Original Article

Short-Term Complications in Preterm Infants with Respiratory Distress Syndrome Treated with Rapid Extubation of Tracheal Tube Following Administration of Surfactant (INSURE) and Mechanical Ventilation Methods

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Abstract

Introduction:
Surfactant injection is used for treatment of respiratory distress syndrome in preterm infants through Intubation-SURfactant-Rapid Extubation and conventional mechanical ventilation. This study aimed to compare the prematurity complications in neonates treated with one of these two methods.

Material and methods:
This descriptive study examined records of 120 preterm neonates hospitalized in NICUs of hospitals affiliated to Babol University of Medical Sciences in 2012-2013. Eligible neonates were non-randomly assigned to conventional treatment based on the admission year (mechanical ventilation in 2012 and Intubation-SURfactant-Rapid Extubation in 2013). Required variables extracted from their records were entered into the questionnaires. Data were analyzed by SPSS version 14 and $p<0.05$ was considered significant.

Results:
The results showed that death, intraventricular hemorrhage, disseminated intravascular coagulation ($p=0.01$), retinopathy of prematurity ($p=0.03$) and pneumothorax ($p=0.001$) were significantly less in the INSURE group than in the mechanical ventilation group. However, no significant difference was observed between the two groups regarding the pulmonary hemorrhage ($p=0.4$), sepsis ($p=0.29$) and patent ductus arteriosus ($p=0.24$).

Conclusion:
Based on the findings of this study, INSURE method is safer than mechinaical ventilation in preterm infants with respiratory distress. Therefore, further studies are suggested in order to use this method for treatment of respiratory distress syndrome in neonatal intensive care units.

Keywords: Intubation, Surfactant, Preterm Infants, Mechanical Ventilation, Respiratory Distress Syndrome, Complications, INSURE

Introduction

Surfactant is produced by epithelial cells type II in the lungs after gestational weeks 30-32 (1). Production of surfactant reduces alveolar surface tension and results in better gas exchange (2) that is necessary for normal lung function (3). Infants born alive before gestational week 37 (4) suffer from respiratory distress syndrome due to

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insufficient surfactant (5 and 6). This syndrome is the most common lung problem (2 & 7) and the main cause of morbidity and mortality in preterm infants (8 and 9), and affects one third of infants in gestational weeks 28 to 34 and less and 5% of infants after gestational week 34 (10). The prevalence of this syndrome increases with lower gestational age and birth weight (11). Clinical symptoms of respiratory distress in infants include apnea, cyanosis, grunting, abnormal breathing sounds, nostril flaring, weak sucking, tachypnea (more than 60 breaths per minute) (10 and 12), and intercostal retraction requiring respiratory support (13), and if untreated may lead to patient's death due to insufficient gas exchange, pneumothorax, emphysema, lung hemorrhage, and cerebral intraventricular hemorrhage (14). Substitute surfactant has been used since early 1990's as an effective and safe treatment for surfactant inadequacy associated with preterm infants (15-16). Infants' respiratory distress is essentially treated by substitute surfactant and mechanical respiratory support (17), which can reduce infant mortality rate by up to 40% (6). There are three strategies for treatment of this syndrome, including 1- establishing Continuous Positive Airway Pressure (CPAP), and intubation and surfactant administration if needed; 2- intubation and surfactant administration in high-risk infants and tracheal extubation and establishing CPAP -this method is referred to as Intubation-SURfactant-Rapid Extubation (INSURE); and 3- tracheal intubation, surfactant administration and continuation of mechanical ventilation according to conventional NICU protocol (18-19). Using mechanical ventilators entails risk of damage to airway and lung parenchyma in infants and can cause pulmonary edema, and lung inflammation, fibrosis, and dysplasia (17). The widespread use of non-invasive ventilation was accepted as the most effective tool for reducing the risk of pulmonary damage due to mechanical ventilation in the first decade of 20th century (18). It is now used in many centers as the first respiratory support for preterm infants (8 and 20), and has been able to reduce the need for substitute surfactant by 50% (21). A study conducted by Naseh et al. showed that post-injection use of INSURE can significantly reduce mortality rate in preterm infants with respiratory distress (6). In their study, Verder et al. argued that using INSURE instead of mechanical ventilator in the first day of life reduces risk of pulmonary dysplasia (8). Post-injection use INSURE instead of mechanical ventilator also obviates the need for re-administration of surfactant in infants with respiratory distress (22). Yet, today, consideration is given to how to minimize the use of mechanical ventilator in infants due to the subsequent risk of damage to lung tissue and progress of bronchopulmonary dysplasia (8 & 23-24). Although post-injection INSURE is considered a beneficial clinical method for controlling respiratory distress in infants (19), there is no consensus on its use in all infants with this syndrome (17). In review of literature, no study was found to compare these two methods in terms of short-term complications in preterm infants with respiratory distress syndrome, including preterm retinopathy, disseminated intravascular coagulation, sepsis, etc. Since previous studies have regarded INSURE as a safe method and mechanical ventilation as a method with many complications, the present study aims to compare complications of these methods in preterm infants.

