Original Article

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Outcome of Surfactant Replacement Therapy for Respiratory Distress syndrome in Preterm babies

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Abstract

Introduction: Surfactant is an important treatment modality in preterm babies with respiratory distress syndrome leading to decrease in mortality, morbidity and cost of treatment. Experiences on surfactant therapy in Nepal are scarce. This study was conceptualised to find the use and immediate outcome of surfactant therapy in preterm babies in a tertiary care hospital in Nepal.

Methods: A cross-sectional study was done in preterm babies who received surfactant over period of five years at neonatal / pediatric intensive care unit at Patan Hospital, Lalitpur, Nepal. After approval from Institutional review committee, information on gestational age, sex, birth weight, doses of dexamethasone, doses and time surfactant delivery, complications and immediate outcome was retrieved from the files. Comparison between early and late rescue group was done. Data was analysed using SPSS 16.

Results: Twelve babies (11.2%) needed a repeat dose of surfactant. Only 12 (11.2%) babies received early rescue surfactant. About 53 (49.5%) babies developed complications with hypotension being the most common seen in 38 (35.5%) babies. Complications were 75% and 46% in the early and late rescue group respectively (p - 0.22). The mortality was inversely proportional to the gestational age (p - 0.002) and birth weight (p < 0.05). Mortality was 16% in both the groups but the deaths related to complications of surfactant was all in the late rescue group.

Conclusions: Complications were more in early rescue group and mortality was similar in both the groups, but mortality related to complications of surfactant was all in the late rescue group. Complications of surfactant therapy and mortality were inversely proportional to the gestational age and birth weight.

Introduction

Surfactant is an important treatment modality in preterm babies with respiratory distress syndrome (RDS). Since its use in early 1990s it has led to decrease the mortality, morbidity and cost of treatment.[1,2] Surfactant can be given as prophylactic, early or late rescue. Prophylactic surfactant is given solely based on gestational age and / or expected high risk of RDS. In rescue therapy, surfactant is given after

failure of continuous positive airway pressure (CPAP) which is defined as inspired oxygen concentration of more than 30% along with clinical assessment of work of breathing, direction of improvement or worsening and general clinical condition of the baby. Surfactant given within two hours is termed early rescue while given after two hours is termed late rescue. Repeat dose is given only when there is lack of improvement, persistent high oxygen requirement more than 30%, increased work of breathing on non-invasive or continuing need for mechanical ventilation.[3]

Although, there are various types of surfactant,[4] the only surfactant easily available in Nepal is Beractant (Survanta) which has to be given via intratracheal route at the dose of 4ml / kg.[5] Prophylactic surfactant use in delivery room has been out of practice now due to the use of antenatal maternal steroid and use of CPAP in the delivery room which has decreased the requirement of surfactant in preterm babies.[6] Early rescue therapy has been shown to be beneficial in view that it has decreased the risk of acute lung injury, neonatal death and chronic lung disease compared to delayed treatment in babies with RDS.[7] Short term risks include bradycardia, hypoxemia, blockage of endotracheal tube, pulmonary haemorrhage, hyperventilation, hypocarbia, pneumothorax, hypotension.[8,9]

Very few data regarding surfactant use has been published in Nepal.[10-13] Previous studies done on surfactant therapy in preterm babies were prospective study but included few babies over short period of time. The objective of this study is to find out about the use, complications and mortality of surfactant replacement therapy in preterm babies in a tertiary care hospital in Nepal over a five year period. It also compares its use between the different gestational age and weight. This study adds on to the experience of surfactant use in our setting.

Methods

This was a retrospective cross-sectional study done in preterm babies who received surfactant at Patan Academy of Health Sciences (PAHS) over a period of five years (January 2016 to January 2021). All the babies who received Beractant (Survanta) were intubated and after confirmation of correct placement of endotracheal tube, surfactant was given through the endotracheal tube using a nasogastric tube at the dose of 4 ml / kg. Babies who received surfactant before onset of respiratory distress was termed prophylactic. If baby developed respiratory distress and received surfactant before two hours after delivery, it was termed early rescue and if received after two hours after delivery, it was late rescue. After approval from the institutional review committee (IRC) of PAHS, data collection was done. All the preterm babies who received surfactant during the study period were included in the study. Babies who had incomplete information were excluded. Hospital number of the preterm neonates who received surfactant was retrieved from the neonatal Intensive care unit (NICU) / Pediatric intensive care unit (PICU) register and NICU / PICU and perinatal audits. Using the hospital number, patient's files were retrieved from the medical records section. From the patient's files information regarding the gestational age, sex, birth weight, doses of dexamethasone received (None or complete or incomplete), time of surfactant delivery after birth, complications and immediate outcome (Improved or expired) was retrieved. According to the hospital protocol, antenatal steroids were given to preterm babies ≤ 34 weeks of delivery with risk of premature delivery. Charts were searched for procedural complications during surfactant delivery like endotracheal tube blockade, hypoxia, bradycardia, tachycardia and physiologic complications like apnea, hypotension, pulmonary hemorrhage, intraventricular hemorrhage and pneumothorax. Any above complications leading to death was categorized as mortality due to surfactant therapy. Other long term complications like bronchopulmonary dysplasia was also analyzed. The study period was divided into first and second halves to compare the percentage of pregnant mothers less than 34 weeks of gestation who received antenatal corticosteroids and to compare the time and type of surfactant delivery. The data was entered on MS excel and analysis was done using SPSS 16. Gestational age, weight, time of intubation, time of surfactant delivery after birth was analyzed and expressed as means, standard deviation and range. Sex, dexamethasone doses, complications due to surfactant therapy and cause of death was expressed as proportion and percentage. The number of babies receiving surfactant along with complications due to surfactant and outcome was compared according to gestational age (< 28 weeks, 28 - 34 weeks, 34 weeks) and weight (< 1000 grams, 1000 - 1500 grams,1500 - 2500 grams, 2500 grams) categories. We compared the babies who received early rescue and late rescue in terms of weight, gestational age, complications and mortality. Results are presented as tables. The study period was divided into first and second halves to compare the number of antenatal steroid doses and the time of surfactant delivery after birth. This comparison was done to see the change in the pattern of surfactant therapy in over the five year period. Analysis was done using t - test for continuous data and chi - square test for categorical data. P - value < 0.05 was considered significant.

