Research Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2020.26.004425

Characteristics of Preterm Neonates Treated with Surfactant in Tu Du Hospital, Vietnam

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ARTICLE INFO

Received: March 27, 2020

Published: April 06, 2020

Citation: Ngo Minh Xuan. Characteristics of Preterm Neonates Treated with Surfactant in Tu Du Hospital, Vietnam. Biomed J Sci & Tech Res 26(5)-2020. BJSTR. MS.ID.004425.

Keywords: Neonatology; Preterm infant; Respiratory distress syndrome; Surfactant administration; Ventilation

Abbreviations: ECMO: Extracorporeal Membrane Oxygenation; MAS: Meconium Aspiration Syndrome; ARDS: Acute Respiratory Distress Syndrome; IQR: Interquartile Ranges; BPD: Bronchopulmonary Dysplasia; LISA: Less invasie less Invasive Surfactant Administration; IVH: Intraventricular Hemorrhage

Abstract

Surfactant treatment in preterm infants and term newborns with (Acute Respiratory Distress Syndrome) ARDS-like severe respiratory failure has become part of an individualized treatment strategy in many intensive care units around the world. These babies constitute heterogeneous groups of gestational ages, lung maturity, as well as of the underlying disease processes and postnatal interventions. The pathophysiology of respiratory failure in preterm infants is characterized by a combination of primary surfactant deficiency and surfactant inactivation as a result of plasma proteins leaking into the airways from areas of epithelial disruption and injury. Various pre- and postnatal factors, such as exposure to chorioamnionitis, pneumonia, sepsis and asphyxia, induce an injurious inflammatory response in the lungs of preterm infants, which may subsequently affect surfactant function, synthesis and alveolar stability. Surfactant inactivation-and dysfunction-is also a hallmark in newborns with Meconium Aspiration Syndrome (MAS), pneumonia and other disorders affecting the pulmonary function. Although for the majority of suggested indications no data from randomized controlled trials exist, a surfactant replacement that counterbalances surfactant inactivation seems to improve oxygenation and lung function in many babies with ARDS without any apparent negative side effects. Newborns with MAS will definitely benefit from a reduced need for Extracorporeal Membrane Oxygenation (ECMO). Clinical experience seems to justify surfactant treatment in neonates with ARDS.

Introduction

Treatment with exogenous surfactant has saved the lives of thousands of premature babies in the past few decades [1]. The therapeutic efficiency of a given surfactant preparation correlates with its lipid and protein composition (and other factors), but it is also highly dependent on the technique used for administration. It is important to use a delivery strategy that optimizes surfactant distribution into the pulmonary airways to maximize its beneficial effects [2]. In 2014, the Committee on Fetus and Newborn – American Academy of Pediatrics published a clinical report on the use of surfactant replacement therapy for respiratory distress in the preterm and term neonate [1]. Among several recommendations, the report stated that “the optimal method of surfactant administration in preterm infants has yet to be clearly proven”. Unfortunately, the scientific literature provides conflicting and limited data regarding the methods or techniques of surfactant administration. The majority of studies were performed long ago and tested in more mature infants (gestational age >28 weeks), which does not reflect the population of preterm infants that actually undergo endotracheal intubation and surfactant treatment.

Moreover, respiratory care has changed substantially since these studies were conducted. Exogenous surfactant preparations must spread rapidly and efficiently into the air-liquid interface once instilled in the proximal airways, with the goal of achieving a homogenous distribution throughout the lungs. However, rapid administration of liquid into the lungs may elicit transient oxygen desaturation and bradycardia, or significant complications such as severe airway obstruction, pulmonary hemorrhage, pneumothoraces or pulmonary hypertension [3]. Therefore, surfactant should be administered according to a well-established protocol under the supervision of clinicians and respiratory therapists experienced in tracheal intubation, ventilator management and general care of the premature infant. The present article reviews the characteristics of preterm neonates treated with surfactant in Tu Du Hospital, Vietnam

