Brief Reports

Surfactant Therapy in Neonatal Respiratory Distress Syndrome

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Respiratory distress syndrome (RDS) is the leading cause of neonatal respiratory distress in our country and is the commonest disorder requiring assisted ventilation all over the world(l,2), Exogenous surfactant administration is now an established mode of therapy in neonatal RDS (hyaline membrane disease, HMD). Ever since the first report of successful surfactant replacement therapy in neonates with established RDS(3), numerous clinical trials conducted worldwide have shown exogenous surfactant therapy to reduce the mortality rate, requirements for mechanical ventilation and air leak complications in RDS(4). Four surfactant preparations are now available commercially. Of these, two have been naturally extracted (SURVANTA-bovine lung source and CUROSURF-porcine lung source) and two are synthetic (Colfosceril palmitate-EXOSURF and artificial lung expanding compound-ALEC). Not many centres in India have tertiary level care neonatal units with facilities for ventilation. Experience with ventilation for neonatal RDS is limited to a few centres only(5). However, there is as yet no report of any experience using established surfactant replacement therapy for RDS in the Indian literature. We report here 'exogenous surfactant replacement treatment' in addition to mechanical ventilation and other intensive care measures. This is probably the first such report from India, of having successfully used surfactant replacement therapy for neonatal RDS.

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Case Report

A male baby was born at 34-35 weeks of gestation to a multiparous woman (gravida six and parity four) in a nursing home. The mother had an uneventful antenatal period. The baby was delivered by a Cesarean section. The mother had received two doses of betamethasone intramuscularly twelve hours apart prior to the delivery. The baby cried normally at birth and the Apgar score was reported to be normal by the attending Pediatrician. Within half an hour after birth, the baby was noted to have respiratory distress with grunting, alae nasi flaring, subscostal and intercostal recessions and cyanosis (in air). Progressive worsening in the respiratory distress occured over the next 2-3 hours inspite of giving the baby humidified oxygen through

a hood. The child was, therefore, referred and transported to our tertiary level care neonatal unit at the Manipal Hospital, Bangalore at 4 hours of age.

On admission here, the baby was noted to be in severe respiratory distress, cyanosed in air, poorly perfused peripherally and hypotensive (mean BP 40 mmHg). His weight was 2.1 kg. Oxygen saturation in air was 55% and he required an FiO_2 of 0.9 through oxygen hood to maintain SaO_2 more than 90%. An arterial blood gas analysis done revealed hypoxemia and metabolic acidosis secondary to the increased work of breathing. The alveolar-arterial oxygen gradient ($(A\text{-}a)DO_2$) and PaO_2/PAO_2 ratio (kPa units) were determined to be 534.5 and 0.08, respectively. An X-ray chest revealed evidence of severe RDS (HMD) with complete 'white out' of both lung fields, air bronchogram and obliteration of the cardiac outline *(Fig. 1)*. The clinical and radiological picture suggested severe RDS in the baby.

The baby was intubated endotracheally and was given intermittent mandatory

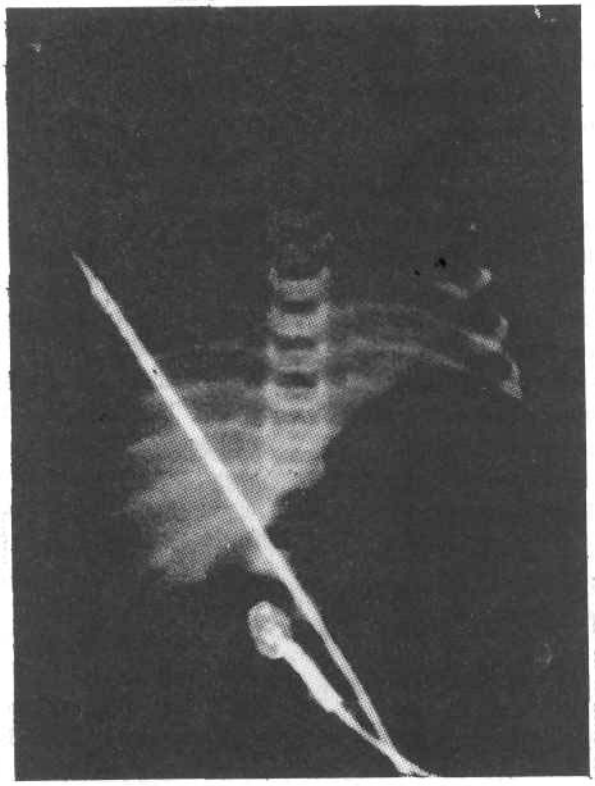

Fig. 1. Chest X-ray showing complete 'white out' of both lung fields (severe RDS).

