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Role of surfactant therapy in reducing oxygen requirement and mortality among neonates suffering from respiratory distress syndrome: A Prospective study at Al – Batool teaching hospital in Diyala province

Sura Qais Mahmood Almaroof [1], Shaima Hussein Alwan [2], Estabraq abed hasan Al gburi [3], Issam Tariq Abdul-Wahaab [4]

[1,2,3]Department of pediatrics/neonatology unit, Diyala health directorate, Iraq
[4]Department of Surgery (radiology)/ college of medicine/ University of Baghdad, Iraq

Correspondence: Sura Qais Mahmood Almaroof

Email: suraqais20@gmail.com

Website: https://djm.uodiyala.edu.iq/index.php/djm

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Abstract

Background: Respiratory distress syndrome (RDS) is a major cause of neonatal morbidity and mortality. It is a breathing disorder characterized by a deficiency or inactivity of surfactant in the lungs of preterm and term babies and if not treated, it leads to serious complications like pneumothorax, emphysema, bronchopulmonary dysplasia and death.

Objective: To estimate the effect of surfactant therapy on oxygen requirement and neonatal mortality as well as the incidence of RDS in the special care neonatal unit (SCNU) in the AL Batool Teaching Hospital in Diyala Governorate.

Patients and Methods: A sample of 2000 patients with signs and symptoms of RDS at the time of presentation was prospectively collected from the 1st of July 2022 until the 1st of March 2023 in SCNU at Al-Batool Teaching Hospital. Gestational age, body weight, the use of oxygen, surfactant therapy, and continuous positive airway pressure (CPAP) were taken into consideration in assessing the outcome of RDS neonates.

Results: There was a significant relationship between surfactant administrations, the period of staying on CPAP, and oxygen demand as the p-value was < 0.001 for both. Neonates who received surfactant had a lower mortality rate, with an incidence of 2.5%; the p-value was < 0.001. Incidence of neonatal RDS was 694 (34.7%).

Conclusion: Since the incidence of RDS was 34.7%, surfactant therapy should be routine in neonatal special and intensive care units. Proper use of surfactant (proper timing and mode of administration) reduces oxygen demand, the need for CPAP, hospitalization, and mortality among those neonates.

Keywords: Neonates, respiratory distress syndrome, Incidence, continuous positive airway pressure.

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Introduction

Respiratory distress syndrome (RDS) is observed in premature babies due to a deficiency of surfactant and in term neonates who have meconium aspiration; pneumonia; sepsis; and pulmonary hemorrhage due to surfactant inactivity. RDS, if untreated, might end with respiratory failure (1). Early surfactant therapy decreases mortality and morbidity in neonates with respiratory distress. The incidence of RDS is higher at small gestational ages. About 60 – 80% with gestational age < 28 weeks will develop RDS, 30% of neonates with gestational age between 28 – 34 weeks develop RDS and those with gestational age > 36 weeks develop RDS in 5% of cases (2, 3). Surfactant is a mixture of dipalmitoyl phosphatidylcholine (lecithin), Phosphatidylglycerol, Apo proteins, and cholesterol (4). Surfactant reduces the surface tension of alveoli and keeps the alveoli open. Because of immaturity, the amount produced is not enough. Surfactant is synthesized in the fetal lung by 20 weeks of gestation and appears in amniotic fluid between 28 and 32 weeks of gestation. RDS is manifested by dyspnea, tachypnea, grunting, nasal flaring, intercostal and subcostal retraction and cyanosis (5). Deficiency of surfactant leads to atelectasis and perfused but not ventilated alveoli, resulting in hypoxia and hypercapnia. This causes pulmonary arterial vasoconstriction, which ends with ischemic injury, together with oxygen toxicity results in the effusion of proteinaceous material into the alveolar spaces causing apnea, irregular respiration, and cyanosis. If the cases are untreated, there will be more apnea and cyanosis, resulting in mixed respiratory-metabolic acidosis. This will cause more complications represented by edema, paralytic ileus, oliguria, emphysema, pneumothorax, pulmonary hemorrhage, and sometimes intraventricular hemorrhage (IVH). Respiratory failure may occur in RDS infants with rapid progression (6). RDS can be diagnosed by clinical features, chest x-ray (CXR) findings, and blood gas analysis. CXR shows ground glass opacity of lung parenchyma with the characteristic air bronchogram appearance or white lung (Figure 1) (7). In spite of that, CXR might be normal during the first few hours. Laboratory investigation might reveal hypoxemia, hypercapnia, which might be associated with metabolic acidosis. RDS must be differentiated from early onset sepsis, congenital pneumonia, cyanotic heart disease, persistent pulmonary hypertension, meconium aspiration, spontaneous pneumothorax, pleural effusions, congenital lung anomalies, diaphragmatic hernia, and lobar emphysema (8, 9). Transient tachypnea of newborn (TTN) has shorter and milder clinical course (neonate needs 24 hours oxygen supplementation). Symptoms usually improve after 24 hours. CXR shows perihilar streaking, representing perihilar interstitial edema, or it may be normal (10).

