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ARTICLE

Comparison of Effects between Nasal Bi-Level Positive Airway Pressure and Nasal Synchronized Intermittent Mandatory Ventilation in Neonatal Respiratory Distress Syndrome

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Abstract

Aims/Background Neonatal respiratory distress syndrome (NRDS) is characterized by progressive aggravation and rapid progression of respiratory distress, with a high incidence rate among premature infants. If left untreated, NRDS results in a poor prognosis. In recent years, various respiratory support modalities have received extensive attention in clinical practice. The therapeutic effect of different respiratory support modes on NRDS has gradually become the focus of clinical research. The aim of this study was to explore the therapeutic effects of nasal bi-level positive airway pressure (nBiPAP) and nasal synchronized intermittent mandatory ventilation (nSIMV) on NRDS.

Methods This study retrospectively analyzed the clinical data of 157 newborns with NRDS in the Mudanjiang Medical University Affiliated Second Hospital from January 2021 to December 2023, finally including 153 cases after excluding 4 cases with missing clinical data. According to the non-invasive ventilation method, these newborns were categorized into a nBiPAP group (receiving nBiPAP treatment, n = 77) and an nSIMV group (receiving nSIMV treatment, n = 76). The blood gas indices, using time of ventilator, hospitalization time, therapeutic effects, and incidence of complications were compared between the two groups.

Results The $PaCO_2$, PaO_2, and pH levels in the nBiPAP group were basically consistent with those in the nSIMV group before and after treatment ($p > 0.05$). The use time of ventilator, hospitalization time, and therapeutic effects in the nBiPAP group were similar to those in the nSIMV group ($p > 0.05$). Additionally, both groups demonstrated no significant difference in the incidence of complications such as intraventricular hemorrhage, apnea, necrotizing enterocolitis, and feeding intolerance ($p > 0.05$). The incidence rates of ventilator-associated lung injury and neonatal bronchopulmonary dysplasia in the nBiPAP group were lower than those in the nSIMV group, with a significant difference ($p < 0.05$).

Conclusion Both nBiPAP and nSIMV have shown good effects in treating NRDS, with nBiPAP showing a significant advantage in reducing the incidence rates of complications such as ventilator-associated lung injury and neonatal bronchopulmonary dysplasia.

Key words: neonatal respiratory distress syndrome; positive airway pressure; complications; blood gas analysis

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Introduction

Neonatal respiratory distress syndrome (NRDS) is a respiratory dysfunction caused by insufficient pulmonary surfactant (PS) (Wang et al, 2021), mainly mani-

fested as polypnea, shortness of breath, and progressive respiratory distress (Zambrano et al, 2022). NRDS is one of the most common diseases in newborns (Rong et al, 2020), and it may result in neonatal death. Newborns with NRDS are commonly treated with PS therapy and respiratory support (Qing et al, 2023). Respiratory support includes invasive assisted ventilation, non-invasive assisted ventilation, and oxygen therapy. However, invasive respiratory support may cause pressure injury, shear force injury, and biological lung injury in newborns (Yuan et al, 2021). Recently, non-invasive assisted ventilation has emerged, and while nasal continuous positive airway pressure (NCPAP) is commonly used, newborns receiving NCPAP are at risk of respiratory failure, sometimes requiring re-intubation for invasive mechanical ventilation (Nasef et al, 2020). Nasal synchronized intermittent mandatory ventilation (nSIMV) is a respiratory support method that achieves a certain frequency of synchronized intermittent positive pressure based on NCPAP, which can provide more substantial respiratory support than NCPAP. In nSIMV, breaths are patient-triggered or time-triggered, flow-limited, and volume-cycled, and patients can breathe spontaneously between mandatory ventilator-cycled breaths (Alikiaii et al, 2022). Furthermore, nSIMV allows patients to breathe spontaneously at the breathing rate set by the machine, thereby reducing respiratory muscle fatigue. The challenge with nSIMV is that patients must have a certain level of spontaneous breathing ability, which may not be suitable for patients who rely solely on ventilators. In addition, the synchronization requirement for nSIMV is high. If the patient's respiratory rate is not synchronized with the ventilator, it may lead to poor ventilation.

