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Original Research

TREATMENT RESULTS OF RESPIRATORY DISTRESS SYNDROME IN PRETERM INFANTS AT THE PEDIATRIC CENTER OF HUE CENTRAL HOSPITAL

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ABSTRACT

Background: *Acute respiratory distress syndrome (ARDS) in premature infants is one of the leading causes of death. Surfactant replacement therapy has been the mainstay of treatment for preterm infants with RDS. This study aimed to evaluate the results of surfactant therapy for premature infants with RDS at the Pediatric Center of Hue Central Hospital.*

Methods: *A prospective, descriptive, and comparative study was conducted on 52 preterm infants with RDS based on clinical and chest radiographic findings before and after intervention. All infants received conventional surfactant therapy or INSURE. Evaluation of treatment results after 6 hours based on: SpO2, FiO2, a/APO2, and chest X-ray.*

Results: *Surfactant treatment markedly reduced the need for FiO2 and Surfactant treatment markedly reduced FiO2. requirement and improved SpO2. The average SpO2 of 91.15% increased to 95.67%. The average FiO2 of 51.54% decreased to 40.5%. Lung lesions on X-ray have markedly improved after treatment, as shown in the improvement of lesions. Alveolar and arterial oxygen rates (a/APO2) improved significantly after surfactant administration. 33/52 (63.5%) cases eventually improved within 6 hours after treatment without any complications.*

Conclusion: *A surfactant replacement that counterbalances surfactant inactivation seems to improve oxygenation and lung function in many preterm infants with respiratory distress syndrome without any apparent negative side effects.*

I. INTRODUCTION

Respiratory distress syndrome (RDS), formerly known as hyaline membrane disease, is one of the most common medical emergencies in preterm neonates resulting from lung immaturity. This disorder accounted for 1% of all infants and 5-10% of preterm ones. Additionally, the risk is highest in preterm infants or those weighing less than 1200 grams [1-3].

In VietNam, RDS in preterm neonates is one of the most leading causes of respiratory failure and death. According to the World Health Organization and United Nations Children's Fund, there are approximately 18000 newborn deaths annually, of which 35% are due to preterm birth complications, and RDS is primarily the leading cause [4].

Nowadays, the use of surfactants is applied in many hospitals. Much research on the use of surfactants is "common" in many hospitals such as Vietnam National Children's Hospital, Tu Du Hospital, Children's Hospital 1, Dong Nai Hospital, showing potential results [5].

We conducted this research to evaluate surfactants' effectiveness in managing RDS in preterm infants in Pediatric center of Hue Central Hospital.

II. MATERIALS AND METHODS

2.1. Study population

The diagnosis of RDS in preterm infants consists of the following 2 criteria:

- Two or more signs of increased work of breathing within 6 hours, including: (1) newborn's respiratory rate > 60 breaths per minute or <30 breaths per minute; (2) chest retractions; (3) grunting.
- The typical radiographic features of neonatal RDS in a preterm infant [6].

Therapeutic indications for surfactant replacement therapy include [7]: Neonates born before 29 weeks: required CPAP and FiO2 ≥ 30%; or need to be intubated with FiO2 ≥ 30%; or those born before 26 weeks required positive pressure ventilation. Neonates born after 29 weeks: required CPAP and FiO2 ≥ 40%; or need to be intubated with FiO2 ≥ 40% and mean airway pressure ≥ 7 cmH2O.

Exclusion criteria: Infants with congenital anomalies of the respiratory system or other accompanied respiratory diseases. Infants who needed resuscitation at birth and then died.

Location and survey period: Pediatric center – Hue Central Hospital from 6/2020 to 10/2021.

2.2. Methods

A prospective, descriptive, and comparative study was conducted on 52 newborns who met the mentioned criteria.

The standard technique for surfactant administration: A sonde is cut to a standard length that is 0,5 – 1 cm shorter than the endotracheal tube. At the next stage, a medical practitioner draws up the required dose of surfactant into a syringe. After attaching the pre-cut sonde to the syringe, the practitioner fills the sonde with surfactant to the end. Then, an assistant disconnects the endotracheal tube from the ventilator and the medical practitioner administers the surfactant via the pre-cut tube within 2-3 seconds. Following instillation, the patient is reconnected to the ventilator. Unless significant airway obstruction occurs, medical staff do not suction airways for 1 hour after surfactant instillation.

