon as possible to prevent infection. Ventilation can be assisted by a ventilator, and PS substitutes are used to relieve symptoms and improve quality of life before premature

infants can secrete enough pulmonary surfactant (PS). The traditional treatment of NRDS is mechanical ventilation, which is easy to cause bronchopulmonary dysplasia and other complications [2].

Studies in recent years have shown that the function of simulating PS can be achieved by supplementing similar PS externally to premature infants so as to expand the lungs of premature infants and relieve the symptoms of NRDS. Representative drugs include bovine lung surfactant for injection, which has been proved to have good clinical

efficacy [3]. In addition, studies have confirmed that local use of glucocorticoids (GCs) can directly alleviate lung diseases. Anti-inflammatory effect of GCs such as inhibition of inflammatory mediator release and cytokine-mediated immune response may play an important role in the treatment of NRDS. The endogenous potency of budesonide (Bun) was 15 times higher than that of prednisolone in terms of hormone affinity for GC receptors. A clinical study comparing the effects of inhaled and oral Bun on NRDS confirmed a significant difference between inhaled Bun and placebo, but there were no significant differences between oral Bun and placebo [4].

At present, physical examination, X-ray examination, and echocardiography are mainly used in clinical diagnosis of NRDS. Doctors carefully examine premature infants' skins and lips to see if they turn blue or purple during the physical examination. Doctors also auscultate premature infants' chests to examine whether there are abnormal breath sounds. Blood gas analysis (BGA) helps doctors determine whether and to what extent premature infants have been deprived of oxygen. Serological examination is performed after birth. X-ray examination is the best examination method of NRDS because it can observe lung imaging in premature infants and clearly examine pulmonary function of premature infants. Echocardiography is used when NRDS cannot be completely confirmed by the above examinations, and the corresponding conditions of arterial catheter can be observed. In addition, recent studies have shown that lung ultrasound (LUS) can effectively diagnose NRDS and contribute to early prediction of the risk of bronchopulmonary dysplasia [5]. There is a certain correlation between LUS score and oxygen exchange index, which can be used to evaluate the respiratory status of premature infants [6]. In summary, this study aimed to treat NRDS with GCs Bun combined with PS and observe its clinical effect and influence on the blood gas index by LUS. The main contents of this study were as follows.

2. Materials and Methods

2.1. Basic Information. A total of 78 premature infants with NRDS occurring within 4 hours of birth and less than 35 weeks of gestational age and less than 2.5 kg of birth mass admitted to our hospital from January 2017 to June 2019 were selected as the subjects. The families of the sick children have been informed and agreed to this study. All children were randomly divided into experimental group and control group, with 39 cases in each group. In experimental group, there were 20 males and 19 females with the gestational age of 30.12 ± 3.06 weeks and body mass of 1.71 ± 0.53 kg. In the control group, there were 21 males and 18 females with the gestational age of 31.81 ± 2.85 and body mass of 1.68 ± 0.48 kg. There was no significant difference in gender, gestational age, and body mass between the two groups ($P > 0.05$), and the general data were comparable. All the procedures of this study were approved by the Ethics Committee of the hospital, and all the legal guardians of premature infants signed informed consents.

2.2. Research Methods. Two groups of children were given routine treatment; after admission, heat preservation was conducted. In addition, electrocardiogram monitoring was conducted to monitor arterial blood gas (ABG) indicators, and intravenous nutrition was given. The airway was cleaned prior to administration. Control group was given PS (70 mg/kg), and experimental group was given a mixture of PS and Bun (0.25 mg Bun/70 mgPS). It was injected into lung through trachea within 4 hours after birth, and if necessary, it can be injected once more within 6–12 h after birth. The ventilator can be used to support breathing if needed. Ventilator parameters were adjusted according to the patient's condition and blood and gas analysis, and the ventilator was withdrawn until the patient's physical signs returned to normal.

2.3. Pulmonary Ultrasonography. In this study, the LUS testing was performed on all patients before and after treatment. The testing equipment used was Philips CX50 ultrasonic diagnostic instrument, high-frequency linear array probe L12-3, and frequency of 8–12 MHz, and chest conditions were selected for the instrument settings. As the reference chest X-ray examination, Shimadzu bedside X-ray machine was used, with the parameter setting tube voltage of 50 kV and tube current of 2.0 mAs. The BGA test adopted the Danish Radiometer ABL 800 FLEX analyzer.

