Experience of Surfactant Therapy and Outcome in Preterm neonates with Respiratory Distress Syndrome

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ABSTRACT
Background:
To share the experience and assess the outcome in preterm babies receiving surfactant as prophylactic and rescue therapy.

Methods:
Prospective hospital based observa-tional study conducted in the Neonatal intensive care unit of Manipal Teaching Hospital, Pokhara Nepal, and study period was from 1st January 2015 to 31st December 2017. Surfactant was administered to preterm babies less than 37 weeks with the diagnosis of respiratory distress syndrome.

Results:
A total of 40 newborns received surfactant of which 19 neonates received prophylactic whereas 21 received rescue therapy .The mean gestation (weeks) was 30.68±1.974 in prophylactic and 32±2.168 in rescue therapy groups. Mean Birth weight in prophylactic group was 1302.26 ±253.15 grams and 1455.24±344 grams in rescue group. Complications of surfactant adminis-tration were noted in 25(62.5%) neonates. Desaturation 13 (52%) and bradycardia 5(20%) were common complications during surfactant administration. Mean hospital stay was 14.26±7.56 (days) in prophylactic and 12.52±7.16 (days) in rescue groups (p value 0.46).Difference in duration of continuous positive airway pressure, ventilations, oxygen, requirement of inotropes were also not statically significant.

Conclusions:
Rescue surfactant therapy was found to be as effective as prophylactic therapy in preterm babies with respiratory distress syndrome.

Key words: Hyaline membrane disease, Newborn, Pulmonary Surfactants.

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INTRODUCTION
Respiratory distress syndrome (RDS) is an important cause of morbidity and mortality in newborn infants especially those born prematurely. Surfactant replacement has been established as an effective and safe treatment modality in premature neonates since early 1990s. Surfactant administration improves respiratory status, decreases ventilator requirement, hospital stay and over all outcome. Subsequent trials have indicated that prophylactic or early administration of surfactant resulted in fewer pneumothoraces, less pulmonary interstitial emphysema and improved survival without bronchopulmonary dysplasia (BPD). However, other recent studies have found the
benefit of prophylactic surfactant is no longer evident in group of infants when continuous positive airway pressure (CPAP) is used routinely.

There is limited information about experience of surfactant use in our part of the world. The study aims to share the experience and outcome of surfactant in preterm babies and to know the advantages of prophylactic over rescue therapy in RDS.

MATERIALS AND METHODS

This study was a prospective hospital based observational study conducted in the neonatal intensive care unit (NICU) of Manipal Teaching Hospital, Pokhara, Nepal which is a 22 bedded NICU with three ventilators and four continuous positive airway pressure (CPAP) machines. The study period was from 1st January 2015 to 31st December 2017. All the neonates less than 37 weeks who received surfactant during the study period were eligible for the study. Newborns with major congenital anomalies, hemodynamically unstable neonates and parental refusal for the administration of surfactant were excluded from the study.

Bovine surfactant was administered to preterm neonates less than 37 weeks with the diagnosis of RDS. Diagnosis of RDS was established on the basis of clinical features along with chest radiography. Surfactant was administered in two or four divided doses through nasogastric tube after endotracheal intubation. Neonate was put on supine, right lateral and left lateral position with slight head elevation after that bag and mask ventilation was given to spread surfactant over alveoli. Dose of administration was 4 ml/kg body weight. Prophylactic use is indicated in neonates less than 32 weeks and as soon as birth till 6 hours of life and rescue therapy for all neonates with the diagnosis of RDS up to the 72 hours of life.

Approval for the research was obtained from the institutional review committee (IRC) of Manipal Teaching Hospital. Written consent was taken from the parents prior to the commencement of the study. Demographic parameters and maternal details were recorded in a preformed Performa. Timing of surfactant administration in hours, duration of oxygen administration, CPAP and ventilator support and duration of hospital stay were also recorded. Administration of prophylactic as well as rescue therapy was recorded. Complications of surfactant adminis-tration and final outcome i.e. discharge; death, referral and left against medical advice were noted. Data analysis was done using SPSS version 16. Continuous data was recorded as mean± S.D. and categorical variables as number and percentage. Chi square and independent ‘t’ test were used as appropriate. Level of significance was taken as 0.05.