INSURE technique for surfactant administration [8]: Infants are intubated with an appropriate size endotracheal tube and surfactant is administered as in standard technique. However, Extubation takes place when premature neonates are stable with SpO2 >90%. After extubation, CPAP with PEEP5-7 cmH20 is started in these patients, depending on the clinical manifestations and SpO2, to adjust possible FiO2 and PEEP to maintain SpO2 ≥ 90%.

The evaluation of treatment after 6 hours involves:

- Clinical response: depending on the infants' requirement of FiO2 to maintain SpO2 ≥ 90%.
- Chest x ray improvement.

2.3. Statistical analysis

Data were analyzed using SPSS 26.0. To evaluate the treatment response, we compare SpO_2, FiO_2 and a/APO_2 before and after treatment using paired sample T test

$$a/APO_2 = \frac{PaO2}{(713xFiO\ 2 - 1{,}25xPaCO2\ )}$$ [9]

Making comparisons of respiratory failure levels and chest x-ray findings before and after surfactant administration to indicate: improvement, no improvement and deterioration.

III. RESULTS

3.1. General characteristics

Table 1: Gestational age distribution of births

Gestational age (weeks)	Number of patients (n)	Rate (%)
< 28	12	23.1
28 – <32	28	53.8
32 – <34	7	13.5
34 – <37	5	9.6
Total	52	100

Neonates born between 28 and 32 weeks had the highest disease incidence, with 53.8%.

Table 2: Distribution of birth weight

Birth weight (gram)	Number of patients (n)	Rate (%)
<1000	11	21.1
1000 – <1500	23	44.2
1500 – <2500	17	32.7
2500 – <4000	1	1.9
Total	52	100

Neonates who were born weighing between 1000 and 1500 grams had the highest incidence of the disease, with 44.2%.

Table 3: The time interval from birth to disease onset

Time interval	Number of patients (n)	Rate (%)
Less than 1 hour	49	94.2
More than 1 hour	3	5.8
Total	52	100

The onset of respiratory failure occurred within 1 hour after delivery, with 94.2%.

Table 4: Methods of respiratory support

Methods of respiratory support	Number of patients (n)	Rate (%)
Nasal Cannula	8	15.4
CPAP	15	28.8
Mechanical Ventilation	29	55.8

Methods of respiratory support	Number of patients (n)	Rate (%)
Total	52	100

All infants with RDS required respiratory support, in which mechanical ventilation accounts for 55.8%.

Table 5: Radiographic stage of chest x-ray

Radiographic stage	Number of patients (n)	Rate (%)
Stage 2	20	38.5
Stage 3	21	40.4
Stage 4	11	21.2
Total	52	100

Most chest x ray in these patients showed radiographic findings in stage 2 and 3. Additionally, the proportion of patients with radiographic findings in stage 4 was 21.2% and there was no patient with chest x ray in stage 1.

3.2. Evaluation of surfactant replacement therapy effects

Table 6: Methods of surfactant administration

Methods	Number of patients (n)	Rate (%)
Standard technique	38	73.1
INSURE	14	26.9
Total	52	100

INSURE method was used in 14/52 neonates, accounting for 26.9%, compared with 38/52 (73.1%) patients using the standard technique for surfactant administration.

Table 7: Changes in SpO2 and FiO2 in groups of patients

	Before instillation (n)		6 hours after instillation (n)		p
	n	%	n	%	
$SpO_2 < 90\%$	14	26.9	3	5.8	< 0.05
$SpO_2 \geq 90\%$	38	73.1	49	94.2	
$FiO_2 \leq 40\%$	21	40.4	25	48.1	> 0.05
$FiO_2 > 40\%$	31	59.6	27	51.9	

Before instillation, 14 of 52 patients had less than 90% oxygen saturation. However, the figure decreased to only 3 patients after instillation. The average SpO2 increased from 91.15% to 95.67% after surfactant administration. Additionally, 31 of all neonates required FiO2 ≥ 40%, which reduced to 27/52 after instillation, and the average demand for FiO2 declined from 51.54% to 40,50%. The improvement of SpO2 was statistically significant.

