THE EFFICACY AND SAFETY OF SURFACTANT THERAPY IN PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME: CASE CONTROL OBSERVATIONAL STUDY

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ABSTRACT

Background: Respiratory distress syndrome (RDS) is the main cause of respiratory failure in preterm neonates and its incidence differs depending on gestational age and birth weight. The use of surfactant therapy has greatly reduced mortality from RDS; however, some authors have concluded no significant change in the outcome of preterm infants with RDS when treated with surfactant. The lack of consensus about the efficacy and safety of surfactant therapy for treatment of preterm infants provided the rationale for planning and conduction of the current study.

Aim of the study: To compare the outcome of preterm infants with RDS receiving surfactant therapy with group of preterm infants having RDS but did not receive surfactant therapy.

Patients and methods: In this hospital based cases control observational study, in order to evaluate the role of surfactant therapy in preterm infants with respiratory distress syndrome, via evaluation of preterm infants (26 to 36 weeks gestation) with clinical and radiological proof of having RDS. At the end of study we were able to include 114 cases and 114 controls. The control patients represented those preterm infants who unfortunately did not receive surfactant therapy because of unavailability of that medication at some periods. The study started on February the 1st 2019 and ended at September the 1st 2019.

Results: The outcome of patients was classified into good “the neonate is discharged well and tolerate oral feeding” and poor “the neonate died because of respiratory failure”. Regarding study group, following surfactant therapy in addition to O2 the outcome was as following: 92 patients out of 114 showed good outcome accounting for 80.7 %; whereas, 22 patients out of 114 showed poor outcome accounting for 19.3 %. While, Regarding control group, following O2 therapy the outcome was as following: 44 patients out of 114 showed good outcome accounting for 38.6 %; whereas, 70 patients out of 114 showed poor outcome accounting for 61.4 %. Therefore, good outcome was more frequently associated with surfactant therapy, 80.7 % versus 38.6 % and the difference was highly significant (P< 0.001)

Conclusion: Surfactant therapy is an effective mode of therapy leading to significant reduction in poor outcome in preterm infants with RDS with negligible adverse effects.

KEYWORDS: surfactant therapy; preterm infants; respiratory distress syndrome: Case control.

I. INTRODUCTION

Preterm labor is parturition that occurs when birth occurs between 20 0/7 weeks of gestation and 36 6/7 weeks. It further categorizes into early and late preterm. Early preterm is when the baby is born before 33 weeks, and late preterm is when a baby is born between 34 and 36 weeks (American College of Obstetricians and Gynecologists’ Committee on Practice Bulletins—Obstetrics, 2016).

Table 1. Risk factors for preterm birth (Oskovi Kaplan et al., 2018)

| Maternal characteristics
| Family history of preterm birth

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Respiratory distress syndrome

Respiratory distress syndrome (RDS) is the main cause of respiratory failure in preterm neonates and its incidence differs depending on gestational age and birth weight. RDS was originally known as “hyaline membrane disease”, based on its histological appearance and re-named RDS after the acceptance that it was caused by primary surfactant deficiency (Tridente et al., 2019).

Predisposing and risk factors

Among the long list of recognized risk factors, the following are the principal predisposing factors (Wang et al., 2015):

- Maternal age > 30
- Gestational diabetes mellitus
- Cesarean section
- Parity > 2
- Placental abnormalities
- Male infant
- Premature rupture of membrane
- Low Apgar score

Clinical features

Thorough clinical assessment of the newborn infant is the most important aspect of accurately diagnosing the underlying respiratory condition. An infant with breathing difficulties displays classic clinical signs of respiratory distress regardless of the underlying cause. These consist of tachypnoea (respiratory rate >60 breaths-min⁻¹),
tachycardia (heart rate >160 beats·min$^{-1}$), nasal flaring, grunting, chest wall recessions (suprasternal, intercostal and subcostal), cyanosis and apnoea. (Gallacher et al., 2016).