RESULTS

Out of 40 newborns who met our inclusion criteria, 19 neonates received prophylactic therapy whereas 21 received rescue therapy. The mean gestation (weeks) was 30.68±1.974 in prophylactic and 32±2.168 in rescue group. There was no statistical difference in between the group (p value - 0.217). Mean birth weight in prophylactic group was 1302.26±253.15 grams and 1455.24±344.636 in rescue group (p value - 0.520) as shown on Table 1.

Out of 40 neonates only 17 preterm mothers received antenatal steroid therapy to prevent hyaline membrane disease. On prophylactic 10(52.63%) and rescue 7(33.33%) neonate mother received steroid that's also not significant. Regarding the hospital stay it was 2 days higher in prophylactic as compared to rescue as mean hospital stay was 14.26±7.56 (days) in prophylactic and 12.52±7.16 (days) in rescue group (p=0.46) since premature and low birth babies were more included in prophylactic group.

Table 1: Demographics characteristics of enrolled newborns

<table>
<thead>
<tr>
<th></th>
<th>Prophylactic n(%)</th>
<th>Rescue n(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>19(47.5%)</td>
<td>21(52.5%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11(57.89%)</td>
<td>12(57.1%)</td>
<td>0.962</td>
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<tr>
<td>Female</td>
<td>8(42.10%)</td>
<td>9(42.85%)</td>
<td></td>
</tr>
<tr>
<td>Gestation(Weeks)</td>
<td>30.68±1.974</td>
<td>32±2.168</td>
<td>0.217</td>
</tr>
<tr>
<td>Birth weight(Grams)</td>
<td>1302.26±253.15</td>
<td>1455.24±344.636</td>
<td>0.520</td>
</tr>
<tr>
<td>Apgar 1 min</td>
<td>6±1.247</td>
<td>5.81±1.778</td>
<td>0.535</td>
</tr>
<tr>
<td>Apgar 5 min</td>
<td>7.63±1.116</td>
<td>7.86±1.424</td>
<td>0.258</td>
</tr>
<tr>
<td>Antenatal steroid</td>
<td>10(52.63%)</td>
<td>7(33.33%)</td>
<td>0.218</td>
</tr>
<tr>
<td>Antepartum Hemorrhage</td>
<td>0</td>
<td>3</td>
<td>(0.043)</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>7(36.84%)</td>
<td>29(52.5%)</td>
<td>0.039</td>
</tr>
<tr>
<td>PROM</td>
<td>5(26.31%)</td>
<td>5(23.80%)</td>
<td>0.885</td>
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</table>
Mean duration of ventilation and oxygen was also not statistically significant in this group.

**Table 2: Outcome variables in prophylactic and rescue therapy groups**

<table>
<thead>
<tr>
<th></th>
<th>Prophylactic</th>
<th>Rescue</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>19 (47.5%)</td>
<td>21 (52.5%)</td>
<td></td>
</tr>
<tr>
<td>Hospital stay days</td>
<td>14.26±7.56</td>
<td>12.52±7.16</td>
<td>0.46</td>
</tr>
<tr>
<td>CPAP days</td>
<td>3.00±1.79</td>
<td>3.14±2.1</td>
<td>0.82</td>
</tr>
<tr>
<td>Ventilation days</td>
<td>0.89±1.56</td>
<td>0.57±9.26</td>
<td>0.425</td>
</tr>
<tr>
<td>Oxygen days</td>
<td>4.58±2.85</td>
<td>3.95±2.41</td>
<td>0.457</td>
</tr>
<tr>
<td>Required inotropes</td>
<td>6 (31.6%)</td>
<td>4 (19.0%)</td>
<td>0.381</td>
</tr>
<tr>
<td>Discharged (Good outcome)</td>
<td>13 (68.4%)</td>
<td>11 (52.4%)</td>
<td>0.301</td>
</tr>
<tr>
<td>Bad outcome</td>
<td>6 (31.6%)</td>
<td>10 (47.6)</td>
<td></td>
</tr>
<tr>
<td>Complications</td>
<td>12 (63.15%)</td>
<td>13 (62.0%)</td>
<td>0.935</td>
</tr>
</tbody>
</table>