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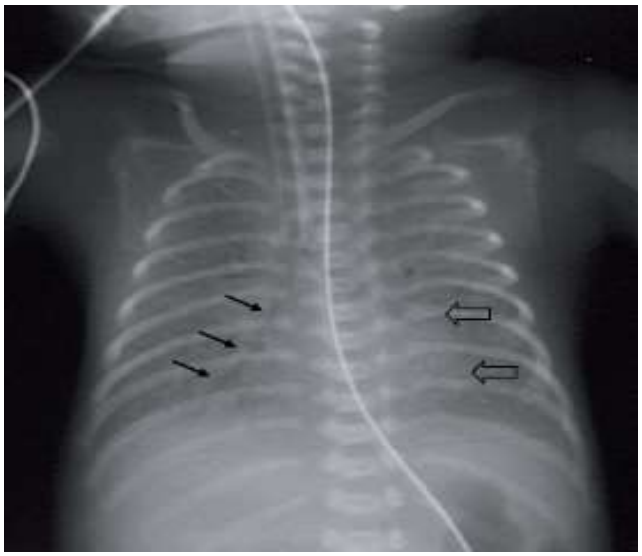

Figure 1: CXR of 4 hours old neonate with respiratory distress syndrome showing bilateral ground-glass opacification of the lung fields, air-bronchogram (small arrows) and loss of cardiac borders (black arrows)

Surfactant is the treatment of choice, and it is given by endotracheal tube in two ways: prophylactic method for premature neonates with very low birth weight (≤ 1500 g) and those with gestational age ≤ 32 weeks immediately after birth, or the rescue method for those with RDS above these limits, as the surfactant should be given during the first 24 hours of life. When oxygen saturation cannot be kept at about 91-95% with nasal oxygen between 50 and 70 mmHg, the neonates should be connected to CPAP at pressure of 5-10 cm H2O via nasal prongs after administration of surfactant. CPAP reduces the collapse of surfactant deficient alveoli and improves ventilation perfusion matching (11 – 13). Effects of surfactant replacement therapy can be noticed by improvement of Alveolar oxygenation, reduced ventilator support and improvement of chest radiographic appearance (14 – 16).

Aim of the study

To estimate the effect of surfactant on decreasing mortality, and the duration of oxygen requirements as well as the incidence of RDS in a special care neonatal unit in Al-Batool Teaching Hospital in Diyala Governorate.