All children with RDS in the two groups underwent LUS and chest X-ray before and after treatment. During the LUS examination, the children took the supine position and the lateral position. The lung was divided into the front chest, side chest, and back area with the front and back axillary line as the boundary. The probe scanned the abovementioned areas horizontally and vertically, and the corresponding image information were recorded and stored. In addition, the children in the study group were followed up twice a week until the ventilator was withdrawn or the gestational age was corrected for 36 weeks to further monitor the progress of children with RDS. During the study period, the LUS examination was not used for clinical disease diagnosis, and there was no intervention in the treatment plan of the children.

2.4. Efficacy Evaluation and Observation Indicators. The use time, oxygen use time, and hospitalization time of the two groups of ventilators were recorded, and the LUS scores and blood gas index changes of the two groups before and after treatment were compared, including arterial partial pressure of oxygen (PaO_2), arterial partial pressure of carbon dioxide (PaCO_2), and oxygenation index ($\text{PaO}_2/\text{FiO}_2$). Among them, the LUS scoring reference standards used in this study were given as follows: normal aerated lung tissue was recorded as 0 points; a large amount of B-line was recorded as 1 point; dense B-line was recorded as 2 points; and lung consolidation was recorded as 3 points [7].

The changes in clinical symptoms and monitoring indicators of the two groups of patients were analyzed after medication, and the efficacy of the two groups was evaluated. If the patient's groaning disappeared after the medication, breathing was smooth, there was no acid-base imbalance and

electrolyte imbalance, blood gas indicators were normal, the lung texture was clear after LUS examination, and the LUS score was obviously reduced; it was judged that the treatment showed a significant effect. If the patient's groaning disappeared after treatment, breathing was stable, blood gas indicators were improved but not completely returned to normal, abnormal LUS shadows were better, and LUS scores were significantly reduced, then the treatment was judged to be effective. If the patient's condition did not improve after treatment or was even worse than before, the treatment was judged to be ineffective.

2.5. Statistical Analysis. SPSS21.0 software was used for statistical processing. *T* test was used to compare the measured data ($X \pm s$) between the two groups. Statistical data (%) were compared by χ^2 test. The results of intergroup comparison were $P < 0.05$, which indicated that the differences were statistically significant.

3. Results

3.1. Comparison of Ventilator Use Time, Oxygen Use Time, and Hospital Stay between the Two Groups. After medication, the duration of ventilator use, oxygen use, and hospital stay in experimental group was significantly shorter than that in the control group ($P < 0.05$), as shown in Table 1.

3.2. Comparison of ABG before and after Treatment between the Two Groups. There was no significant difference in PaO_2 , PaCO_2 , and $\text{PaO}_2/\text{FiO}_2$ levels between the two groups before treatment ($P > 0.05$). After treatment, the PaO_2 and $\text{PaO}_2/\text{FiO}_2$ levels in the two groups significantly increased, while the PaCO_2 levels significantly decreased, with statistically significant differences ($P < 0.05$). After treatment, the PaO_2 and $\text{PaO}_2/\text{FiO}_2$ levels of children in the experimental group were significantly higher than those in the control group ($P < 0.05$), as shown in Table 2.

3.3. Comparison on the Results of LUS before and after Treatment between the Two Groups. Figure 1 shows images of the lungs before and after treatment in the two groups of patients. The X-ray images of the two patients selected from the two groups of patients before treatment showed reduced lung transparency, bronchial signs, ground glass shadows, and diffuse white lung signs. The ultrasound images before treatment showed that the A-line of both lungs disappeared, the pleural line was abnormal, and a certain degree of pulmonary edema and lung consolidation appeared in the two patients. After different treatments, it was shown that the diffuse white lung and lung consolidation characteristics of LUS in the experimental group disappeared, the diffuse white lung characteristics of the LUS in the control group disappeared, and the degree of lung consolidation was improved.

