Research Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2020.27.004448

Less Invasive Surfactant Administration Versus Intubation For Surfactant Delivery In Preterm Infants With Respiratory Distress Syndrome: An Experimental Study In Vietnam

Ngo Minh Xuan*

Pham Ngoc Thach Medical University, 2 Duong Quang Trung street, District 10, Ho Chi Minh City, Vietnam

***Corresponding author:** Ngo Minh Xuan, Pham Ngoc Thach Medical University, 2 Duong Quang Trung street, District 10, Ho Chi Minh City, Vietnam

ARTICLE INFO

Received: April 02, 2020

Published: April 17, 2020

Citation: Ngo Minh Xuan. Less Invasive Surfactant Administration Versus Intubation For Surfactant Delivery In Preterm Infants With Respiratory Distress Syndrome: An Experimental Study In Vietnam. Biomed J Sci & Tech Res 27(1)-2020. BJSTR. MS.ID.004448.

Abbreviations: RDS: Respiratory Distress Syndrome; LISA: Less Invasive Surfactant Administration; BPD: Bronchopulmonary Dysplasia; CPAP: Continuous Positive Airway Pressure; ET: Endotracheal Tube; PDA: Patent Ductus Arteriosus; IVH: Intraventricular Haemorrhage; ROP: Retinopathy Of Prematurity,

ABSTRACT

Purpose: To compare the outcome between LISA (less invasive surfactant administration) method and conventional INSURE method (INtubation SURfactant administration and Extubation) in preterm infants with respiratory distress syndrome (RDS).

Methods: This is An experimental study which conducted at Neonatal Intensive Care Unit of Tu Du Hospital, from August 2017 to July 2018.A total of 106 preterm infants 26-32 weeks gestation, with respiratory distress syndrome (RDS) were included in the study and divided randomly into two groups, 53 each.

Results: There were 29 (50.9%) males in LISAand 29 (54.7%) in the INSURE group. Mean birth weight was 1248.1 grams in LISA, while 1308.5 grams in INSURE infants. C-section rate was 60.4% (n=32) and 56.6% (n=30) in LISAand INSURE, respectively. Pre-natal steroids were given to 16 patients (30.2%) in LISAand 16 patients (30.2%) in INSURE group. The median duration of mechanical ventilation was 54. daysand 4.9 days in LISAand INSURE, respectively. Similarly, mean FiO2 reduction was 11.7% in LISA group and it was 8.5% in INSURE group, with p-value <0.05. There was no significant difference in mortality, hospital stay and complications.

Conclusion: LISA technique was safe, non-invasive approach of surfactant administration, with reduced need of mechanical ventilation rate and duration.

Introduction

Respiratory distress syndrome (RDS) is a common neonatal condition in premature infants. Its treatment often requires the use of surfactants, which have been shown to reduce the risk of death and bronchopulmonary dysplasia (BPD) in this population [1,2]. The most common technique for surfactant delivery currently involves endotracheal intubation and short-duration mechanical ventilation. However, the lungs of premature infants are particularly susceptible to ventilator-induced lung injury [3-5]. The use of non-invasive ventilation with nasal continuous positive airway pressure (CPAP) has been shown to cause less alveolar injury compared with mechanical ventilation via endotracheal tube [6,7]. Currently, the preferred strategy for management of RDS is nasal CPAP at onset with selective use of surfactant for those infants with increasing oxygen requirements [8,9]. Infants meeting the criteria for surfactant use are intubated and briefly ventilated for surfactant delivery by a protocol often referred to as InSurE (Intubation, Surfactant administration and Extubation) [10,11]. To prevent intubation for surfactant delivery in preterm infants with RDS, less invasive surfactant administration (LISA) techniques have been described [12,13]. Of these techniques, the use of a thin catheter for intratracheal surfactant delivery in spontaneously breathing preterm infants on nasal CPAP is the most studiedwith

proposed benefits in terms of better survival and decreased need for mechanical ventilation [14]. The aim of our study was to assess the efficacy and the feasibility of LISA technique without medication and to compare the effects with the conventional management.