ventilation (IMV) using a continuous flow, pressure limited and time cycled ventilator (INFANT STAR). Initial ventilator settings were 60 breaths per minute, inspiratory time (Ti) of 0.5 sec, (I:E ratio 1:1), FiO_2 of 0.9, peak end expiratory pressure (PEEP) of 5 cm H_2O using a flow rate of 10 litres per minute. The peak inspiratory pressure (PIP) was adjusted at a level enough to improve oxygenation and produce good air entry on chest auscultation. Initially, PIP of as much as 32 cm of H_2O was required. The child was given one dose of pancuronium (0.1 mg/kg) intravenously at the time of initiation of ventilation. Subsequently, an infusion of intravenous morphine (10 (µg/kg/hour) was given to sedate the baby. Other supportive therapy included care in a servocontrolled environment, intravenous alimentation and antibiotics. Dopamine was infused at a rate of 3 µg/kg/min. Close monitoring of all vital functions (heart rate, respiratory rate, BP, temperature) was done through a continuous monitor (Criticare 508).

An indwelling low umbilical arterial catheter (at L3-L4 level) was inserted to record blood pressure continuously (through a Nihon Kohden Life Scope Monitor) and for arterial blood gas sampling. Arterial blood gas (ABG) analysis was done 4-6 hourly and whenever necessary, full blood counts, serum ttectrotytes, WoodNtextrose, blood culture andxenal functions were tested. These were normal at admission and were repeated subsequently as and when necessary.

The baby continued to require high ventilatory peak inspiratory pressures (PIP 32 cm H_2O) and FiO_2 requirements rose to 0.95 by 7 hours of age. The PaO_2/PAO_2 calculated at this time was 0.15. The (A-a) Do_2 was 529.35. Since the baby had established RDS and PaO_2/PAO_2 ratio was less than 0.22, a decision to administer surfactant as a "rescue therapy", was taken after informed parental consent. A bovine surfactant preparation (SURVANTA, Ross Laboratories, USA, Lot No. 7883527.) was administered to the baby slowly by the intratracheal route through a 'side port adaptor' connected to the ventilator circuit(4). A total of 8 ml *i.e.,* 200 mg of Survanta containing 200 mg of the phospholipid (at a recommended dose of 100 mg/kg/dose) was administered slowly over 20 minutes with half the dose, *i.e.,* 4 ml (100 mg) each being delivered into each lung by positioning the baby in the left and right lateral positions, respectively. Surfactant was taken in a sterile syringe and administered with a No. 5 FG catheter slowly through a side port adaptor connected to the endotracheal tube and ventilatory circuit without interrupting the ventilation to the baby. Close monitoring of the baby's vital functions,' BP and O_2 saturation was undertaken during and after the procedure. Ventilator settings including FiO_2 were changed during and following surfactant administration depending on the baby's oxygen saturation and arterial blood gas analysis, as recommended(4).

The subsequent course of the baby's respiratory status revealed a dramatic improvement in oxygenation with FiO_2 requirements falling to 0.65 within 4 hours and 0.3 within 16 hours of surfactant therapy. A dramatic improvement in lung compliance was reflected through decreased pressure requirements with peak inspiratory pressure (PIP) falling to 16 cm H_2O over the next 16 hours *(Fig. 2).* Good aeration of the lungs was observed within 12 hours of surfactant administration *(Fig. 3).*