Materials and Methods

This was a retrospective study in which a total of 426 preterm newborns less than 34 weeks gestation were studied. The study was carried in Tu Duc Hospital from August 2017 – July 2018. The inclusion criteria were designed to include newborn babies who were less than 34 weeks gestational age at the time of birth. The gestational age assessment was based on antenatal records and postnatal assessment based on expanded new Ballard scoring system. The babies with congenital malformations and the babies born to mothers with chorioamnionitis were excluded from the study. All preterm newborns less than 34 weeks gestation who satisfied the inclusion criteria were administered exogenous surfactant by endotracheal route (4 mL/Kg of the surfactant preparation equivalent to 100 mg/Kg of phospholipids) after resuscitation and stabilisation of the neonates shortly after birth. Further management of these babies was guided by their cardiorespiratory status and was as per the existing protocols in the neonatal intensive care unit. We report demographic and clinical characteristics variables using frequencies and proportions for categorical data and medians with Interquartile Ranges (IQR) for continuous data. Continuous normally distributed variables (such as birth weight and gestational age) were analysed using unpaired Student ‘t’ test. Various proportions of neonatal morbidity were analysed using Chi square test or Fisher›s exact test when an expected cell value was < 5.

Results

From August 2017 to July 2018, there were 1926 premature babies ≤ 32 weeks admitted to the Tu Du Hospital’s neonatal department. A total of 426 children (22.12%) received surfactant treatment. There were 53 infants born with nCPAP that met the sampling criteria and were enrolled in the minimally invasive LISA group. Table 1 shows the average gestational age of the LISA group with less invasive technique was 29.1 ± 1.9 weeks. The average gestational age of the group using INSURE technique was 29.7 ± 1.6 weeks. The average gestational age of LISA group was lower than the INSURE group but the difference was not statistically significant, p = 0.07. Table 2 shows the birth weight in the LISA group was 1248.1 ± 311.6, lower than the birth weight in the INSURE group was 1308.5 ± 309.1. The difference is not statistically significant, p = 0.32. The smallest birth weight in the LISA group was 600g, the highest was 1800g. The smallest birth weight in the INSURE group was 800g, the highest in 1950g.

Table 1: Average gestational age.

Technique	Mean± SD	CI 95%	Min	Max	*p*-value
INSURE	29.7± 1.6	29.3 – 30.2	26.1	32	0.07
LISA	29.1 ± 1.9	28.5 – 29.6	26.0.	32	

Table 2: Weight at birth.

Technique	Mean± SD	CI 95%	Min	Max	*p*-value
INSURE	1308.5 ± 309.1	1223.3 – 1393.7	800	1950	0.032
LISA	1248.1 ± 311.6	1162.2– 1334.0	600	1800	

The gender distribution of the two treatments was similar, with 50.9% of the boys in the LISA group being less invasive compared to 54.7% of the boys treated with INSURE, the difference was not Statistically significant with p = 0.69 (Table 3). There was no difference in using sufficient prenatal steroids dose between 2 groups INSURE and LISA by less invasive technique, p>0.05. The caesarean group had a lower rate of invasive LISA (60.4%) than the treatment with INSURE (56.6%), the difference was not statistically significant with p = 0.69 (Table 4). The average CRIB score of the LISA group was 2.28 ± 1.16, the INSURE group was 2.07 ± 1.45. The average CRIB score of the LISA group was 0.2 points higher than the INSURE group, the difference was not statistically significant, p = 0.42 (Figure 1). According to Table 5, the average age of LISA in the INSURE group was (243.49 ± 13.6) minutes (equivalent to 4 hours ± 13.6 minutes), the average age at the LISA in the LISA group was (204.53). ± 13.6) minutes (equivalent to 3 hours 24 minutes ± 13.6 minutes). The LISA group was implemented earlier than the INSURE LISA group. The difference was statistically significant p = 0.04.

 DOI: 10.26717/BJSTR.2020.26.004425

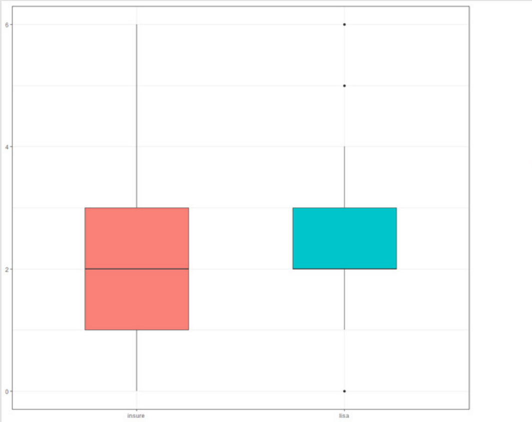

Figure 1: CRIB score.