Nasal bi-level positive airway pressure (nBiPAP) is derived from NCPAP. It uses positive pressure to help patients breathe spontaneously by delivering airflow at two different pressures during inspiration and expiration (Kumari et al, 2024). nBiPAP can maintain high airflow and stable support pressure, expand collapsed and closed alveoli, improve lung compliance, reduce breathing workload, and enable newborns to breathe spontaneously to varying degrees (Lv et al, 2020). Due to its non-invasive characteristics, nBiPAP can also reduce the infection risk and improve patients' comfort. However, the application of nBiPAP also faces some challenges. nBiPAP may not be the best choice for patients with impaired consciousness or those unable to remove airway secretions autonomously.

While the above two ventilation methods have shown good therapeutic effects in clinical practice, relatively few studies directly compare them. This situation not only limits our in-depth understanding and evaluation of the two ventilation methods but also affects the ability of clinicians to make optimal choices when facing specific cases. Along with diversified clinical needs, patients must choose between different ventilation methods to match their unique physiological status and treatment needs. Therefore, it is important to clarify the differences between these ventilation methods for clinical practice. To understand the advantages and disadvantages of nBiPAP and nSIMV in treating NRDS, we conducted an in-depth retrospective study on the two non-invasive ventilation methods.

Methods

Data Selection Criteria and Potential Selection Bias

To ensure the reliability and validity of the research results, this study strictly formulated the data selection criteria. The subjects were NRDS children who were treated in our hospital from January 2021 to December 2023.

The inclusion criteria were: (1) Newborns who met the diagnostic criteria for NRDS as outlined in the European Consensus Guidelines on the Management of Neonatal Respiratory Distress Syndrome in Preterm Infants (Sweet et al, 2013). (2) Newborns with gestational age of 28–38 weeks. (3) Newborns with no organ failure.

The exclusion criteria were: (1) Newborns with congenital lung tissue dysplasia; (2) newborns with severe infection and anemia; (3) newborns with severe intracranial hemorrhage and pulmonary hemorrhage; and (4) newborns with missing or incomplete clinical data.

This study was retrospective in nature. Researchers could not intervene or control the subjects at the beginning of the study. The choice of subjects was based on their past state. Given that these events have occurred, researchers could not randomly assign research subjects before the event occurred, so randomization could not be achieved. In addition, retrospective studies rely on existing data, such as medical records, archives, or historical databases. Therefore, researchers could only randomly allocate the data after data collection.

Research Subjects

This study retrospectively analyzed the clinical data of 157 newborns with NRDS in Mudanjiang Medical University Affiliated Second Hospital from January 2021 to December 2023, finally including 153 cases after excluding 4 cases with missing clinical data. According to the non-invasive ventilation method, they were categorized into the nBiPAP group (receiving nBiPAP treatment, n = 77) and the nSIMV group (receiving nSIMV treatment, n = 76).

Methods

Both groups of patients received PS therapy. The medical staff actively supplied warming measures for newborns, closely monitored their vital signs, and applied multiple treatment methods such as correcting acidosis and providing nutritional support and anti-infection therapy.

The nBiPAP group was given nBiPAP treatment using the ACUTRONIC non-invasive ventilator (Fabian Hfo; ACUTRONIC Medical Systems AG; Hirzel, Switzerland) for non-invasive mechanical ventilation. The parameters were: peak airway pressure of 12–15 cmH_2O, oxygen flow of 6–10 L/min, respiratory rate of 20–30 times/min, inhaled oxygen concentration of 30–50%, and positive end-expiratory pressure of 4–6 cmH_2O. The clinical indications of the newborns were closely monitored. The machine was removed, and bilateral nasal cannula oxygen therapy was given when one of the following situations occurred: inhaled oxygen concentration

<0.4; average airway pressure <8 cmH_2O; and positive end-expiratory pressure <3 cmH_2O.

The nSIMV group received nSIMV treatment using the Drager neonatal ventilator (Babylog 8000 plus; Delger Medical Company; Lubeck, Germany) for noninvasive mechanical ventilation. The ventilator mode was set to nSIMV. The parameters were: respiratory rate of 30–45 times/min, peak airway pressure of 10–20 cmH_2O, positive end-expiratory pressure of 4–6 cmH_2O, inhaled oxygen concentration of 0.21–0.5, and blood pressure saturation of 88–93%. The clinical indications of the newborns were closely monitored. The machine was removed, and bilateral nasal cannula oxygen therapy was given when one of the following situations occurred: inhaled oxygen concentration <0.4; average airway pressure <8 cmH_2O; and positive end-expiratory pressure <3 cmH_2O.

Observation Indicators

Baseline Information

The baseline data, including sex, gestational age, birth weight, PS dosage, NRDS degree, mode of delivery, number of pregnancies, complications, and history of prenatal hormone use by puerperae, were collected from the medical record system of Mudanjiang Medical University Affiliated Second Hospital.