**Surfactant replacement therapy**

**Surfactant production**

Pulmonary surfactant is a complex mixture of phospholipids (PL) and proteins (SP) that reduce surface tension at the air-liquid interface of the alveolus, thus preventing its collapse during end-exhalation. It also participates in innate host defense against inhaled pathogens. Surfactant is synthesized and secreted by Type II alveolar epithelial cells, also called pneumocytes, which differentiate between 24 and 34 weeks of gestation in the human. It is made up of 70% to 80% phospholipids, approximately 10% protein and 10% neutral lipids, mainly cholesterol (Nkadi et al., 2009).

**Contraindication** (Walsh et al., 2013)

Relative contraindications to surfactant administration are:

- The presence of congenital anomalies incompatible with life beyond the neonatal period
- Respiratory distress in infants with laboratory evidence of lung maturity
- Diagnosis of congenital diaphragmatic hernia
- Patient hemodynamically unstable
- Active pulmonary hemorrhage

**Complications** (Walsh et al., 2013)

**Procedural complications resulting from the administration of surfactant**

- plugging of endotracheal tube (ETT) by surfactant
- hemoglobin desaturation and increased need for supplemental O2
- bradycardia due to hypoxia
- tachycardia due to agitation, with reflux of surfactant into the ETT
- pharyngeal deposition of surfactant
- administration of surfactant to only one lung (ie, right mainstem intubation)
- administration of suboptimal dose

**Physiologic complications of surfactant replacement therapy**

- Apnea
- pulmonary hemorrhage from right to left shunting
- increased necessity for treatment for patent ductus arteriosus
- marginal increase in retinopathy of prematurity
- volutrauma resulting from increase in lung compliance following surfactant replacement and failure to change ventilator settings accordingly

**Assessment surfactant need**

- Reduction in FIO2 requirement
- Reduction in work of breathing
• Improvement in aeration, as indicated by chest radiograph
• Improvement in pulmonary mechanics (compliance, airways resistance) and lung volume (functional residual capacity)
• Reduction in ventilator support (peak inspiratory pressure, PEEP, airway pressure)
• Improvement in ratio of arterial to alveolar PO2 and oxygen index

II. AIM OF STUDY
The aim of the current study is to compare the outcome of preterm infants with RDS receiving surfactant therapy with group of preterm infants having RDS but did not receive surfactant therapy.

III. PATIENT AND METHODS
Study design and sample size
this study, in order to evaluate the role of surfactant therapy in preterm infants with respiratory distress syndrome, via evaluation of preterm infants (26 to 36 weeks gestation) with clinical and radiological proof of having RDS. At the end of study we were able to include 114 cases and 114 controls. The control patients represented those preterm infants who unfortunately did not receive surfactant therapy because of unavailability of that medication at some periods. The study started on February the 1st 2019 and ended at September the 1st 2019.

The study was carried out at the intensive neonatal care unit (INCU) of Al-Diwaniyah maternity and children teaching hospital in Al-Diwnaiyah province/ Iraq.

Inclusion criteria
Preterm infants (26 to 36 weeks gestation) with clinical and radiological proof of having RDS.

Exclusion criteria
Multiple congenital anomalies
Congenital heart disease

Variables under investigation
The following variables were included in the questionnaire form: gestational age, birth weight, gender, mode of delivery, antenatal steroid administration, need for mechanical ventilation, surfactant therapy (2nd dose administration and clinical indications).

Ethical consideration
The study was approved by the institutional ethical approval committee and formal agreement was obtained from the directorate of Health in Al-Diwaniyah province, the formal representative of Iraqi Ministry of health.

Verbal consent was obtained from each parent after full illustration of the aim and procedures related to the current study.

Questionnaire form
A questionnaire form was established depending on information obtained from reviewing published articles and consultation specialists dealing with pediatrics. The questionnaire form is shown in appendix I.

Diagnosis of prematurity and RDS
Clinical evidence for RDS include: tachypnea > 60 breaths/min, prominent grunting, shallow breathing, intercostals and subcostal recessions, nasal flaring and cyanosis; while radiological evidence include: reticulgranular appearance and airbronchogram.