Patients and Methods

A sample of 2000 patients was prospectively collected over a period of 7 months extending from the 1st of July 2022 until the 1st of March 2023 in the SCNU at Al-Batool Teaching Hospital. All cases with clinical signs and symptoms of respiratory distress at the time of presentation were included in this study and classified into RDS and TTN on the bases of clinical examination, CXR, and laboratory findings. Approximately 2mL of venous blood was aspirated into a heparinized syringe and sent to the laboratory for blood gas analysis. RDS neonates were followed for their response to natural surfactant (Survanta 4 ml vial 25 mg / ml, AbbVie Inc, United states), which was administered in a dose of 100mg/kg during the first 24 hours of life, in four positions with separate doses (15 seconds apart) by using an ambu bag with the INSUR technique (intubation, administration of surfactant, and extubating) (17, 18). Then we put the patient on CPAP. Bubble CPAP at 5 cm H2O is used to maintain Spa O2 within the range of 89-95%. Weaning from CPAP commences after improvement and the

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neonates change to nasal oxygen (19, 20). RDS neonates were assessed according to gestational age, body weight, surfactant administration, period of stay on CPAP, oxygen demand, and outcome. The cut point for giving surfactant was the birth weight and gestational age. Those with very low birth weight (≤ 1500 g) and those with gestational age ≤ 32 weeks received surfactant as prophylactic, while those above this level were given surfactant according to the rescue method. Birth asphyxia and congenital anomalies were excluded.

Statistical analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 22 software. The variables are expressed as frequencies and percentages. The relationship between neonatal RDS and gestational age, body weight, surfactant administration, oxygen demand, CPAP stay, and the outcome were tested by the Chi - square test. A P-value of less than 0.05 was regarded as statistically significant.

Ethical considerations

The research will not expose patients to further risk. Only the main investigator has the right to access the patient's information. The research was conducted after the approval of the research proposal by the ethical committee at Al-Batool Teaching Hospital. (Document no. 2023SQM804).

Results

The collected data were analyzed to find the effect of surfactant therapy on the number of hours spent on CPAP, oxygen demand, and their outcome as well as the incidence of neonatal RDS and its relation to various risk factors. Descriptive statistics revealed that among the studied sample, there were 1037 (51.9%) male and 963 (48.2%) female neonates. RDS accounts for 694 (34.7%) of cases, while the remaining 1306 (65.3%) suffered from TTN. Neonates who received surfactant were 297 (14.9%) and those who did not receive it represented 1703 (85.2%). The gestational ages of the newborns at the time of delivery were: 22 (1.1%) found to be less than or equal to 27 weeks; 65 (3.3%) had gestational age from 28 – 31 weeks; 396 (19.8%) were from 32 – 36 weeks (i.e., preterm neonates account for 24.2 % of all cases); and those with gestational age above or equal to 36 weeks were 1517 (75.9%). In addition to that, neonates who had been born with a body weight less than 1kg were 7 (0.4%), those who weighed between 1 and 1.499 kg were 88 (4.4%), those weighing from 1.5 – 2.499 kg were 325 (16.3%) i.e., low birth weight neonates account for 21.1%, while those with a body weight above 2.5 kg account for 1580 (79%). CPAP usage was 34.4%. 1314 (65.7%) neonates did not necessitate the use of CPAP, 65 (3.3%) of neonates needed the CPAP for less than 4 h, 187 (9.4%) of neonates needed the CPAP for 5 – 12 h, 246 (12.3%) of neonates needed the CPAP from 13 – 24 h, 166 (8.3%) neonates needed the CPAP from 24 – 48 h, and 22 (1.1%) of neonates require the use of CPAP for more than 48 h. Neonates who required oxygen for less than 24 h were 1476 (73.8%), those who needed oxygen from 24 – 48 h were 215 (10.8%) and those who needed oxygen for more than 48 h were 309 (15.5%). The outcome of neonates in the studied sample was 1861(93.1%) alive neonates while, the remaining 139 (6.9%) died as shown in Table 1.