Blood Gas Indexes

In brief, 2 mL of arterial blood was collected from all subjects before treatment and 48 hours after treatment. The $PaCO_2$, PaO_2, and pH levels were measured using an automatic blood gas analyzer (GEM Premier 3500; National Instruments; Austin, TX, USA).

Treatment Times

The ventilator usage time and hospitalization time at the end of treatment were compared.

Clinical Efficacy

The clinical efficacy of the two groups was compared (markedly effective: the newborns had normal blood gas indexes and steady breathing, without cyanosis and moaning, and the radiographs showed clear lung texture; effective: the symptoms of cyanosis, moaning, and dyspnea were relieved, and the blood gas indexes and radiographs showed significant improvement compared with those before treatment; ineffective: the symptoms of the newborns were not significantly improved, or even deteriorated). Effective rate = (markedly effective + effective) cases/total cases × 100%.

Incidence of Complications

The short-term and long-term complications, including ventilator-associated lung injury, intraventricular hemorrhage, apnea, neonatal bronchopulmonary dysplasia, necrotizing enterocolitis, and feeding intolerance, of the two groups within two months of treatment were compared.

Statistical Analysis

The clinical data were processed using Statistical Package for the Social Sciences (SPSS) 26.0 software (IBM Corp., Armonk, NY, USA). The categorical variables were expressed as (n (%)) and analyzed by the following tests: (1) Fourfold table test: (i) Pearson chi-square test was employed when all theoretical numbers (T) $\geq$5 and total sample size (n) $\geq$40. (ii) Continuity correction was utilized when $1 \leq T < 5$ and n $\geq$40. (iii) Fisher's exact test was adopted when T $<$1 or n $<$40. (2) R $\times$ C table test: The cells with theoretical number less than 5 were less than 20%, or the theoretical number T $\geq$1, and the Pearson chi-square test was used. Conversely, Fisher's test was used (cells with theoretical number less than 5 $>$20%, or theoretical number T $<$1). The continuous variables were tested using the Shapiro-Wilk method, and the data not adhering to a normal distribution were represented by (M (P_{25}, P_{75})) and tested by the Mann-Whitney U test. $p < 0.05$ was considered statistically significant.

Results

Comparison of Baseline Data

As shown in Table 1, the baseline characteristics, such as sex, gestational age, birth weight, PS dosage, NRDS degree, mode of delivery, number of pregnancies, complications, and history of prenatal hormone use by puerperae were similar across groups ($p > 0.05$).

Comparison of Blood Gas Indexes

The $PaCO_2$, PaO_2, and pH levels in the nBiPAP group were basically consistent with those in the nSIMV group before and after treatment ($p > 0.05$, Table 2).

Comparison of Treatment Time

The duration of ventilator use and hospitalization time in the nBiPAP group were similar to those in the nSIMV group ($p > 0.05$, Table 3).

Comparison of Therapeutic Effect

After treatment, no significant difference was observed in the effective rate between the nBiPAP group (92.21%) and the nSIMV group (94.74%) ($p > 0.05$, Table 4).

Comparison of Incidence of Complications

Table 5 shows the short-term and long-term complications within two months of treatment. Both groups demonstrated no significant difference in the incidence of complications such as intraventricular hemorrhage, apnea, necrotizing enterocolitis, and feeding intolerance ($p > 0.05$). The incidence rates of ventilator-associated lung injury and neonatal bronchopulmonary dysplasia in the nBiPAP group were lower than those in the nSIMV group, with a significant difference ($p < 0.05$).

Table 1. Comparison of baseline data [M (P_{25}, P_{75}), n (%)].

Characteristic	nBiPAP group (n = 77)	nSIMV group (n = 76)	χ^2/Z	*p*
Neonatal sex			1.479	0.224
Male	36 (46.75)	43 (56.58)		
Female	41 (53.25)	33 (43.42)		
Gestational age (weeks)	32.00 (30.00, 35.00)	33.00 (31.00, 35.00)	–0.643	0.520
Birth weight (g)	1821.28 (1703.22, 2071.40)	1889.85 (1758.87, 2027.27)	–1.014	0.310
Neonatal PS dosage (mg/kg)	152.13 (143.73, 166.89)	155.42 (142.30, 166.29)	–0.166	0.868
NRDS degree			0.554	0.758
Mild	38 (49.35)	33 (43.42)		
Moderate	24 (31.17)	27 (35.52)		
Severe	15 (19.48)	16 (21.05)		
Mode of delivery			0.577	0.447
Vaginal delivery	44 (57.14)	48 (63.16)		
Cesarean section	33 (42.86)	28 (36.84)		
Number of pregnancies (times)	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	–1.448	0.148
Maternal complications			2.856	0.414
Gestational hypertension	17 (22.08)	11 (14.47)		
Gestational diabetes	14 (18.18)	17 (22.37)		
Oligohydramnios	12 (15.58)	8 (10.53)		
No	34 (44.16)	40 (52.63)		
History of hormone use			0.843	0.358
Yes	20 (25.97)	15 (19.74)		
No	57 (74.03)	61 (80.26)		