Assessment of gestational age in our study according to:

1. Calculation of gestational age according to LMP
2. perinatal ultrasound.

3. Ballard score.

Ballard scoring system: in which estimation of gestational age by physical examination by assessment of physical and neurological criteria of prematurity, this scoring system is accurate to ± 2 weeks (Lee et al., 2016).

**Surfactant replacement therapy**

For all patients the source of surfactant was Animal-derived Beractant minced bovine lung extract. SURVANTA® (beractant) Intratracheal Suspension is a sterile, non-pyrogenic pulmonary surfactant intended for intratracheal use only. It is a natural bovine lung extract containing phospholipids, neutral lipids, fatty acids, and surfactant-associated proteins (dipalmitoylphosphatidylcholine), palmitic acid, and tripalmitin are added to standarize the composition and to mimic surface-tension lowering properties of natural lung surfactant. The resulting composition provides 25 mg/mL phospholipids (including 11.0-15.5 mg/mL disaturatedphosphatidylcholine), 0.5-1.75 mg/mL triglycerides, 1.4-3.5 mg/mL free fatty acids, and less than 1.0 mg/mL protein.

**Procedure:**

The procedure must be done under aseptic conditions, keep the infant warm under radiant warmer with cardiorespiratory monitor, calculated the exact dose was according to body weight(100mg/kg), then intubated with appropriate size ETT and the ordered dose of surfactant was given followed by manual ventilation using ambu bag connected to oxygen source, after that, we put the infant according to his condition on CPAP or mechanical ventilator followed by chest x-ray monitor (4-6 hours), suction should be avoided till after 2 hours after administration of surfactant.

To ensure homogenous distribution of SURVANTA throughout the lungs, each dose is divided into four quarter-doses.

Each quarter-dose is administered with the infant in a different position. The recommended positions are:

Head and body inclined 5-10° down, head turned to the right

Head and body inclined 5-10° down, head turned to the left

Head and body inclined 5-10° up, head turned to the right

Head and body inclined 5-10° up, head turned to the left

**Neonatal monitoring**

Included the following: vital signs, chest wall movements and breath sounds, oxygen saturation by pulse oximetry, position of patient, proper placement and position of ETT, reflux of surfactant into ETT, setting of CPAP or mechanical ventilator, blood gas analysis, and serial chest x-ray monitoring.

**Assessment of outcome**

Assessment of short term outcome of involved preterm infants during their hospital stay in NICUs (within 1st 30 days of life); including:

1. Assessment of response to treatment by:
   - Reduction in work of breath
   - Improvement in aeration, as indicated by chest radiograph
   - Reduction in FiO2 requirements
   - Reduction in ventilation support (peak inspiratory pressure, PEEP, airway pressure)
Assessments of neonatal mortality and morbidity and development of complications following replacement therapy in both studied groups; as pulmonary hemorrhage, air leak, BPD and IVH.

IV. STATISTICAL ANALYSIS

Data were collected and transformed into a spreadsheet of Microsoft Office Excel 2010 and then into an SPSS (statistical package for social sciences) version 23. Numeric quantitative data were expressed as mean, range and standard deviation (SD), whereas, qualitative data were expressed as number and percentage. Comparison of mean between any two groups was done according to independent sample t-test, while chi-square test was used to evaluate association between any two categorical variables. The level of significance was considered at $P \leq 0.05$.

Limitation of study

The most important limitation was the short time period.

V. RESULTS

General characteristics of patients enrolled in the present study

The present study included 228 patients with respiratory distress syndrome (RDS) who were chosen in such a way that 114 patients has received surfactant therapy, serving as a study group, and 114 patients received no surfactant therapy because of unavailability of this therapy at some periods, serving as a control group. The characteristics of those patients are demonstrated in Table 3.1.