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Table 1: Frequencies and percentages of neonatal RDS, possible risk factors & the need for surfactant therapy

Variables		Frequency n=2000	Percentage 100.0%
Cases	RDS	694	34.7%
	TTN	1306	65.3%
Surfactant	Yes	297	14.9%
	No	1703	85.2%
Gestational age	≤27W	22	1.1%
	28-31W	65	3.3%
	32-36W	396	19.8%
	≥36 W	1517	75.9%
Weight	<1kg	7	0.4%
	1-1.499kg	88	4.4%
	1.5-2.499kg	325	16.3%
	>2.5	1580	79%
Sex	Male	1037	51.9%
	Female	963	48.2%
CPAP	No CPAP	1314	65.7%
	<4h	65	3.3%
	5-12h	187	9.4%
	13-24h	246	12.3%
	25-48h	166	8.3%
	>48h	22	1.1%
Oxygen	<24h	1476	73.8%
	24-48h	215	10.8%
	>48h	309	15.5%
Outcome	Alive	1861	93.1%
	Dead	139	6.9%

Analytic statistics showed a significant relationship between the development of RDS and the gender of the neonates, since RDS appeared to be more common in male infants, as the p –value was < 0.001, as shown in Table 2.

Table 2: The relationship between RDS and neonatal gander

Respiratory distress	Gender		Total	P-Value
	Male	Female		
RDS	398 (57.3 %)	296 (42.7)	694	< 0.001
TTN	639	667	1306	
Total	1037	963	2000	

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On the other hand, the relationships between parenteral administrations of surfactant and various relevant parameters were tested by using the Chi – square test as shown in Table 3 which revealed the presence of significant relationships between surfactant administration and neonatal distress, neonatal outcome, oxygen demand, neonatal boy weight, gestational age at time of delivery, and the period of staying on CPAP, as the p – values were < 0.001 for each relation. It was clear that RDS neonates necessitate the use of surfactant, while those with TTN do not need surfactant therapy. Neonates with RDS showed a significant improvement in neonatal outcome with the use of surfactant therapy. Oxygen demand was significantly reduced in RDS neonates after using parenteral surfactant. It was evident that the lower the birth weight and gestational age at the time of delivery, the more risk for RDS development and the more the need for parenteral surfactant therapy. With the administration of surfactant, RDS neonates needed less hours on CPAP.

Table 3: The relationship between administration of surfactant and various relevant parameters

		Administration of surfactant		Total	P-values
		Yes	No		
Neonatal distress	RDS	297	397	694	< 0.001
	TTN	0	1306	1306	
	Total	297	1703	2000	
Outcome	Alive	246	1615	1861	< 0.001
	Dead	51	88	139	
	Total	297	1703	2000	
O2 demand	< 24 h	112	1364	1476	< 0.001
	24 – 48 h	92	123	215	
	> 48 h	93	216	309	
	Total	297	1703	2000	
Body weight	< 1 kg	7	0	7	< 0.001
	1 – 1.499 kg	53	35	88	
	1.5 – 2.499 kg	158	167	325	
	> 2.5 kg	79	1501	1580	
	Total	297	1703	2000	
Gestational age	< 27 w	15	7	22	< 0.001
	28 – 31 w	42	23	65	
	32 – 36 w	171	225	396	
	> 36 w	69	1448	1517	
	Total	297	1703	2000	
Staying on CPAP	0 h	0	1314	1314	< 0.001
	< 4 h	48	17	65	
	5 – 12 h	103	84	187	
	13 – 24 h	100	146	246	
	24 – 48 h	42	124	166	
	> 48 h	4	18	22	
	Total	297	1703	2000	