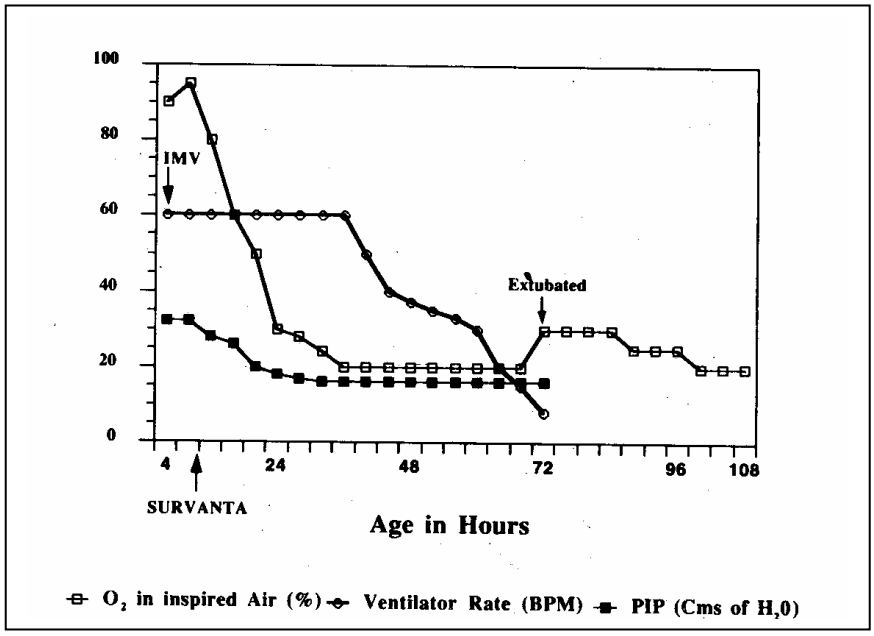

Fig.2. Ventilatory settings and respiratory status before and after 'Survanta' administration.

Other ventilatory settings' were weaned down gradually as an improvement in the baby's condition was noted. Morphine infusion was stopped and intravenous naloxone was given when ventilatory rate had been brought down to 30 breaths per minute.

The baby's oxygenation improved dra matically after administration of Survanta. The PaOjP A02 ratio was calculated to be 0.26 and 0.55 at 6 hours and 24 hours, respectively after giving surfactant. The values for (A-a) D02 were 256.3 and 33.4 respectively, at these times *(Table* J). The baby did not require a second dose of surfactant. The baby's cardiorespiratory status, BP, blood urea, serum creatinine, serum electrolytes, blood counts remained within normal limits after surfactant adminLtration till discharge. Cranial ultrasonography done at 48 hours of age was normal.

The baby was discharged home on breast feeds on the 17th day of life. On follow up, a retinal check revealed no evidence of any retinopathy of prematurity at 5 weeks of age.

Discussion

It is now well accepted that 'surfactant replacement therapy' early in the course of RDS significantly reduces morbidity and mortality by 40-60%(4,6). Particularly there is reduction in the incidence of air leak complications encountered during ventilation and the severity of Bronchopulmonary Dysplasia due to barotrauma(4,6,7). Both, natural surfactants (Survanta-Bovine, Curosurf-porcine) and synthetic surfactant (Exosurt) have been clearly shown to improve survival, decrease ventilatory support requirements and reduce the incidence of air leak complications(4,6). 'Rescue therapy'