Materials and Methods

Population

The study was conducted in the Neonatal Intensive Care Units of Tu Du Hospital (Ho Chi Minh city, Vietnam) from August 2017 to July 2018. The Ethics Committee of the hospitalapproved the study. A written informed consent for participation in the study was obtained from the parent of infants.

Inclusion criteria were:

(1) Infants born at 26 to 32 week's gestational age.

(2) Infants with RDS and need PS administration with 2 hr after birth.

Exclusion criteria were:

(1) Infants who had been previously intubated and

(2) Infants with a congenital anomaly affecting respiratory function.

The diagnosis of respiratory distress syndrome (RDS) was based on the occurrence of classic signs of respiratory distress such as the need for oxygen, tachypnea, intercostal muscle retractions, grunting, and the exclusion of other causes of respiratory failure. The diagnosis was confirmed radiologically by reduced lung volumes, a reticulogranular pattern of lung consolidation, and air bronchograms [15]. Nasal continue positive airway pressure (nCPAP) was the initial means of respiratory support. Distending pressure ranged from 5 to 8 cm H_2O, titrated according to oxygen requirement and work of breathing. Infants with signs of RDS, who were received nCPAP treatment and required nCPAP pressures ≧7 cm H_2O and FiO2 ≧0.3 (28+0-29+6 weeks gestation) or ≧0.35 (30+0–32+6 weeks) to maintain SpO^2 levels between 85% and 95%, were randomized to receive PS treatment (Curosurf, Chiesi Farmaceutici, Parma, Italy) at a dose of 200 mg/kg either by LISA procedure or conventional intubation. Infants were intubated, if FiO_2 was ≧0.5, or if there was respiratory acidosis (pH <7.2) or significant apnea.

Surfactant Administration

During process of surfactant administration, the concentration of oxygen (FiO^2) was adjusted using a blender to maintain oxygen saturation within the range of 85–95%.

LISA procedure: A 16 gauge, 130 mm vascular catheter (16G Angiocath, BD, Sandy, Utah, USA) was marked to indicate desired depth of insertion (28–29 weeks: 1.5 cm, 30–32 weeks: 2 cm). Direct laryngoscopy was performed, and the vascular catheter was inserted beyond the vocal cords to the required depth, and held in position at lips. If catheterization of the trachea was not possible within 20–30 s, the procedure was discontinued and attempted again once the baby was stable. Once the catheter was correctly positioned, surfactant was given at a standard dose as 5 boluses or more over 3-5 min. The tracheal catheter was immediately withdrawn. Infants were continued on nCPAP throughout the procedure. Positive pressure inflations were given by mask, if the infant developed apnoea or bradycardia.

Conventional Intubation Procedure: Surfactant instillation via endotracheal tube (ET) was performed with some brief mechanical ventilations, a standard dose of surfactant was always divided into 2 or 3 boluses. The endotracheal tube was withdrawn as soon as clinically possible after PS instillation, and the baby switched to nCPAP. The whole procedure took about 3 min and occurred without continuous distending pressure.

Management after Surfactant Administration

After procedure, infants were stabilized on nCPAP. If FiO2 was >0.6, or if there was sustained respiratory acidos (pH <7.2) or repeated apnea, infants were intubated and receive MV. A further dose of surfactant (100 mg/kg) was given after intubation if clinically indicated. Care throughout hospitalization was as per routine for all infants, including monitoring for, and treatment of, patent ductus arteriosus (PDA), and screening for intraventricular haemorrhage (IVH) and retinopathy of prematurity (ROP) according to standard schedules of our center.

Data collection

For each eligible infant, details during the PS instillation, including pulse oximetry saturation, heart rate and FiO2, were recorded prospectively every 30 seconds for about 3 min, along with pO_2 and pCO_2 values from blood gas samples before, and 1 h after PS administration. Changes in nCPAP pressure were recorded every 30 min in the first 4 hr, and at 12 and 24 h of life. Demographical dataand early neonatal outcomes were recorded for all infants including need for intubation and mechanical ventilation in the first 72 h (and thereafter), further PS therapy. The duration of respiratory support, including respiratory assistance (mechanical ventilation and/or nCPAP), oxygen therapy and intensive care admission were also recorded.