Table 3: The sex of preterm newborn.

Sex	LISA (n=53)	INSURE (n=53)	OR (CI 95%)	*p*-value
Male	29 (50.9)	7 (54.7)	0.85 (0.37 – 1.98)	0.69
Female	26 (49.1)	24 (45.3)		

Table 4: Corticoids using before birth.

	LISA (n=53)	INSURE (n=53)	OR (CI 95%)	*p*-value
Corticoids using before birth				
No use	28 (52.8)	24 (45.3)		
Less dose use	9 (17.0)	13 (24.5)	0.59 (0.21 – 1.62)	0.31
Full dose use	16 (30.2)	16 (30.2)	0.86 (0.35 – 2.07)	0.73
Delivery method				
Normal delivery	21 (39.6)	23 (43.4)		
Caesarean delivery	32 (60.4)	30 (56.6)	0.85 (0.37 – 2.00)	0.69

Table 5: The age of baby at time of procedure.

Technique	Mean± SD	CI 95%	Min	Max	*p*-value
INSURE	243.49 ± 13.6	216.3 – 270.7	65	360	0.07
LISA	204.53 ± 13.6	177.1 – 231.9	50	360	

Discussion

Respiratory distress syndrome in preterm infants is a disorder caused by a primary deficiency of surfactant or surfactant in immature lungs, resulting in progressive, widespread alveolar collapse, resulting in early respiratory failure. Birth, which is an important cause of morbidity and mortality in preterm infants. Surfactant replacement therapy reduces the risk of death and complications of bronchopulmonary dysplasia (BPD) [4]. The combination of prenatal sterocorticoids, early postpartum NCPAP and alternative surfactant therapy improved outcomes for preterm neonates. There have been many studies on techniques of pumping surfactant into the lungs. Until now, the INSURE technique has been considered the standard in surfactant replacement therapy. However, with INSURE technique, endotracheal intubation is still needed to pump surfactant and consequently the child undergoes mechanical ventilation during the procedure. To minimize the child's exposure to invasive mechanical ventilation, clinicians have improved the technique of pumping surfactant into the lungs without the need for mechanical ventilation, called a minimally invasive surfactant (LISA - Less invasie less Invasive Surfactant Administration (MIST).

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Attempts to introduce surfactant into the lungs by aerosol spray or laryngeal mask have not shown clinical evidence [5]. A recommended minimally invasive technique is to open the glottis with a laryngoscope and insert a small catheter into the trachea. Surfactant is introduced into the lungs through this catheter. There have been many studies on the feasibility and effectiveness of this technique. Recently, Christin S and colleagues published in the journal Global Pediatric health Meta-analysis of low-invasive LISA technology that reduces the need for invasive mechanical ventilation in preterm neonates. The authors selected 3 studies of Kanmaz et al. [6-8] out of 219 published studies to be included in the analysis [9]. Author Mohamma dizadeh et al. [7] used 4F gastric catheter and used Magill forceps to insert catheter into trachea. Surfactant is pumped for 1 - 3 minutes. Kanmaz et al. [6] used a 5F gastric tube and did not need Magill nipper to insert the gastric tube into the trachea.

The surfactant used is Poractant alpha and injects rapidly within 30-60 seconds [10]. Dargaville PA uses a vascular catheter and does not require Magill nipper to enter the trachea [11]. Authors Bao et al. [8] used a 16G vascular catheter and did not use Magill nipper to insert the catheter into the trachea. Surfactant is pumped for 3-5 minutes [12]. Author Wolfgang Gopel 2016 uses endotracheal tubes 2.5 and does not need Magill nippers [13]. According to author Cristina Ramos-Navarro, a small 5-6 F catheter is specially designed to pump surfactant without using Magill nipper [14]. In our study, 5 - 6 F gastric catheter was used and inserted directly into the trachea through laryngoscope without using Magill nipper. The advantage is that gastric catheters are readily available, inexpensive while vascular catheters are expensive, and specially designed catheters by author Cristina Ramos-Navarro are not available in Vietnam. As for the endotracheal tube 2.5, the inner diameter of the tube is 2.5 mm, the outer diameter is 4.1 mm, the rest for children to breathe when doing small procedures, children breathe harder.