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Discussion

RDS is one of the main causes of morbidity and mortality among preterm neonates in the SCNU and NICU. Therefore, understanding pathophysiology and risk factors and the proper use of therapeutic methods, including antenatal steroids, monitoring oxygenation and ventilation, exogenous surfactant, and supportive care can reduce the mortality rate among those neonates (21). In this study, we found that 34.7% were RDS cases and among them 57.3 % were male neonates. Preterm neonates account for 24.2 % of all cases, while low birth weight neonates account for 21.1%. Neonates with RDS who received surfactant and required oxygen for less than 24 h were 16.1% versus 8% who did not take surfactant; those who needed oxygen from 24 – 48h were 9.5% versus 17.7% and those who needed oxygen for more than 48h were 13.4% versus 31.1%. In RDS neonates who received surfactant, CPAP usage less than 4 hours was 6.9% versus 2.4% in the untreated neonates while those who needed CPAP from 13-24 hour were 14.4% versus 21%, those who needed CPAP from 24-48 hour were 6% versus 17.8% those who needed CPAP more than 48 hours among the treated neonates were 0.57% versus 2.59 %. Neonates that died from RDS were 6.9% those who took surfactant were 2.5% versus 4.4% in the untreated neonates. It was obvious that parenteral administration of surfactant therapy decreased with increasing gestational age and neonatal body weight at the time of delivery. The use of rescue method and early administration of surfactant in premature and low birth weight neonates (less than 2.5 kg) have decreased the hours of demand for oxygen and CPAP usage since the p-value was < 0.001 and this coincides with a study conducted by Rojas-Reyes et al (2012) in which they stated that all infants delivered at a gestational age less than 32 weeks should be treated with surfactant as soon as they are intubated since the need for mechanical ventilation was lower in the treated group, which was 26% compared with the control group, which was 39% (22). In addition to that Kattwinkel et al (1993) reported that prophylaxis use of surfactant associated with less neonatal RDS, less mechanical ventilation or supplemental oxygen during the first four days, and fewer neonatal deaths (23). Plavka et al (2002) mentioned that early use of surfactant has decreased oxygen consumption and the death rate among premature neonates suffering from RDS (29% early treated versus 64% delayed treated) since the p – value was 0.02 (24). Previous studies stated that the early use of surfactant therapy can improve the duration on mechanical ventilation and oxygen therapy in premature infants with insignificant relationship with mortality rate (25 – 27). On the other hand, the Osiris Collaborative Group (1992) (28) reported a 16% reduction in mortality rate among neonates who received surfactant in early and late groups, which was (early 7% versus delayed 25%) which appeared to be similar to our result. Similarly, Sankar et al (2016) found that giving surfactant to distressed neonate decreases the rate of mortality (29), while others reported a insignificant reduction in the mortality rate among neonates receiving surfactant with NIPPV/CPAP, and those who connected to NIPPV/CPAP and did not receive surfactant (30, 31). Preterm neonates were more likely to develop RDS, but in spite of that, full – term infants could also develop RDS due to the inactivity of surfactant as in congenital pneumonia, sepsis (32) and meconium aspiration. This runs in parallel with a study performed by et al who showed that using surfactant wash in neonates suffering from meconium aspiration leads to an improvement in arterial oxygen saturation, which reach up to 80% within 12 minutes in most cases (33). In this study, the mortality rate among neonates who received

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surfactant was 2.5% while for untreated neonates, due to the unavailability of surfactant in the hospital at that time and the inability of their families to bring it due to its high cost, it was 4.4%. Untreated neonates were connected to CPAP and ventilators. These results coincide with a study done by Hamvas et al (1993) in which he reported that 20% of premature babies with RDS have little or no response to surfactant. due to: structural lung immaturity; they may have other diseases such as pneumonia or pulmonary hypoplasia; pulmonary edema from lung damage results in inactivation of surfactant; or it occurs from left-to-right shunting through the patent ductus arteriosus, and maldistribution of surfactant in the lungs (34).

Conclusion

The mortality rate has decreased after administration of surfactant from 4.4% to 2.5%, and the period of staying on CPAP has also decreased, which allowed for the rapid turnover of neonates on CPAP, also needed less time on oxygen and thus decreased the period of staying in hospital.

Source of funding

No source of funding

Conflict of interest

The author acknowledges no conflict of interest in this study.