nBiPAP, neonatal respiratory distress syndrome; nSIMV, nasal synchronized intermittent mandatory ventilation; PS, Pulmonary Surfactant; NRDS, Neonatal Respiratory Distress Syndrome.

Discussion

NRDS is a disease that seriously threatens the lives of newborns (Liu and Xu, 2023). Timely treatment is crucial for improving the prognosis. This study compared the effects of nBiPAP and nSIMV in treating NRDS to guide the selection and formulation of clinical programs.

This study showed that nBiPAP and nSIMV can effectively improve blood gas indices, including $PaCO_2$, PaO_2, and pH, in newborns with NRDS. nBiPAP is a flow-triggered-pressure support ventilation method of non-invasive mechanical ventilation with two different pressure levels, equivalent to pressure support ventilation plus positive end-expiratory pressure. High airway pressure levels can expand pulmonary functional residual capacity. In contrast, low levels can maintain normal pulmonary functional residual capacity, keeping alveoli dilated, thereby improving alveolar ventilation and oxygenation (Zhuang et al, 2020). In addition, the mixed ventilation mode of nBiPAP can improve gas distribution throughout the lungs, increase the PaO_2 level, and remove CO_2 from the alveoli, substantially improving respiratory function and reversing hypoxia symptoms (Sadeghnia et al, 2016). nSIMV is based on non-invasive positive pressure ventilation. As an inter-

Table 2. Comparison of blood gas indexes [M (P_{25}, P_{75})].

Group	Cases	$PaCO_2$ (mmHg)		PaO_2 (mmHg)		pH	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
nBiPAP group	77	56.81 (53.63, 60.55)	41.58 (40.83, 42.27)	55.82 (54.22, 58.27)	82.80 (78.58, 86.88)	7.05 (7.01, 7.07)	7.38 (7.36, 7.41)
nSIMV group	76	57.75 (53.43, 60.73)	41.70 (40.99, 42.34)	55.71 (53.67, 58.52)	80.34 (77.99, 84.37)	7.04 (7.02, 7.07)	7.39 (7.35, 7.41)
Z	-	–0.206	–0.033	–0.339	–1.883	–0.062	–0.823
p	-	0.837	0.974	0.734	0.060	0.950	0.410

Table 3. Comparison of treatment time [M (P_{25}, P_{75})].

Group	Cases	Using time of ventilator (h)	Hospitalization time (d)
nBiPAP group	77	38.71 (36.05, 41.32)	12.00 (11.00, 13.00)
nSIMV group	76	38.74 (35.98, 41.93)	12.00 (11.00, 13.00)
Z	-	–0.109	–0.028
p	-	0.913	0.978

Table 4. Comparison of therapeutic effect [n (%)].

Group	Cases	Markedly effective	Effective	Ineffective	Total effective rate
nBiPAP group	77	33 (42.86)	38 (49.35)	6 (7.79)	71 (92.21)
nSIMV group	76	30 (39.47)	42 (55.26)	4 (5.26)	72 (94.74)
χ^2	-	-	-	-	0.093
p	-	-	-	-	0.760

Table 5. Comparison of incidence of complications [n (%)].

Group	Cases	Ventilator-associated lung injury	Intraventricular hemorrhage	Apnea	Neonatal bronchopulmonary dysplasia	Necrotizing enterocolitis	Feeding intolerance
nBiPAP group	77	2 (2.60)	3 (3.90)	2 (2.60)	3(3.90)	1 (1.30)	1 (1.30)
nSIMV group	76	9 (11.84)	1 (1.32)	3 (3.95)	10 (13.16)	2 (2.63)	3 (3.95)
χ^2	-	4.899	0.243	0.000	4.220	0.000	0.270
p	-	0.027	0.622	0.988	0.040	0.991	0.603

mittent positive pressure with a specific frequency synchronization, it can synchronize with the breathing of newborns (Wang et al, 2015). The effective combination of spontaneous breathing and ventilator use in newborns can increase ventilation efficiency and tidal volume (Tao et al, 2016), improve arterial blood gas analysis indices, and then release CO_2 (Kaltsogianni et al, 2023).