Table 2. The characteristics of patients enrolled in the current study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study group $n = 114$</th>
<th>Control group $n = 114$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (week)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>31.53 ±2.05</td>
<td>31.70 ±1.44</td>
<td>0.597 NS</td>
</tr>
<tr>
<td>Range</td>
<td>26 -36</td>
<td>26 -36</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, $n$ (%)</td>
<td>60 (52.6 %)</td>
<td>54 (47.4 %)</td>
<td>0.574 NS</td>
</tr>
<tr>
<td>Female, $n$ (%)</td>
<td>54 (47.4 %)</td>
<td>60 (52.6 %)</td>
<td></td>
</tr>
<tr>
<td>Mode of delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NVD, $n$ (%)</td>
<td>74 (64.9 %)</td>
<td>84 (73.7 %)</td>
<td>0.310 NS</td>
</tr>
<tr>
<td>CS, $n$ (%)</td>
<td>40 (35.1 %)</td>
<td>30 (26.3 %)</td>
<td></td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>1.75 ±0.29</td>
<td>1.73 ±0.24</td>
<td>0.627 NS</td>
</tr>
<tr>
<td>Range</td>
<td>0.8 -2.5</td>
<td>0.9 -2.5</td>
<td></td>
</tr>
</tbody>
</table>

NS: not significant at $P > 0.05$

There was no significant difference in mean gestational age between study and control groups ($P = 0.597$), 31.53 ±2.05 weeks versus 31.70 ±1.44 weeks, respectively, table 3.1. There was also no significant difference in the distribution of patients according to gender between study and control groups ($P = 0.574$), table 3.1. There was in addition no significant difference in the distribution of patients according to mode of delivery between study and control groups ($P = 0.301$), table 3.1. Moreover, there was no significant difference in mean weight between study and control groups ($P = 0.627$), 1.75 ±0.29 kg versus 1.73 ±0.24 kg, respectively, table 3.1.

Surfactant therapy

The characteristics of surfactant therapy are shown in table 3.2. Most of patients required half an hour duration of therapy and they accounted for 80 (70.2 %) cases.

Significant number of patients required one hour duration of therapy and they accounted for 32 (28.1 %), in addition, 2 patients required two hours duration of therapy, table 3.2. A single dose was sufficient in 84 (73.7 %) cases; however, 2 doses were required in 30 (26.3 %) cases, table 3.2. The mean $O_2$ saturation after surfactant therapy was 95.25 ±3.32 % with a range of 88 to 100 %, table 3.2. The improvement in $O_2$ saturation has been
shown in figure 3.1. The mean O2 saturation was improved from 83.56 ±4.50 % to 95.25 ±3.32 %. The difference was highly significant (P< 0.001) from statistical perspective, figure 1.

Complication in the form of apnea was encountered in 3 patients (2.6 %), table 3.2.

Table 3. Characteristics of surfactant therapy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of surfactant admin (h)</td>
<td></td>
</tr>
<tr>
<td>Half an hour, n (%)</td>
<td>80 (70.2 %)</td>
</tr>
<tr>
<td>One hour, n (%)</td>
<td>32 (28.1 %)</td>
</tr>
<tr>
<td>Two hours, n (%)</td>
<td>2 (1.8 %)</td>
</tr>
<tr>
<td>Number of doses</td>
<td></td>
</tr>
<tr>
<td>One, n (%)</td>
<td>84 (73.7 %)</td>
</tr>
<tr>
<td>Two, n (%)</td>
<td>30 (26.3 %)</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
</tr>
<tr>
<td>Apnea, n (%)</td>
<td>3 (2.6 %)</td>
</tr>
</tbody>
</table>

Figure 1. Bar chart showing mean O2 saturation % before and after surfactant therapy

Outcome following surfactant therapy

The outcome of patients was classified into good “the neonate is discharged well and tolerate oral feeding” and poor “the neonate died because of respiratory failure”.

Regarding study group, following surfactant therapy in addition to O2 the outcome was as following: 92 patients out of 114 showed good outcome accounting for 80.7 %; whereas, 22 patients out of 114 showed poor outcome accounting for 19.3 %; While, Regarding control group, following O2 therapy the outcome was as following: 44 patients out of 114 showed good outcome accounting for 38.6 %; whereas, 70 patients out of 114 showed poor outcome accounting for 61.4 %, as shown in table 3.3.

Therefore, good outcome was more frequently associated with surfactant therapy, 80.7 % versus 38.6 % and the difference was highly significant (P< 0.001), as shown in table 3.3.