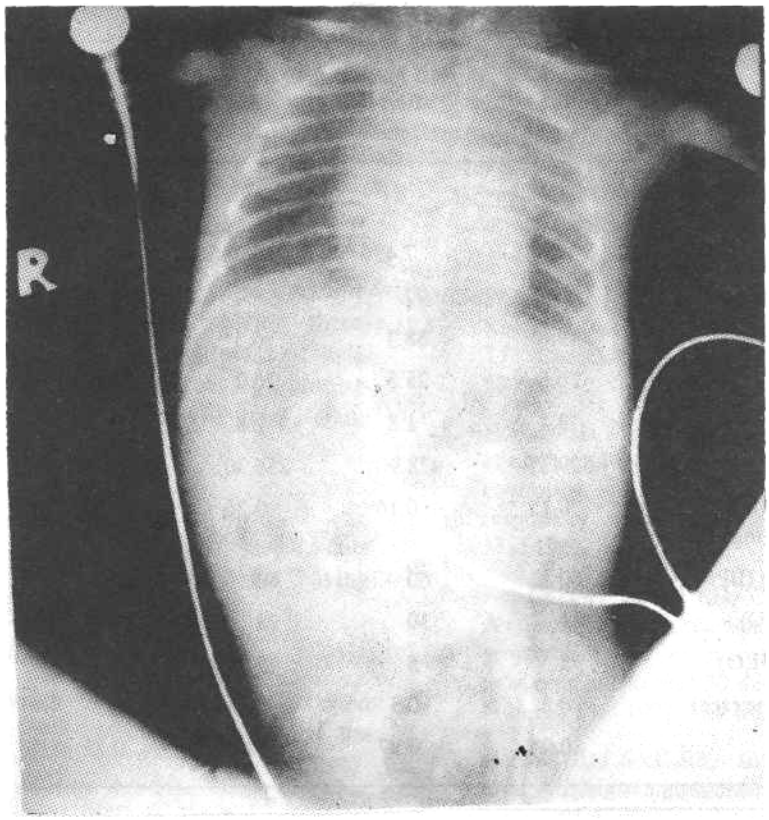

Fig. 3. Chest X-ray showing better aeration of lung fields 12 hours after surfactant administration.

wherein surfactant is administered to a ventilated baby with confirmed and established RDS is reported to be as equally efficacious as early 'prophylactic' administration of surfactant into the 'at risk' preterm baby's lungs at the time of birth(8). Both, single and multiple doses of Survanta at 12 hours intervals have been shown to improve survival in low birth weight preterm neonates(4). Two doses of Survanta or Exosurf may be adequate treatment though some babies may benefit from one dose itself or even additional doses(4,9). Current data do not recommend the use or superiority of one surfactant preparation over the other(4,6). Surfactant therapy, especially Exosurf use, is associated with an increased risk of pulmonary hemorrhage in extremely low birth weight babies less than 700 g(6). Also there is possibly an increased incidence of PDA due to surfactant therapy(4,6). No long term physical or neurodevelopmental handicaps or other complications have been noted with surfactant therapy(6).

Surfactant replacement therapy can

TABLE I-*Arterial Blood Gases, Oxygenation and Ventilator Settings Before and After Surfactant Administration*

Parameters	One hour before surfactant	Half hour after surfactant	6 hours later	24 hours later	48 hours later
Arterial blood gases					
PH	7.368	7.426	7.286	7.636	7.435
$Pa0_2$ (nun Hg)	96	97	96.4	84	64
$PaC0_2$ (mm Hg)	49.6	38.3	56.3	25.6	41.2
$HC0_3$ (meq/L)	26.6	25.5	26.2	20.9	28.0
Base excess	3.4	1.8	2.8	0.4	4.0
(A-a) $D0_2$ (mm Hg)*	529.35	478.90	256.30	33.40	7.40
a/A ratio (Kpa)**	0.15	0.16	0.26	0.55	0.59
Ventilator settings (IMV)					
Ventilator rate (BPM)	60	60	60	60	35
PIP (cm of H_2O)	32	30	28	17	16
PEEP (cm of HP)	5	5	5	5	5
Inspiratory time (sec)	0.5	0.5	0.5	0.5	0.5
$Fi0_2$	0.95	0.87	0.6	0.25	0.21

* (A-a) D02 = Alveolar arterial oxygen gradient.

** a/A ratio = Ratio of arterial/alveolar oxygen tension (PaO/PA02)

reduce the overall cost in the management of sick babies with severe RDS by as much as 16%(10). Especially, in India, where 4he financial burden of treating sick babies in neonatal intensive care units either falls on the Government or the family, surfactant replacement therapy can prove to be cost effective. This is through reduction in the length of stay in the NICU, reduction in rate of complications, less oxygen dependency, lesser ventilatory requirements, less time spent by the baby on the ventilator and thereby lesser complications like air leaks and infection, which otherwise prolong stay in the NICU. Also, in a country like ours, "single dose" surfactant therapy could prove to very cost effective. The case reported above suitably exemplifies successful outcome with a single dose of surfactant leading to less morbidity, early discharge and thereby cost effective therapy. However, this needs to be further evaluated and confirmed through controlled trials in tertiary levels care units in the country. Surfactant therapy in the management of premature infants with RDS is a useful adjunct to mechanical ventilation and other intensive supportive care. However, its use should be

restricted to tertiary care neonatal units where equipment and trained staff necessary or mechanical ventilation and close monitoring (oxygen monitoring, pulse oximetry and cardio pulmonary monitoring) are available along with appropriate radiological and laboratory support. More importantly, only those Pediatricians who are trained in the care of low birth weight babies and their ventilation should administer surfactant after familiarizing themselves thoroughly with all aspects of indications for its use, techniques of administration, monitoring protocol and acute adverse effects.

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