This study revealed that the incidence of ventilator-associated lung injury and neonatal bronchopulmonary dysplasia in the nBiPAP group was significantly lower than that in the nSIMV group, which may be related to the characteristics of nBiPAP. This finding is similar to that of Lin and Yang (2022). Long-term respiratory distress can induce pulmonary pressure injury in newborns with NRDS, causing lung inflammation and increasing the risk of bronchopulmonary dysplasia (Wu et al, 2021). nBiPAP maintains the open state of the alveoli by providing high positive pressure support during inspiration and low positive end-expiratory pressure during expiration. This method is conducive to preserving uniform ventilation and gas exchange in the lungs, thereby reducing mechanical damage caused by repeated opening and closing of the alveoli. In addition, nBiPAP provides stable ventilation support, thereby improving lung blood circulation, nutritional supply, and lung compliance, as well as protecting lung tissue from damage and effectively reducing the incidence of neonatal bronchopulmonary dysplasia (Zhou et al, 2023). While nSIMV can reduce mean arterial pressure, improve oxygenation, coordinate spontaneous breathing with ventilators, and improve respiratory muscle function, it requires intubation. Long-term maintenance of artificial airways can increase the incidence of ventilator-associated pneumonia, and long-term oxygen stress may damage lung tissue and cause bronchopulmonary dysplasia in newborns (Lee et al, 2017; Marseglia et al, 2019). In addition, this study showed no significant difference in treatment time and clinical efficacy between the nBiPAP group and the nSIMV group, indicating both ventilation methods improve the symptoms and signs of newborns without significantly affecting their recovery time, thereby achieving good outcomes in treating NRDS.

While exploring the potential mechanisms of nBiPAP and nSIMV, we also recognize that clinicians need to comprehensively consider the specific conditions of the child when selecting ventilation methods, such as the severity of the disease, respiratory center function, and oxygenation needs. In addition, different ventilation methods have similar limitations. For example, nSIMV is highly dependent on the respiratory center and may not be effective for children with respiratory center dysfunction. nBiPAP requires experienced operators who must closely monitor the child's response and physiological parameters to ensure ventilation effectiveness. In conclusion, BiPAP and nSIMV have their applications and limitations, and they should be flexibly selected according to the specific conditions of the child to achieve the best therapeutic effect. However, because of the retrospective nature and small sample size, this study has some limitations. Future studies should expand the sample size and conduct prospective, multi-center randomized controlled trials to further verify the difference in the effects of the two ventilation methods in treating children with NRDS.

Conclusion

Both nBiPAP and nSIMV have good effects in treating NRDS. nBiPAP surpasses nSIMV in reducing the incidence of complications such as ventilator-associated lung injury and neonatal bronchopulmonary dysplasia. In clinical practice, the appropriate ventilation method should be selected according to the specific conditions of the newborn and the equipment available at the hospital. At the same time, comprehensive treatment and management of newborns with NRDS should be strengthened to improve the effect and prognosis.

Key Points

- nBiPAP and nSIMV can effectively improve blood gas indices in treating NRDS.
- No significant difference was found in using time of ventilator, hospitalization time, and therapeutic effect between nBiPAP and nSIMV in newborns with NRDS.
- nBiPAP has advantages in reducing the incidence of complications such as ventilator-associated lung injury and neonatal bronchopulmonary dysplasia.
- In clinical practice, appropriate ventilation methods should be selected according to the specific conditions of the newborn and the equipment available at the hospital.

Availability of Data and Materials

The corresponding author will provide the data that underpin the study's conclusions with a reasonable application.

Author Contributions

YZ designed the study; both authors conducted the study; JZ collected and analyzed the data. YZ and JZ participated in drafting the manuscript, and both authors contributed to the critical revision of the manuscript for important intellectual content. Both authors gave final approval of the version to be published. Both authors participated fully in the work, took public responsibility for appropriate portions of the content, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

The ethical committee of Mudanjiang Medical University Affiliated Second Hospital has approved the study (approval no.: 20201104). This study conforms to the principles of the Declaration of Helsinki. The legal guardian of the newborns signed the informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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