3.4. Analysis on LUS Scoring Results of Two Groups of Patients. Figure 2 shows a comparison chart of the LUS scores before and after treatment of the two groups of patients. The figure

illustrates that the average LUS scores of patients in the experimental group after treatment with Bun and pulmonary surfactant for 0 h, 6 h, 12 h, 18 h, and 24 h were 22.9 ± 2.8 points, 17.4 ± 3.6 points, 16.5 ± 2.3 points, 14.2 ± 2.9 points, and 12.1 ± 3.7 points, respectively. The LUS scores of the control group after treatment with pulmonary surfactants were 23.1 ± 2.5 points, 21.8 ± 3.1 points, 21.2 ± 2.1 points, 19.6 ± 2.4 points, and 18.2 ± 2.3 points, respectively. According to the above data, the average LUS scores of patients in the experimental group at 6 h, 12 h, 18 h, and 24 h after treatment were obviously lower than those of the control group, and the differences were statistically remarkable ($P < 0.05$).

Figure 3 shows a scatter diagram of the correlation between the patient's $\text{PaO}_2/\text{FiO}_2$ and the LUS score. It indicated that the LUS score and oxygenation index of all patients in this study showed a significant negative correlation, that was, the lower the oxygenation index, the higher the LUS score. In this case, the patient's condition was also more serious. On the contrary, if the $\text{PaO}_2/\text{FiO}_2$ was higher, the LUS score would be lower. In this case, the patient's condition was also relatively mild.

Figure 4 shows the accuracy of LUS diagnosis in the two groups of patients. It revealed that with X-ray as a reference, the accuracy of LUS diagnosis in the experimental group and the control group was 96.2% and 95.3%, respectively.

3.5. Comparison of Clinical Efficacy between Two Groups after Treatment. After medication, the clinical signs of children in both groups improved significantly, and the total effective rate of treatment in the experimental group was significantly higher than that in the control group, with statistically significant differences ($P < 0.05$), as shown in Table 3.

4. Discussion

NRDS is a common respiratory disease in premature infants, which may cause premature infant death if not treated in time. Traditional mechanical ventilation treatment is easy to cause damage to premature infants' immature lungs and affect their growth and brain development [8]. In recent years, the use of exogenous PS as an alternative therapy clinically can significantly improve the lung function of children [9]. Bun is a glucocorticoid inhaled with strong anti-allergic inflammatory effect, which can enhance the stability of endothelial cells, smooth muscle cells and lysosomal membrane, inhibit the synthesis and release of bronchoconstrictor substances, and reduce the contraction response of smooth muscle. It is often used in the treatment of bronchial asthma and chronic obstructive pulmonary disease. There is still some controversy about the therapeutic effect of NRDS [10, 11].

In this study, pulmonary ultrasound was used to evaluate the efficacy of Bun and PS in the treatment of NRDS in preterm infants. The results showed that after the combined treatment of Bun and PS, the ventilator use time, oxygen consumption, and hospital stay were significantly shortened, indicating that the combined treatment can improve the

TABLE 1: Comparison of ventilator use time, oxygen use time, and hospital stay between the two groups ($X \pm s$).

Group	Case	Ventilator use time (h)	Oxygen use time (h)	Hospital stay (d)
Experimental group	39	88.36 ± 12.41	105.62 ± 20.21	12.76 ± 1.58
Control group	39	97.24 ± 16.35	116.74 ± 22.58	14.38 ± 2.31
<i>T</i>		2.702	2.292	3.615
<i>P</i>		0.009	0.025	0.001

TABLE 2: Comparison of ABG before and after treatment between the two groups ($X \pm s$).

Group	Case	PaO ₂ (mmHg)		PaCO ₂ (mmHg)		PaO ₂ /FiO ₂	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	39	44.61 ± 10.83	$65.59 \pm 12.46^*$	48.72 ± 11.21	$40.24 \pm 8.92^*$	72.14 ± 14.22	$112.57 \pm 19.35^*$
Control group	39	45.12 ± 11.21	$57.31 \pm 14.23^*$	49.21 ± 11.75	$41.22 \pm 9.24^*$	71.29 ± 17.01	$101.28 \pm 21.36^*$
<i>T</i>		-0.204	2.734	-0.188	-0.477	0.239	2.446
<i>P</i>		0.839	0.008	0.851	0.635	0.812	0.017

Note. *indicated that compared with that before treatment, the difference was statistically significant; $P < 0.05$.