Results

There were 111 babies who received surfactant over the study period. Four babies were excluded from the study due to incomplete information in the files. Out of 107 babies, there were 75 males (70%) and 32 (30%) female babies with the male : female ratio of 2.34. The mean gestational age of all the babies was 31.3 ± 2.86 weeks ranging from 25 weeks to 36.29 weeks. The mean weight of all the babies was 1540.61 ± 511.68 grams ranging from 600 grams to 2955 grams. Most of the babies were in the gestational age of 28 - 34 weeks (66.35%) and weight of 1500 - 2500 grams (49.5%) as shown in table 1 and 2.

Table 1. Surfactant therapy and its outcome according to gestational age

Parameters	Total N (%)	< 28 weeks N (%)	28 - 34 weeks N (%)	> 34 week N (%)	P - value
Number of babies	107 (100)	15 (14)	73 (68.2)	19 (17.8)	
Complications due to surfactant therapy	53 (49.5)	9 (60)	36 (49.3)	8 (42.1)	0.30
Mortality	18 (16.8)	7 (46.7)	11 (15.1)	0	0.002
Mortality due to complications of surfactant	3 (2.8)	1 (6.7%)	2 (2.7)	0	0.829

Table 2. Surfactant therapy and its outcome according to birth weight

Parameters	Total N (%)	< 1000 grams N (%)	1000 - 1500 grams N (%)	1500 - 2500 grams n (%)	> 2500 grams n (%)	P - value
Number of babies	107 (100)	13(12.1)	35 (32.7)	53 (49.5)	6 (5.6)	
Complications due to Surfactant Therapy	53 (49.5)	8 (61.5)	19 (54.3)	24 (45.2)	2 (33.3)	0.55
Mortality	18 (16.8)	7 (53.8%)	9 (25.7%)	2 (3.77%)	0	0.000054
Mortality due to complications of surfactant	3 (2.8)	1 (7.7)	1 (2.9)	1 (1.9)	0	0.401

Out of 107 babies, 54 (50.46.5%) babies received antenatal steroids among which only 29 (27.1%) babies received full doses. Out of babies born in the first half of the study, 21.7% babies received complete doses of antenatal steroids while in the second half of the study, 31.1% babies received complete doses. There was some improvement in the percentage of mothers receiving complete doses of antenatal steroids although not statistically significant (p - value - 0.27).

None of the babies received prophylactic surfactant. Twelve (11.2%) babies received early rescue whereas 95 (88.8%) babies received late rescue. Twelve (11.2%) babies needed a repeat dose of surfactant. The mean time of intubation after delivery was 8.66 ± 13 hours ranging from at birth to 69 hours. The mean time of surfactant delivery after intubation was 5.93 ± 7.8 hours ranging from 30 minutes to 43 hours after intubation. Time of surfactant delivery after birth in the first and second half of study period was 17.5 ± 19.4 hours and 12.3 ± 14.5 hours after intubation respectively (p-value - 0.127).

Following surfactant delivery, 54 (50.5%) babies did not develop any complications due to surfactant therapy while 32 babies developed single complication and 21 babies developed multiple complications. Hypotension was the most common complications seen in 38 patients. Other serious complications like pulmonary hemorrhage was seen in 11 patients, intraventricular haemorrhage (IVH) in four cases and pneumothorax was seen in two babies. Seven babies developed bronchopulmonary dysplasia (BPD). Out of all the babies who received surfactant, 78 survived, 18 babies expired, 10 withdrew from treatment and one baby was transferred to another centre. Out of 18 mortalities, 15 deaths were due to late onset sepsis. In rest of the cases, the cause of death was due to complications related to surfactant therapy. Two deaths were pulmonary and one death was due to pulmonary haemorrhage with IVH. As seen in tables 1 and 2, both mortality and complications due to surfactant therapy were inversely proportional to the gestational age and birth weight. Mortality was significantly more in the younger gestation and lower birth weight (p-value < 0.05). There was no mortality in the gestational age > 34 weeks and birth weight > 2500 grams.