Complications were seen in 25 (62.5%) neonates, 12 (48%) neonates from prophylactic and 13 (52%) from rescue group. Complications included desaturation in 13 (52%), bradycardia 5 (20%), PDA 3 (12%), seizure 3 (12%) and pulmonary hemorrhage in 1 (4%) as shown in Fig. 1.

**DISCUSSION**

World health organization (WHO) has estimated around 1.1 million preterm neonatal deaths every year. Many clinical trials carried out in the 1980s and 1990s to decrease the mortality of preterm babies found surfactant use as one of the strategies to reduce mortality and complication.8-9

Randomized controlled trials have shown that surfactant therapy in RDS results in overall 40% reduction in morality and 35-50% reduction in air leak.10-12 Few countries like Kuwait, South Africa, India and Iran have reported regarding the benefits of surfactant13-16 In our study 34 neonates were put on CPAP out of 40 so early use of CPAP along with surfactant may have reduced morbidity and mortality in neonates which is similar and comparable to others trial from different developed countries. Only 17 received antenatal steroids might be attributed most of the un-booked mothers present in the second stage of labor as well as preterm babies are referred from peripheral centers.

Cochrane review had shown surfactant along with CPAP may have reduced ventilation days and lower mortality in preterm neonates17-19 The most common morbidities seen in our study was desaturation accounting for 52.5%. Other complications seen were bradycardia, patent ductus arteriosus (PDA), seizure and one (4%) case of pulmonary hemorrhage. Researchers have shown medical morbidities such as intraventricular hemorrhage (IVH), necrotising enterocolitis (NEC), Patent Ductus Arteriosus (PDA) has not change with use of surfactant16 We have also noted PDA as complications similar to other findings but were unable to note long term complications like Broncho Pulmonary Dysplasia (BPD) and Retinopathy of Prematurity (ROP).

In our study difference in the overall outcome, duration of CPAP, ventilation, complications, hospital stay between prophylaxis and rescue surfactant group was statistical insignificant which is also similar to other meta-analysis studies (National Institute of child health and Human Development Support Trial and Vermont...
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Oxford Network) 6,21 Mean hospital stay was two days more in prophylactic group compared with rescue group which might be due to enrollment of more premature and less birth weight neonates in prophylactic group.

The mortality was 2 out of 40 neonates which account for 5% which in contrast to other studies where mortality is higher (21%-80%). 22-25 This could be as these were babies who got discharged on left against medical advice (LAMA) or were referred to other centers. We couldn't find out the numbers of mortality in those babies. All the NICU, surfactant expenses had to be borne by the patient party so that may be also the factor for LAMA and refusal for further treatment. Antenatal steroid administration has not shown significant in prophylactic and rescue therapy in morbidity which is also similar to other studies 26 The results have shown that the mortality was very low among study subject and majority of them improved and got discharged. This is similar to the study conducted by Suresh and Soll (2005) 27 in 23 and 34 weeks gestational aged premature neonates. Sankar et al., (2016) 28 however found no difference in the risk of mortality in their randomized control trial. Higher mean gestation (weeks) is 30.68±1.974 and 32±2.168 and birth weight is 1302.26±253.15 grams and 1455.24±344.636 on prophylactic and rescue therapy respectively which is also one of the factor contributing better outcome.

CONCLUSION
Our study does not show the added benefit of early administration of surfactant in the prognosis of premature neonates compared with rescue surfactant replacement therapy. Small sample size, lack of follow up and new borns were not randomized were the potential limitation of our study. In future large scale, prospective and randomized controlled trial studies might be beneficial. Significant cost of surfactant procurement is also the concern for developing countries.

REFERENCES
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