Statistical analysis

Data were expressed as proportion, mean ± standard deviation (m ± SD) or median (interquartile range). Proportions were compared by Chi-square analysis. Continuous variables were compared by Student's t test or Mann–Whitney U test according to their distribution. A p value <0.05 was considered statistically significant. Statistical analysis was carried out using the SPSS software, version 19.0 for Windows (SPSS, Chicago, IL, USA).

Results

During the study period, 1926 infants with 26–32 gestational age, were born in our hospital. 53 infants in LISA group and 53 infants in conventional group were eligible for the statistical analysis. Demographic and clinical characteristics of the infants receiving surfactant by LISA were generally well matched with those managed by conventional intubation (Table 1). The average gestational age of LISA group was lower than the INSURE group but the difference was not statistically significant, p = 0.07. 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. 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. 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. 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.

Table 1: Demographic and clinical characteristics.

Characteristics	LISA (n=53)	Intubation (n=53)	P value
Gestation age (weeks), mean (SD)	29.1 (1.9)	29.7 (1.9)	0.07
Birth weight (grams), mean (SD)	1248.1 (311.6)	1308.5 (309.1)	0.032
Male gender, n (%)	29 (50.9)	29 (54.7)	0.69
Singleton, n (%)	23 (43.4)	22 (41.5)	0.86
Complete antenatal corticosteroids, n (%)	16 (30.2)	16 (30.2)	-
Cesarean section, n (%)	32 (60.4)	30 (56.6)	0.69
CRIB score	2.28 ± 1.16	2.07 ± 1.45	0.42
Mechanical ventilation at anytime(n,%)	12 (22.6)	11 (20.8)	0.81
Mechanical ventilation in the first-3-day after birth (n,%)	5 (9.4)	8 (15.1)	0.37
Total time of mechanical ventilation (day), mean (SD)	5.4 (3.8)	4.9 (3.3)	0.73

The percentage of infants who were treated with LISA for mechanical ventilation for more than 1 hour during hospitalization was 22.6%. The percentage of infants in INSURE group requiring mechanical ventilation for more than 1 hour during hospitalization was 20.8%. The difference is not statistically significant with p = 0.81 (Table 1). (Table 2) shows the mean of post-treatment SpO_2 increasing and the post-treatment FiO_2 reducing when comprare to those pre-treatment, respectively. The FiO_2 after treatment in the LISA group was (29.2 ± 3.8)%, and in the INSURE group was (33.1 ± 5.2)%, which was significant different between the two groups (p = 0.001). Pneumothorax was seen in 2 patients in INSURE group, accounted for 3.8%. Pneumonia was the most common complication in both group, but more frequency in INSURE group. Death was occurred in 5 (9.4%) patients of LISA group and 8 (15.1%) of INSURE group. The hospital stay was shorter in LISA group than that in INSURE group (Table 3).

Table 2: Comparison SpO_2 between pre- and post-treatment.

	LISA (n=53)	Intubation (n=53)
SpO_2(%), mean (SD)		
Pre-treatment	92.1 (2.9)	92.0 (2.4)
Post-treatment	95.3 (1.9)	94.9 (2.1)
P value	<0.001	<0.001
FiO_2(%), mean (SD)		
Pre-treatment	40.8 (6.7)	40.6 (5.9)
Post-treatment	29.1 (3.8)	32 (5.2)
P value	<0.001	<0.001

Table 3: Outcome and complication.