Recommendation

1. Encourage the use of the prophylactic method in the administration of surfactant to any neonate less than or equal to 1500 g or less than 32 weeks gestation.
2. Encourage the use of the rescue method for any neonate above 32 weeks gestation or 1500 g with severe RDS.
3. Give surfactant to any intubated neonate with RDS.
4. Proper monitoring of heart rate, respiratory rate, SP O2, blood gas analysis and repeat CXR after 8 – 12 hours if the baby is still on CPAP in order to give another dose of surfactant.

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دور الفاعل بالسطح في تقليل متطلبات الأكسجين ومعدل الوفيات عند الولدان المصابين بعسر التنفس الولادي. دراسة استطلاعية في مستشفى البتول التعليمي في ديالى

سرى قيس محمود المعروف[١]،شيماء حسين[٢] ,أستبرق عبد حسن الجبوري[٣] ,عصام طارق عبدالوهاب[٤]

الملخص

الخلفية الدراسية: تعتبر متلازمة عسر التنفس السبب الرئيسي لوفيات الأطفال حديثي الولادة. هو اضطراب في التنفس يتميز بنقص أو عدم نشاط الفاعل بالسطح في رئتي الأطفال الخدج والأطفال الناضجين وإذا لم يتم علاجه؛ فهو يؤدي إلى مضاعفات خطيرة مثل استرواح الصدر وانتفاخ الرئة وخلل التنسج القصبي الرئوي والوفاة.

الهدف من الدراسة: معرفة معدل حدوث متلازمة عسر التنفس الولادي في وحدة الرعاية الخاصة لحديثي الولادة (SCNU) في مستشفى البتول التعليمي في محافظة ديالى وتأثير العلاج بالسطح على متطلبات الأكسجين ووفيات الأطفال حديثي الولادة.

المرضى وطرق العمل: تم جمع عينة من ٢٠٠٠ مريض يعانون من علامات وأعراض عسر التنفس الولادي بأثر تقدمي في الفترة من ١ تموز ٢٠٢٢ حتى ١ اذار ٢٠٢٣ في وحدة العناية الخاصة لحديثي الولادة بمستشفى البتول التعليمي. تم أخذ عمر الحمل ووزن الجسم واستخدام الأكسجين والعلاج بالسطح وضغط بالاعتبار عند تقييم نتائج حديثي الولادة (CPAP) مجرى الهواء الإيجابي المستمر

النتائج: كشفت هذه الدراسة أن معدل حدوث الضائقة التنفسية عند الأطفال حديثي الولادة كان ٦٩٤ (٣٤,٧٪). وهناك علاقات هامة بين إعطاء الفاعل بالسطح وانخفاض فترة البقاء على الأكسجين وجهاز الضغط العالي للاوكسجين حيث كانت القيمة الاحتمالية ٠,٠٠١ لكليهما. كان لدى حديثي الولادة الذين تلقوا الفاعل بالسطح معدل وفيات أقل بنسبة ٢,٥٪، وكانت القيمة الاحتمالية ٠,٠٠١.

الاستنتاجات: بما أن نسبة حدوث متلازمة عسر التنفس كانت ٣٤,٧٪ ، يجب أن يكون العلاج بالفاعل بالسطح روتينيًا في وحدات العناية المركزة والخاصة لحديثي الولادة ، فالاستخدام السليم للفاعل بالسطح (التوقيت المناسب وطريقة الإعطاء) يقلل من الطلب على الأكسجين، والحاجة الى جهاز الضغط العالي للاوكسجين والاستشفاء والوفيات بين حديثي الولادة.

الكلمات المفتاحية: RDS حديثي الولادة، الإصابة، ضغط مجرى الهواء الإيجابي المستمر.

البريد الالكتروني: suraqais20@gmail.com
تاريخ استلام البحث: ٢٨ تشرين الثاني ٢٠٢٣
تاريخ قبول البحث: ١ نيسان ٢٠٢٤

[١،٢،٣]دائرة صحة ديالى- مستشفى البتول التعليمي- قسم الأطفال
[٤]كلية الطب - جامعة بغداد - فرع الجراحة