Table 8: Changes in arterial/alveolar oxygen tension ratio (a/APO2)

	First time	Second time	p
a/APO_2	0.21 ± 0.13	0.26 ± 0.15	< 0.05

The improvement of a/APO2 was statistically significant.

Table 9: Changes in radiographic stage in chest x ray of the neonates

Results	Number of patients (n)	Rate (%)
Improvement	47	90.4
No improvement	4	7.7
Deterioration	1	1.9
Total	52	100

Most patients after surfactant administration showed improvement in chest x ray findings. Only 4 patients (7.7%) showed no improvement and 1 newborn (1.9) presented the deterioration.

Table 9: Results after 6 hours of treatment

Results	Number of patients (n)	Rate (%)
No improvement	19	36,5
Improvement	33	63,5
Total	52	100

There was a significant improvement in 33 newborns after being treated with surfactant, accounting for 63,5%.

3.3. The factors related to treatment outcomes Table 10: The correlation between treatment outcome and gestational age

Gestational age	No improvement		Improvement		p
	n	%	n	%	
Extremely preterm	8	15.4	4	7.7	< 0.05
Very preterm	10	19.2	18	34.6	
Moderate preterm	1	1.9	6	11.5	
Late preterm	0	0	5	9.6	
Total	19	36.5	33	63.5	

The later gestational age, the greater possibility of improvement.

Table 11: The correlation between treatment outcome and birth weight

Birth weight	No improvement		Improvement		p
	n	%	n	%	
Extremely low birth weight	8	15.4	3	5.8	< 0.05
Very low birth weight	7	13.5	16	30.8	
Low birth weight	4	7.7	13	25.0	
Normal	0	0	1	1.9	
Total	19	36.5	33	635	

The improvement ratios in normal and low-weight newborns are higher than the figure for very low birth weight and extremely low birth weight.

Table 12: The correlation between treatment outcome and radiographic stage on x ray

Stage	No improvement		Improvement		p
	n	%	n	%	
2	4	7.7	16	30.8	> 0.05
3	9	17.3	12	23.1	
4	6	11.5	5	9.6	
Total	19	36.5	33	63.5	

The correlation between treatment outcome and the radiographic stage was not statistically significant.

IV. DISCUSSION

4.1. Methods of surfactant administration

In Vietnam, we currently use three techniques of surfactant administration: Conventional surfactant therapy is used for infants of low gestational age and low birth weight because these infants frequently have severe dyspnea that prevents effective spontaneous breathing. INSURE and LISA, each with its unique benefits, are available to newborns at a higher gestational age. The strategy to intubate, give surfactant, and extubate (INSURE) has been widely accepted in clinical practice. The disadvantage of this technique remains the need for intubation and positive pressure ventilation during the procedure. In some cases, the endotracheal tube could not be removed after this therapy. Additionally, even brief periods of invasive mechanical ventilation still cause harm to the immature lungs of the preterm neonate. These factors contribute to the delay in the INSURE method indication. Another technique developed to address this issue is less invasive surfactant administration (LISA), also known as minimally invasive surfactant therapy (MIST). It aims to make the procedure as minimally invasive as possible.

In our study, we used 2 methods for surfactant replacement therapy: the conventional method and the INSURE method. One of the concerns of clinicians is the regurgitation of surfactant during the procedure, particularly when using minimally invasive surfactant therapy and no mechanical ventilation at all. While the newborn breathes naturally with CPAP support, the surfactant is administered into the trachea. That is one of the main barriers keeping physicians from applying the LISA approach. As a result, 38 patients in our research received the conventional technique, accounting for 73.1%, and the remaining 14 patients we performed by INSURE technique accounted for 26.9%.