FIGURE 1: Images of lungs before and after treatment in the two groups of patients. (a-b) Images of chest X-ray and LUS of a patient before treatment in experimental group. (c) The image of LUS of the patient after treatment. (d-e) Images of chest X-ray and LUS of a patient in control group. (f) The image of LUS of the patient after treatment.

FIGURE 2: Comparison on LUS scores before and after treatment between the two groups. Notes: *indicated that the average LUS score of experimental group and control group was significantly different, with statistical significance ($P < 0.05$).

FIGURE 3: Scatter diagram of correlation between the patient oxygenation index and LUS score.

FIGURE 4: The accuracy of lung ultrasound diagnosis in the two groups.

TABLE 3: Comparison of clinical efficacy after treatment between two groups (%).

Group	Case	Obvious effect	Effective	Ineffective	Total effective rate
Experimental group	39	22	15	2	37 (94.87)
Control group	39	13	16	10	29 (74.36)
χ^2					6.303
P					0.012

treatment efficiency and shorten the course of treatment. Traditional treatment of NARDS often uses mechanical ventilation, which will lead to the immature reconstruction of the lung tissue structure of premature infants, reduce the number of alveoli, simplify the structure, and decrease lung function. At the same time, it will seriously affect the development of children's brain nerves [12]. Combination medication can reduce the use of mechanical ventilation and is of great significance to the growth and development of children. In addition, it was observed that the improvement effect of PaO_2 , PaCO_2 , and $\text{PaO}_2/\text{FiO}_2$ levels in children after combined treatment was significantly better than that of PS alone ($P < 0.05$). Besides, the average LUS scores of the children after the combined treatment were much lower than those of the PS group alone. Comparison on the total effective rate of treatment between the two groups of patients suggested that the total effective rate of the combination of Bun and PS was significantly higher than that of PS alone ($P < 0.05$). This shows that, on the basis of exogenous PS, the

combination of Bun in the treatment of premature neonatal respiratory distress syndrome shows a better effect on improving the condition of the child. Taking X-ray as a reference, the diagnostic accuracy rates of LUS in the experimental group and the control group were 96.2% and 95.3%, respectively, indicating that lung ultrasound imaging has a high application value in the clinical diagnosis of respiratory distress syndrome in preterm neonates. Such results are consistent with the research results of Peng et al. [13], confirming that LUS shows good diagnostic accuracy, can be used to assess the level of lung ventilation in children, and is fast, safe, and radiation-free.

The reason why Bun combined with PS exhibits a good therapeutic effect may be that after exogenous PS is injected into the trachea, and it can spread rapidly in the lungs due to the gradient tension on the lung surface. With this traction as a carrier, Bun can be brought to the end bronchial and alveolar tissues of the respiratory tract [14]. As an effective local anti-inflammatory glucocorticoid, Bun has a wide

range of biotransformation forms. In the liver, it can be converted into various low-activity glucocorticoid metabolites. It can not only increase the synthesis of PS and antioxidants in the body, inhibit the synthesis of prostaglandins and leukotrienes, and reduce cytokine-mediated inflammation but also promote cilia vibration, increase lung compliance, reduce carbon dioxide partial pressure, and improve lung ventilation function [15].

5. Conclusion

In this study, Bun was added on the basis of exogenous PS in the treatment of NRDS in premature infants. LUS was used to evaluate the effect of different treatments on NRDS in premature infants. The results showed that the addition of Bun on the basis of exogenous PS in the treatment of pulmonary NRDS in premature infants can effectively improve pulmonary function and greatly enhance respiratory function compared with direct use of PS. LUS imaging showed great efficacy and high diagnostic accuracy in evaluating the efficacy of Bun combined with PS in the treatment of premature NRDS. However, there were still some deficiencies in this study. For example, the total number of samples in this study was small and the sources were relatively single, which might lead to some systematic errors in the study results. The content of the efficacy evaluation indexes of the other two treatment methods was too small, which failed to comprehensively evaluate the efficacy differences of the two treatment methods. In future studies, the efficacy of Bun in the treatment of premature NRDS is expected to be further analyzed and verified by increasing the number of cases and conducting a multicenter joint study on the basis of exogenous PS.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The author declares that there are no conflicts of interest.

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