Table 4. Comparison of neonatal outcome between study and control group

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study group n = 114</th>
<th>Control group n = 114</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>92 (80.7 %)</td>
<td>44 (38.6 %)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Poor</td>
<td>22 (19.3 %)</td>
<td>70 (61.4 %)</td>
<td>HS</td>
</tr>
</tbody>
</table>

¥: Chi-square test; HS: highly significant at P ≤ 0.01.
In order to evaluate possible predictors of outcome following surfactant therapy, characteristics of neonates, in the study group, with good outcome were contrasted to those of neonates with poor outcome and the results were outlined in table 3.

Regarding gestational age, infants with good outcome were older than infants with poor outcome, 31.76 ±2.07 weeks versus 30.55 ±1.69 weeks, but the difference did not reach statistical significance (P = 0.076), however, this level is very close to the significant level of 0.05 and can be considered borderline significant value. The mean birth weight was significantly higher in infants with good outcome in comparison with infants with poor outcome (P = 0.018), 1.79 ±0.29 kg versus 1.57 ±0.20 kg, table 4. There was no significant difference in mean initial O₂ saturation between infants with good outcome and infants with poor outcome (P = 0.295), 83.87 ±4.78 % versus 82.27 ±2.90 %, table 4.

Table 3.4: Predictors of outcome following surfactant therapy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Statistic</th>
<th>Good outcome n = 92</th>
<th>Poor outcome n = 22</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (weeks)</td>
<td>Mean ±SD</td>
<td>31.76 ±2.07</td>
<td>30.55 ±1.69</td>
<td>0.076 †</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>Mean ±SD</td>
<td>1.79 ±0.29</td>
<td>1.57 ±0.20</td>
<td>0.018 †</td>
</tr>
<tr>
<td>O₂ Saturation (%)</td>
<td>Mean ±SD</td>
<td>83.87 ±4.78</td>
<td>82.27 ±2.90</td>
<td>0.295 †</td>
</tr>
<tr>
<td>Gender</td>
<td>n (%)</td>
<td>44 (47.8 %)</td>
<td>16 (72.7 %)</td>
<td>0.036 ¥</td>
</tr>
<tr>
<td>Male</td>
<td>n (%)</td>
<td>48 (52.2 %)</td>
<td>6 (27.3 %)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>n (%)</td>
<td>58 (63.0 %)</td>
<td>16 (72.7 %)</td>
<td>0.800 y</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>n (%)</td>
<td>34 (37.0 %)</td>
<td>6 (27.3 %)</td>
<td>NS</td>
</tr>
<tr>
<td>NVD</td>
<td>n (%)</td>
<td>60 (65.2 %)</td>
<td>20 (90.9 %)</td>
<td>0.012 ¥</td>
</tr>
<tr>
<td>CS</td>
<td>n (%)</td>
<td>32 (34.8 %)</td>
<td>0 (0.0 %)</td>
<td>S</td>
</tr>
<tr>
<td>Antenatal steroids</td>
<td>n (%)</td>
<td>28 (30.4 %)</td>
<td>0 (0.0 %)</td>
<td>0.049 f</td>
</tr>
<tr>
<td>Yes</td>
<td>n (%)</td>
<td>64 (69.6 %)</td>
<td>22 (100.0 %)</td>
<td>S</td>
</tr>
<tr>
<td>No</td>
<td>n (%)</td>
<td>60 (65.2 %)</td>
<td>20 (90.9 %)</td>
<td></td>
</tr>
<tr>
<td>Time of surfactant admin (h)</td>
<td>n (%)</td>
<td>32 (34.8 %)</td>
<td>0 (0.0 %)</td>
<td></td>
</tr>
<tr>
<td>1-2 hours</td>
<td>n (%)</td>
<td>0 (0.0 %)</td>
<td>2 (9.1 %)</td>
<td></td>
</tr>
<tr>
<td>Number of doses</td>
<td>n (%)</td>
<td>74 (80.4 %)</td>
<td>10 (45.5 %)</td>
<td>0.047 y</td>
</tr>
<tr>
<td>One</td>
<td>n (%)</td>
<td>18 (19.6 %)</td>
<td>12 (54.5 %)</td>
<td></td>
</tr>
<tr>
<td>Two</td>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Proportion of male gender was higher in those with poor outcome in comparison with female with poor outcome, 72.2 % versus 27.3 %; the difference was statistically significant (P = 0.036). There was no significant association between mode of delivery and outcome (P = 0.800), table 3.4. The use of antenatal steroid (two doses of Betamethasone 12mg IM at 24hr interval) was significantly associated with good outcome (P = 0.049), table 3.4. The duration of surfactant therapy significantly affected outcome in such a way that half an hour therapy resulted in proportionally more good outcome than poor outcome; whereas, one hour therapy resulted in only good outcome. Single dose was associated with significantly good outcome than 2 doses, 80.4 % versus 45.5 % (P = 0.049), table 3.4.