4.2. Change in SpO2 value and FiO2 requirement in patients

A marked improvement in SpO2 value and FiO2 requirements can be seen in patients receiving surfactant administration, with the improvement in SpO2 being particularly statistically significant. The increase in SpO2 and the decrease in FiO2 demand reflect the improvement of lung function after surfactant therapy. The effectiveness of surfactants acts in three phases: acute response occurring after a few minutes, effects occurring over several hours, and effects lasting for several days. The surfactant-induced lung expansion results in a quick rise in oxygen saturation that might happen immediately. The subsequent response to surfactant therapy results from improved lung mechanics, which takes longer and depends in part on the mode of ventilation.

The obvious improvement of SpO2 and FiO2 after surfactant treatment was also reported in a study by Tran Thi Thuy at Bac Ninh Maternity and Paediatric Hospital [10], a study by Nguyen Viet Dong at Ha Tinh Provincial General Hospital [11], and a study by Vo Tuong Van at Children's Hospital 2 [12].

4.3. Change in a/APO2

According to a study by Mats Blennow et al., infants > 27 weeks of gestational age with acute respiratory distress syndrome were intubated and treated with surfactant when the a/APO2 ratio was below 0.22. a/APO2 increased from 0.2 to 0.5 after 1 hour of surfactant therapy and stayed there for 48 hours. The study by Verder et al. showed that children with acute respiratory distress syndrome who received early surfactant treatment (a/APO2 ranged from 0.22 to 0.35, mean 0.26) had a lower rate of needing mechanical ventilation and mortality than the group who received treatment later. Therefore, surfactants are recommended early for children with acute respiratory distress syndrome [13].

According to our results, the index a/APO2 at the time after surfactant treatment was 0.26, significantly increased compared to before treatment was 0.21. This shows an improvement in lung gas exchange following surfactant therapy. Our findings are consistent with the results of Vo Tuong Van at Children's Hospital 2 [12].

4.4. Change in disease severity on Chest X-ray

In our study, most patients had improved lung lesions on chest X-rays following surfactant therapy, accounting for 90.4% of cases. The degree of lung injury was significantly reduced after surfactant therapy. Clinical improvements in dyspnea following therapy are consistent with improvements in lung damage. However, there are also cases of lung damage that did not get better after treatment. The cause of these cases was that the patient was critically ill and had high FiO2 requirements of up to 100% on admission. In the study of Hoang Thi Thanh Mai [14] at Bach Mai hospital, pre-treatment results on straight chest x-ray showed respiratory distress syndrome (RDS) grade II accounted for the highest rate of 46.7%, grade III was 33.3%, and grade IV was 20% (6/30 cases). There was a noticeable improvement in the first 24 hours of therapy, grade 3 and 4 disease is no longer present. After 48 hours of treatment, the results showed that only 11.8% of the patients on X-ray were grade 1, and 88.2% had no signs of lung damage. Research by Pham Van Anh at the Maternity and Paediatric Hospital in Quang Ngai province also showed a 96.5% improvement in chest X-ray results [15].

4.5. Overall outcome of surfactant replacement therapy

In our study, 33 cases of improvement following therapy accounted for 63.5%. The results are close to those of studies by Nguyen Thanh Thien [16] at Children's Hospital 2 and Le Thi Thuy Loan [17] at Can Tho Children's Hospital, with success rates of mechanical ventilation of 76,9% and 66%, respectively. Although follow-up time varied between studies, their results were similar, indicating a rapid response to surfactant after administration.

In our study, no complications were recorded. The limitation of our study is that we did not evaluate throughout the course of treatment to assess all the complications of the disease as well as the complications of the surfactant administration process.

V. CONCLUSION

Surfactant treatment markedly reduced FiO2 requirement and improved SpO2. The average SpO2 of 91.15% increased to 95.67%, and the average FiO2 requirement of 51.54% decreased to 40.5%. Lung damage on X-ray also improved significantly after treatment, as shown in the improvement of lesion grading (90.4%). Alveolar and arterial oxygen rates (a/APO2) improved significantly after surfactant administration. 33/52 (63.5%) cases eventually improved within 6 hours after treatment without complications.

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