In addition, the gastric tube we use is hard enough to put directly into the trachea without using Magill pliers, simple technical manipulation. These are the advantages of a technique. Simple equipment easy to find, low cost and simple operation easy to carry out. There was no difference between the two groups in the study of primary features or prenatal risk factors, except that the CRIB score was higher in the LISA group, indicating a more severe clinical condition at baseline. In this study, the mean gestational age was 29.7 ± 0.22 weeks in the INSURE group and 29.06 ± 0.26 weeks in the LISA group, the difference was not statistically significant, p = 0.065. In the study of Cristina R et al., The average gestational age in the INSURE group was 29.1 weeks and 28.4 weeks in the LISA group, the difference was not statistically significant [14]. In the study of Bao et al. [8], the average gestational age of two groups of INSURE and LISAs was 29.3 ± 1.6 weeks and 29.1 ± 1.5 weeks, the difference was not significant. Statistically significant p = 0.54 [12]. In the study of Mohammadizadeh Majid et al. [7], the average gestational age was higher in the INSURE group and the LISA (31 ± 2 weeks, 30 ± 2 weeks, p = 0.2) [13].

The mean gestational age in our study was nearly the same as the average gestational age of other studies that studied preterm infants under 32 weeks gestation. When we grouped gestational age groups by smaller groups, we found no difference in each gestational age group, especially the age group below 28 weeks. Babies under the age of 28 weeks are the subjects with worse and worse outcomes in those of higher gestational age, especially the effects of mechanical ventilation on immature lungs. Therefore, this age group is at particular risk for broncho pulmonary dysplasia. In addition, other organs are immature, so this subject is susceptible to systemic infections, pneumonia, arterial duct disease, necrotizing enterocolitis and retinopathy in preterm infants. There was no difference in the rates of caesarean births in the 2 INSURE groups and the LISA Regarding prenatal coticosteroids use, in the study of Cristina R et al., The rate of prenatal coticosteroids use in the INSURE group was 70% and 73% in the LISA group, the difference was not statistically significant [11].

In the study of Bao et al. [8], the use of antenatal coticosteroids 2 groups INSURE and LISA group was 93% and 89.4%, the difference was not statistically significant p = 0.54 [12]. In the study of Mohammadizadeh Majid et al. [7], the use of antenatal coticosteroids in the INSURE group and the LISA group was 89.5% and 84.2%, p = 0.2 [13]. In our study, the rate of adequate use of antenatal corticoids was lower than that of other studies but no difference was found between the two LISA groups and the INSURE. The use of antenatal corticoids for pregnant women at risk of preterm birth contributes to improved adverse outcomes for preterm neonates. The effect of antenatal corticoids reduces the incidence and severity of respiratory endothelial respiratory depression in preterm neonates. In a Systematic review of Robert D 2017 on the Cochrane Library, treatment with prenatal corticosteroids (compared to placebo or no treatment) was associated with a reduction in the most serious adverse outcomes associated with preterm birth, including: perinatal mortality (average risk ratio) RR) 0.72, 95% confidence interval (CI) 0.58 - 0.89; participants = 6729; research = 15; Tau^2 = 0.05; I^2 = 34%; moderate-quality); neonatal mortality (RR 0.69, 95% CI 0.59 - 0.81; participants = 7188; study = 22), RDS (average RR 0.66; 95% CI 0.56 - 0 , 77; participants = 7764; research = 28; Tau^2 = 0.06; I^2 = 48%; moderate-quality); Medium / heavy RDS (RR average 0.59, 95% CI 0.38 - 0.91; participants = 1686; studies = 6; Tau^2 = 0.14; I^2 = 52%); intraventricular hemorrhage (IVH) (RR average 0.55, 95% CI 0.40 - 0.76; participants = 6093; studies = 16; Tau^2 = 0.10; I^2 = 33%; moderate -quality), necrotizing enterocolitis (RR 0.50, 95% CI 0.32 - 0.78; participants = 4702; studies = 10); mechanical ventilation is required (RR 0.68, 95% CI 0.56 - 0.84; participants = 1368; research = 9); and systemic infection in the first 48 hours of life (RR 0.60, 95% CI 0.41 - 0.88; participants = 1753; studies = 8) [14].

Conflicts of Interest

There are no conflicts of interest to declare.

Financial Support and Sponsorship

Nil.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2020.26.004425

Ngo Minh Xuan. Biomed J Sci & Tech Res