VI. DISCUSSION

General characteristics of patients enrolled in the present study
In the current study, complication in the form of apnea has been recorded in a minority of neonates (3) in
hospital/neonatal mortality of neonates with RDS admitted in two time periods—before and after introduction
of SRT (Ho and Chang, 2007; Verhagen et al., 2002; Barriaet al., 2008; Prigenzi et al., 2008; Fustinanaet al., 2009).
these studies reported a significant reduction in mortality between the two time periods. One study from South

In the present study, there was no significant difference in mean gestational age between study and control, a
finding that eliminated any possible bias in the outcome that can be attributed to gestational age. Similarly, there
was also no significant difference in the distribution of patients according to gender, mode of delivery and history
of antenatal care, providing statistical matching between study and control group leading to avoidance of bias in
the primary outcome related to these factors. Furthermore, in the present study, there was no significant
difference in mean weight between study and control groups, thereby avoiding effect of a confounding variable
other than surfactant therapy, and this finding was similar to findings of other authors such as (Barriaet al., 2008;
Prigenzi et al., 2008; Fustinanaet al., 2009).

Surfactant therapy
In the present study, most of patients received the dose of surfactant therapy within half an hour duration of
delivery and they accounted for 80 (70.2 %) cases; however, significant number of patients have received
surfactant one hour after delivery and they accounted for 32 (28.1 %), in addition, two patients have been given
the treatment two hours after delivery. It has been stated that for infants intubated immediately after birth, it is
recommended that surfactant be given as early treatment (<2 h of age) (Nouraeyan et al., 2014); therefore, all
preterm infants in the current study have received surfactant within the recommended period after birth and this
is similar to the trend of other studies such as (Nouraeyan et al., 2014; Soll and Ozek 2009).

In the present study, a single dose was sufficient in 84 (73.7 %) cases; however, 2 doses were required in 30 (26.3
%) cases. Soll and Ozek (2009) in a systematic review looking into the issue of multiple doses vs. a single dose,
reported that the repeated dosing schedule showed further reduction in the risk of pneumothoraces with a trend
ward reduction in mortality. However, there is no much additional benefit from repeating doses beyond two
times. Therefore, in the current study, the maximum number of recommended doses according to (Soll and Ozek,
2009) was not exceeded.

In the current study, the mean O2 saturation after surfactant therapy was 95.25 ±3.32 % with a range of 88 to 100
% and the mean O2 saturation was 83.56 ±4.50 % with a range of 79 to 86 % before surfactant therapy and the
difference was highly significant. Wang et al., 2012; Cai et al., 2012; change in oxygen level reflected the
beneficial effect of surfactant in improving lung function and have significant reduction in poor outcome.

In the current study, complication in the form of apnea has been recorded in a minority of neonates (3) in
association with surfactant administration. 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. 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 (Nouraeyan et al., 2014), and
this was the same as shown by other studies (Barria et al., 2008; Prigenzi et al., 2008; Fustinana et al., 2009).

Outcome following surfactant therapy
In the current study mortality rate has been significantly reduced following using surfactant therapy in preterm
infants with RDS.