OR(CI 95%)	Therapeutics		OR(CI 95%)	p-value
	LISA (n=53)	INSURE (n=53)		
Pneumothorax(n,%)	0 (0.0)	2 (3.8)		0.49
Pneumonia(n,%)	32 (60.4)	40 (75.5)	0.50 (0.20 – 1.23)	0.09
Death(n,%)	5 (9.4)	8 (15.1)	0.59 (0.14 – 2.21)	0.37
Hospital stay (day), mean (SD)	23.1 (29.9)	26.5(12,3)		0.02

Discussion

The effectiveness of the surfactant treatment was assessed based on a decrease in FiO_2 requirement of more than 20%. One of the goals of treating respiratory failure is to reduce oxygen demand. Clinicians are concerned that, with LISA techniques, when a positive pressure is not used to push the drug in, it is guaranteed that the drug will enter the alveoli. In our study, both groups effectively reduced FiO_2 by more than 20% after procedure. However, the LISA group decreased FiO2 by 20% higher than the INSURE group and the difference was statistically significant. The rate of FiO2 reduction over 20% in the LISA group was 90.57% and 71.7% in the INSURE group, p = 0.013. In 5 cases where FiO_2 was not reduced by more than 20% in the first hour, only 1 case had to be intubated again within 72 hours after birth. And in all cases of LISA, no endotracheal intubation is required within 1 hour after procedure. Compared with Christina Ramos - Navarro, this rate is

73.3% and the difference is not statistically significant between the two groups INSURE and LISA [16]. The decrease in oxygen demand within 1 hour after procedure for respiratory failure treatment of endothelial disease proves that adequate exogenous surfactant is provided. It is the reduction of FiO2 within 1 hour after procedure shows that one of the goals of treatment of respiratory failure has been achieved. Contrary to the anxiety of clinicians, the administration of surfactant to the lungs while the child was still breathing completely physiologically, no volume injury, no pressure traumaas well as no influence on the airflow in and out of babies. The use of invasive mechanical ventilation during surfactant administration has been shown to reduce the effectiveness of injected surfactant, contributing to the development of respiratory complications.

In our study, there were 2 cases (3.77%) of pneumothorax in the INSURE group and no cases of pneumothorax in the LISA group, the difference was not statistically significant (p = 0.15). The rate of pneumothorax in our study seems to be lower than other studies, this can be explained by the smaller sample size we have and the criteria for inclusion in the INSURE group are different from other studies. We did not include INSURE cases of endotracheal extubation immediately after procedure. Regarding the incidence of pneumonia, the INSURE treatment group seemed to be higher than the less invasive surfactant treatment group (75.47% compared to 40.38%, p = 0.096) but the difference was not statistically significant. In our study, we recorded all cases of pneumonia from the time he was in the intensive care unit until he was discharged from the hospital, including the schools that ended treatment in NICU but also hospitalized in Kangaroo program for nutrition issues, caring for preterm infants, breastfeeding mothers... pneumonia was also recorded. Although the difference in CRIB scale and gestational age and birth weight differences were not statistically significant, the average gestational age of the surfactant group was less invasive than the INSURE group (29.06 weeks compared to 29.7 weeks, p = 0.06), the CRIB score of the less invasive surfactant group was higher than the INSURE group (2.28 compared to 2.07, p = 0.4) showing a worse clinical situation at starting time. On the other hand, the sample size of 53 children may not be enough to make a statistically significant difference.

The number of hospitalization days of the LISA group was shorter than the number of hospitalization days of the INSURE group and the difference was statistically significant. The average number of days in hospital of the INSURE group and the LISA was 32.24 ± 2.1 days and 26.51 ± 1.68 days, p = 0.016. In this study, although the incidence of invasive mechanical ventilation and duration of mechanical ventilation did not differ between the 2 treatment groups, the total number of hospitalized days of the LISA group was shorter than the total number of hospitalized days in the group. INSURE. Therefore, we believe that this technology will contribute to reducing treatment costs and reducing overcrowding in the Neonatal Department. Shortening the length of hospital stay is one of the hospital's goals. Especially in the current situation, the overload of hospitals is an urgent problem. Every effort to reduce the length of hospital stay contributes to reduce hospital overcrowding. Hospital overcrowding has always been a special concern for residents, health workers and regulators. The consequences of prolonged hospital stay are enormous. Especially in intensive care units, prolonged hospitalization means an increase in infection rates, an increase in the incidence of complications and especially an increase in the death rate. The mortality rate in the LISA group was lower than the INSURE group (9.43% compared to 15.09%, p = 0.37) but the difference was not statistically significant. This is also consistent with other studies where there was no difference in mortality between the two INSURE groups and the LISA. The survey found a 10-fold increase in mortality when failing on aLISA compared to a successful group with aLISA. In addition, it may be due to the small sample size, the research design is not strong enough, so there is no difference and related factors between the LISAand the death.