Materials and Methods

In the present descriptive study, samples were selected randomly from records of preterm infants hospitalized with respiratory distress diagnosis in NICU of a hospital affiliated to Babol University of Medical Sciences during 2012-13 and treated with surfactant in either mechanical ventilation or INSURE methods. All eligible preterm infants included infants

that had undergone mechanical ventilation in 2012 (mechanical ventilation group) and INSURE in 2013 (INSURE group). The two groups were matched in terms of some study variables such as gestational age, birth weight, Silverman respiratory score, type of childbirth, etc. (Tables 1 and 2).

Preterm infants that needed Fio2≥40% to maintain arterial blood oxygen saturation within 85% and 92% range (6) and had received surfactant were included in the study by census method, and were assigned to two groups of 60 infants treated with INSURE (group 1) and mechanical ventilation (group 2). Study exclusion criteria were congenital anomalies, meconium aspiration syndrome, gestational age outside 28-36 weeks range, and birth weight less than 750 grams, death in the first three days of birth, not needing surfactant according to physician's order, history of maternal drug use, the need for advanced resuscitation after birth, and umbilical cord pH less than 7. Group 2 infants with Silverman respiratory distress score of 4 and higher in the first hour of birth were intubated and received surfactant during mechanical ventilation. Group 1 infants with Silverman respiratory distress score of 3 and higher in the first two hours of birth were treated according to INSURE. In the present study, failed treatment was defined as needing mechanical ventilation (po_2<50mmHg, pH<7.2) up to 72 hours later with Fio_2>0.5, pco_2>65mmHg, and repeat of apnea (requiring bag-mask ventilation) (17 & 19). Study variables were extracted from records and entered into a researcher-made questionnaire, such as demographic details of gestational age, birth weight, Silverman respiratory distress score (recorded by physician), receiving steroids before childbirth, prematurity complications, duration of hospitalization, feeding time, infant's outcome in terms of discharge or death during stay. Ethical issues regarding confidentiality of extracted data were observed in the course of the present study. Data were analyzed in SPSS-14 using t-test (for normally distributed data based on Kolmogorov-Smirnov test) and Chi-square (to compare bimodal nominal data) with 95% confidence interval. P<0.05 was considered statistically significant. All ethical requirements were observed in the present study.

Results

The present study recruited 126 eligible infants of 28-36 weeks of gestation and birth weight of 750-2900 grams. Because of death on the first day of birth, 6 infants were excluded. There were no significant differences between the two groups in terms of birth weight, gender, mode of childbirth, gestational age, Silverman respiratory distress score before treatment, and receiving steroids before childbirth (P>0.05) (Tables 1 and 2).

Relative frequency of complications such as disseminated intravascular coagulation, death, pneumothorax, preterm retinopathy, and cerebral intraventricular hemorrhage (irrespective of severity) was significantly lower in INSURE group compared to mechanical ventilation group. In group 1, pulmonary hemorrhage, patent ductus arteriosus, and sepsis were less frequent, but not significantly different from mechanical ventilation group. Treatment failed in equal number of infants from the two groups (needed intubation and mechanical ventilation within 72 hours after extubation) (Table 3).

On average, breastfeeding of infants began on the fourth day in group 1 and on the fifth day in group 2, with no significant difference between them (P=0.06). Mean weight at discharge was 1709 grams in group 1 and 1754 grams in group 2, with no significant difference between the two groups (P=0.49). Mean duration of stay was 28 days in infants treated with INSURE method and 32 days in infants treated with mechanical ventilation, with no significant difference between the two groups (P=0.1).

Table 1: Distribution of study samples in terms of mean and standard deviation of some personal details in two groups

Variable	Mechanical ventilation Mean ± SD	INSURE Mean ± SD	P-value
Birth weight	1517.3±464	1535±489	0.83
Gestational age	30.1±2	30.9±2	0.07
Silverman respiratory distress score	5.8±1.1	5.2±1.2	0.23

Table 2: Distribution of relative and absolute frequencies in terms of some variables in two groups

Variable	Mechanical ventilation Mean ± SD	INSURE Mean ± SD	P-value
Receiving steroid before childbirth	25(41%)	27(45%)	0.71
Gender (female)	26(43%)	28(46%)	0.71
Childbirth mode (cesarean)	60(100%)	60(100%)	>0.05
Bovine surfactant (SURVENTA)	29(48%)	30(50%)	0.85
Swine surfactant (KRASTEV)	31(51%)	30(50%)	