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Africa, which compared the mortality of neonates born between 1991 and 1992 with those born between 1989 and June 1991, did not report any difference (Ballot et al., 1995). However, surfactant was administered only in severe RDS with a high FiO2 requirement in the former period.

It has been shown in the current study that infants with good outcome were older than infants with poor outcome, but the difference did not reach statistical significance. However, the mean birth weight was significantly higher in infants with good outcome in comparison with infants with poor outcome. Consistent with the current study findings, previous studies have shown that mortality rate among preterm infant with RDS was highest among lower birth weight and lower gestational age infant (Vermont Oxford Network Nightingale Database, 2012; Trembath et al., 2013).

In the current study, there was no significant difference in mean initial O2 saturation between infants with good outcome and infants with poor outcome. In the current study also, the proportion of male gender was significantly higher in those with poor outcome in comparison with female with poor outcome, 72.2 % versus 27.3 %. In accordance with current study, Chen et al., (2018) stated that male are significantly more prone to poor outcome than females neonates “Female infants were more sensitive to surfactant treatment than males”; they attributed that to lower lung compliance in males than in females, and that this difference may result from sex differences in surfactant phospholipid composition and function.

Besides, in the present study, there was no significant association between mode of delivery and outcome. However, it has been shown by previous authors that cesarean section is associated with significantly poor outcome in comparison with NVD (Liu et al., 2014); the reason may be there is less activity of amiloride-sensitive sodium channels in alveolar epithelial cells following cesarean section, leading to reduced fluid clearance (Liu et al., 2014).

In the current study in addition, the duration of surfactant therapy significantly affected outcome in such a way that 1-30min therapy resulted in proportionally more good outcome than poor outcome; whereas, 30-60min therapy resulted in only good outcome. It has been stated that for infants intubated immediately after birth, it is recommended that surfactant be given as early treatment (<2 h of age) (Nouraeyan et al., 2014); therefore, all preterm infants in the current study have received surfactant within the recommended period after birth.

In contrast to the present study, Wang et al., in 2015 found that among newborn infants who were diagnosed with RDS, preterm babies < 35 weeks of gestational age had a better response to surfactant treatment than near-term and term babies. The reason for this discrepancy is the inclusion of term infants with RDS in the study of Wang et al. and those children may have other cause of respiratory failure other than surfactant deficiency such as bronchopulmonary dysplasia.

In the current study also, the use of antenatal steroid was significantly associated with good outcome. Large cohort studies indicate that the combination of surfactant and steroids is more effective than exogenous surfactant alone (Chien et al., 2002). A secondary analysis of data from surfactant trials also indicates a reduction in disease severity in babies who received antenatal steroids (Farrell et al., 1989). Two other RCTs (Kari et al., 1994; Sliver et al., 1996) have confirmed that antenatal steroids continue to reduce the risk of poor outcome, even in centres where surfactant is available; one (Costakos et al., 1996) showed a reduction in RDS as well as an increase in survival without ventilatory support and both showed significant reductions in severe intraventricular hemorrhage.

In the current study, single dose was associated with significantly good outcome than 2 doses. This is in accordance with Tsakalidis et al. (2012) who reported that premature infants treated with a single dose of surfactant could usually be successfully extubated. The requirements for retreatment could be attributed to other pathogenic mechanisms (Tsakalidis et al., 2012).

VII. CONCLUSIONS

1. The use of surfactant therapy in preterm infants significantly improves outcome through significant reduction in poor outcome.

2. The use of surfactant therapy in preterm infants is efficient and safe since it is associated with no recognizable adverse effects.
The outcome of surfactant therapy is greatly affected by preterm baby gestational age, birth weight and previous antenatal steroid therapy.

VIII. RECOMMENDATIONS

1 Larger sample size, multicentre study is recommended in order to validate the results of the current study.

2 It is recommended to treat preterm infants with RDS with surfactant therapy as early as possible since delay in treatment may increase risk of mortality.

3 It is recommended to give antenatal steroid to all women at risk of having a preterm baby in order to increase the beneficial effect associated with postnatal surfactant therapy.

REFERENCES


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