Table 3. Type of surfactant delivery and outcome

Parameters	Total n (%)	Early rescue n (%)	Late rescue n (%)	P - value
Number of babies	107 (100)	12 (11.2)	95 (88.8)	
Gestational age (Weeks) Mean ± 2 SD		29.2 ± 2.4	31.5 ± 2.8	0.009
Weight (Grams) Mean ± 2 SD		1211.7 ± 315.6	1582.2 ± 517.7	0.007
Complications due to surfactant therapy	53 (49.5)	9 (75)	44 (46.3)	0.223
Mortality			16 (16.9)	
Late onset sepsis	18 (16.8)	2 (16.7)	13 (13.7)	
Mortality due to complications of surfactant	15 (14)	2 (16.7)	3 (3.2)	0.675
Pulmonary haemorrhage	3 (2.8)	0		
Pulmonary haemorrhage with IVH	2 (1.9)	0	2 (2.1)	
	1 (0.9)	0	1 (1.1)	

Table 3 shows the comparison between babies receiving early and late rescue surfactant therapy. Around 75% of babies in early rescue group developed complications while 46.3% of babies developed complication in late rescue group. All the babies who received early rescue were the babies who received surfactant in the latter half of the study. Mortality in both the early and late rescue groups was 16% but mortality related to surfactant delivery was all in the late rescue group.

Discussion

Surfactant replacement therapy is the standard of care for treatment of RDS in preterm babies.[3] Although not free of complications, its benefit outweighs the risk.[1,2,8,9] This study analyzed the use and immediate outcome of surfactant therapy in 107 preterm baby in NICU at Patan Hospital. In our study, 45.8% of the neonates developed complications due to surfactant therapy. Hypotension was the most common complication seen in our study. This was similar to the findings in a study done by Hellström - Westas et al who showed 21 out of 23 neonates to have significant fall in blood pressure after surfactant therapy.[8] The cause of this hypotension has been attributed to the left to right steal by the large patent ductus arteriosus associated with inability of preterm baby to compensate by increasing left ventricular output.[14] In our study pulmonary hemorrhage was the second most common complication while it was the commonest complication in other studies.[11,15] Overall mortality in this study was 16.8%. This was similar to other studies.[11,16] The most common cause of mortality in our study was late onset sepsis and pulmonary hemorrhage which was similar to other studies.[11,15]

Use of antenatal corticosteroids during pregnancy in women at risk of preterm delivery is effective in prevention of RDS in neonates. Besides it also reduces the need of mechanical ventilator, the incidence of complication like necrotising enterocolitis, IVH, late onset sepsis and the number of neonatal and perinatal death in preterm. Very few major adverse effects have been seen.[17,18] Its benefit is not only limited to babies less than 34 weeks of gestation but also been found to be beneficial in late preterm delivery.[19,20] The response to corticosteroids has been found to be present even after a single dose.[20] Despite the known benefit of antenatal steroids, only 27.1% of our babies received complete doses of antenatal corticosteroids although this number has improved over the study period. This delivery of antenatal steroids is more than shown by other studies like Manandhar et al and Femitha et al[13,18] but is lesser than other studies by Yadal SK, Narang A, Ganesh BK et al etc.[11,12,16] The reason for the less number of babies receiving antenatal steroids may be due to the late presentation of the pregnant mother to the health facility.

None of the babies received prophylactic surfactant in our study. Studies have shown that when routine application of CPAP was done, the benefits of prophylactic surfactant on mortality and air leak was not demonstrated.[9] Twelve (11.2%) babies received early rescue while 95 (88.8%) received late rescue. The cause of our babies receiving late rescue might be due to the unavailability of surfactant at our hospital during study period. All the babies who received early rescue were delivered during the second half of the study. The mean time of surfactant delivery had decreased from the first half to second half duration of study and all of the early rescue surfactant was given in the late half of study. This might be due to the availability of surfactant at our hospital and also the fact that we stored extra surfactant at out NICU / PICU which had to be replaced when used. Various studies have shown that complications and mortality are significantly less in early rescue than in late rescue group.[21] In our study, complications were more in the early rescue group while mortality was similar in both the groups. This is different from other studies which might be due to the less number of cases in early rescue and also the mean gestational age and weight of the babies who received early rescue was less than late rescue (p- value < 0.05).[7]

Out of 107 babies, 6.5% of babies developed chronic lung disease. Another study done by Narang A et al showed the incidence of 8.5%.[16] Comparing our study and study by Narang A et al, the gestational age was comparable but the mean weight of the baby was more in ours which might have led to the less incidence of chronic lung disease. The strength of our study was the duration of over five years. The limitations of our study is the small number of patients in the early rescue group, retrospective nature and single centre study. A larger, prospective and multi centric study with a larger sample size is needed to confirm the findings of this study.

Conclusions

Complications of surfactant therapy and mortality were inversely proportional to the gestational age and birth weight. Mortality was similar in early and late rescue groups but mortality related to surfactant delivery was all in the late rescue group.

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