Table 3: Distribution of relative and absolute frequencies in terms of prematurity complications in two groups

Preterm complications	Mechanical ventilation Number (%)	INSURE Number (%)	P-value
Cerebral intraventricular hemorrhage	25(41.6%)	12(20%)	0.01
Retinopathy	28(46.6%)	17(28.3%)	0.03
Pneumothorax	13(21.6%)	1(1.6%)	0.001
Death	13(21.6%)	4(6.6%)	0.01
Disseminated intravascular coagulation	5(8.3%)	0(0%)	0.01
Patent ductus arteriosus	14(23.3%)	9(15%)	0.24
Pulmonary hemorrhage	5(8.3%)	3(5%)	0.4
Sepsis	6(10%)	3(5%)	0.29
Treatment failure	6(10%)	3(5%)	1

Discussion

Irrespective of statistical significance, compared to mechanical ventilation group, infants in INSURE group had fewer prematurity complications such as retinopathy, pulmonary hemorrhage, pneumothorax, sepsis, patent ductus arteriosus, disseminated intravascular coagulation, cerebral intraventricular hemorrhage, and death, and also their first breastfeeding time and duration of stay were shorter.

In agreement with the present study, Dani et al. showed that if preterm infants of less than 30 weeks of gestation with respiratory distress that need mechanical ventilation immediately undergo INSURE treatment compared to intubated infants connected to mechanical ventilator will have better treatment outcomes including shorter stay, and reduced incidence of nosocomial infections and pneumothorax. Unlike the present study, in Cherif et al. study conducted on 109 preterm infants of 27-34 weeks of gestation, no significant difference was observed between the two groups in terms of incidence of pneumothorax, cerebral intraventricular hemorrhage, or preterm retinopathy, but death, patent ductus arteriosus were higher in the group with failed INSURE treatment that received mechanical ventilation (25). In a study by Huang et al., infants treated with INSURE and mechanical ventilation methods were compared, and no significant difference was found between the two methods in terms of complications such as pneumothorax, cerebral intraventricular hemorrhage, or pulmonary hemorrhage

(P>0.05), and in terms of incidence of pulmonary hemorrhage, their results agreed with those of the present study (26). Kirsten et al. compared survival of infants with very low birth weight (less than 1000 grams) treated with INSURE and mechanical ventilation methods. Contrary to the opinion regarding safety and advantages of INSURE method, survival of infants that only received respiratory support was significantly higher compared to those that were treated with surfactant (80% V 63.4%) (P=0.008) (27). Since intubation is highly stressful for infants that may have undesirable physiological responses (21), and may be risky for highly vulnerable infants; this may be considered as one of the reasons for higher mortality rate of infants treated with INSURE rather than mechanical ventilation. A study by Gharehbaghi et al. also revealed that failure of surfactant administration through INSURE is highly likely in preterm infants with low gestational age and birth weight and higher respiratory distress score (28). Li et al. considered rising arterial carbon dioxide pressure and low ratio of arterial oxygen pressure to inhaled oxygen pressure among factors causing failure in INSURE in preterm infants (29). It seems that safe use of this method in infants with very low birth weight requires further studies. Infant mortality rates in INSURE and mechanical ventilation methods was 14.3%, 28.6% in Nayeri et al. study (30), and 6.6% and 21.6% in the present study respectively, while sample size in the present study was almost three times that in their study. In their study, the incidence of patent ductus arteriosus and cerebral intraventricular hemorrhage in mechanical ventilation group was significantly higher compared to INSURE group (P=0.01 and 0.001 respectively), but no significant difference was observed between the two groups in terms of pneumothorax (P=0.25). This treatment method was up to 90% successful in the present study, 57% in Amit et al., 74% in Naseh et al., 91% in Dani et al., and 76.2% in Nayeri et al. (6, 17, 19 & 30).

In the present study, only short-term complications during stay were compared, which is among study limitations. It is recommended that other complications caused by INSURE or mechanical ventilation methods in infants with respiratory distress be studied. Another study limitation was the use of available data.

Conclusion

Generally, the present study showed that for preterm infants with respiratory distress requiring substitute surfactant, INSURE is a safer method compared to mechanical ventilation in terms of short-term complications, and reduces the risks caused by prolonged mechanical ventilation of infants in NICU. Furthermore, since mean duration of stay in the INSURE group was 4 days shorter compared to mechanical ventilation group, this method can also be beneficial in terms of reducing hospital costs.

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Conflict of interest

The Authors declare that there is no conflict of interest in this paper.

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