Conclusion

As a result of our research, we believe that aLISA technique is feasible, feasible, with an effective reduction of FiO_2 above 20% by up to 90.57%, which may be possible to reduce the need for mechanical ventilation within the first 3 days of life. Reduce the length of hospital stay, reduce the cost of treatment, reduce the overload for the Neonatal Department, contribute to improving the quality of treatment for preterm infants, contributing to improving the outcome of preterm neonates.

References

1 Seger N, Soll R (2009) Animal derived surfactant extract for treatment of respiratory distress syndrome. Cochrane Database Syst Rev (2): CD007836.

2 Soll RF (2000) Synthetic surfactant for respiratory distress syndrome in preterm infants. Cochrane Database Syst Rev (2): CD001149.

3 Attar MA, Donn S (2002) Mechanisms of ventilator-induced lung injury in premature infants. Semin Neonatol 7(5): 353-360.

4 Hillman NH, Kallapur SG, Pillow JJ, Moss TJ, Polglase GR, et al. (2010) Airway injury from initiating ventilation in preterm sheep. Pediatr Res 67(1): 60-65.

5 Schmolzer GM, Te Pas AB, Davis PG, Morley CJ (2008) Reducing lung injury during neonatal resuscitation of preterm infants. J Pediatr 153(6): 741-745.

6 Jobe AH, Kramer BW, Moss TJ, Newnham JP, Ikegami M (2002) Decreased indicators of lung injury with continuous positive expiratory pressure in preterm lambs. Pediatr Res 52(3): 387-392.

7 Polin RA, Sahni R (2002) Newer experience with CPAP. Semin Neonatol 7(5): 379-389.

8 Finer NN, Merritt TA, Bernstein G, Job L, Mazela J, et al. (2010) An open label, pilot study of Aerosurf(R) combined with nCPAP to prevent RDS in preterm neonates. J Aerosol Med Pulm Drug Deliv 23(5): 303-309.

9 Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, et al. (2013) European consensus guidelines on the management of neonatal respiratory distress syndrome in preterm infants--2013 update. Neonatology. 103(4): 353-368.

10 Bohlin K, Gudmundsdottir T, Katz Salamon M, Jonsson B, Blennow M (2007) Implementation of surfactant treatment during continuous positive airway pressure. J Perinatol 27(7): 422-427.

11 Verder H, Robertson B, Greisen G, Ebbesen F, Albertsen P, et al. (1994) Surfactant therapy and nasal continuous positive airway pressure for newborns with respiratory distress syndrome. Danish-Swedish Multicenter Study Group. N Engl J Med 331(16): 1051-1055.

12 Attridge JT, Stewart C, Stukenborg GJ, Kattwinkel J (2013) Administration of rescue surfactant by laryngeal mask airway: Lessons from a pilot trial. Am J Perinatol 30(3): 201-206.

13 Pillow JJ, Minocchieri S (2012) Innovation in surfactant therapy II: surfactant administration by aerosolization. Neonatology 101(4): 337-344.

14 Klebermass Schrehof K, Wald M, Schwindt J, Grill A, Prusa AR, et al. (2013) Less invasive surfactant administration in extremely preterm infants: impact on mortality and morbidity. Neonatology 103(4): 252-258.

15 Gortner L, Bartmann P, Pohlandt F, Bernsau U, Porz F, et al. (1992) Early treatment of respiratory distress syndrome with bovine surfactant in very preterm infants: A multicenter controlled clinical trial. Pediatr Pulmonol 14(1): 4-9.

16 Ramos Navarro C, Sanchez Luna M, Zeballos Sarrato S, Gonzalez Pacheco N (2016) Less invasive beractant administration in preterm infants: a pilot study. Clinics (Sao Paulo) 71(3): 128-134.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2020.27.004448

Ngo Minh Xuan. Biomed J Sci & Tech Res