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Surfactant Replacement Therapy for Respiratory Distress Syndrome in the Newborn

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Abstract

Surfactant deficiency Causing respiratory failure is the major cause of morbidity and mortality in low birth weight premature infants. Surfactant therapy gradually reduces mortality and morbidity for this population. Exogenous surfactant therapy is well established in newbornbabies with respiratory distress. Many aspects of its use have been well assessed in high-quality trials and systematic reviews. In late-preterm and term neonates with meconium aspiration syndrome, pneumonia/sepsis, and maybe pulmonary haemorrhage, secondary surfactant deficiency also leads to acute respiratory morbidity; surfactant substitution can be helpful for these babies. This paper reviews the evidence and provides guidelines for the use of respiratory distress syndrome (RDS) surfactant therapy in newborns.

Keywords: Surfactant therapy Distress Syndrome in newborn

Introduction

As an effective preventive and treatment therapy for prematurity-related surfactant deficiency, exogenous surfactant substitution has been developed.More advanced children with primary pulmonary hypertension or meconium aspiration syndrome may also be recommended for surfactant therapy. The use of surfactant replacement in preventive or treatment modes has been shown to be safe and efficient in single and multicenter randomised controlled trials using synthetic, modified animal, purified animal, and human surfactants. Reduced death rates and increased short-term respiratory status have been reported for preterm babies with respiratory failure due to surfactant-deficiency. New experiments continue to tackle refinements in the use of surfactants that can maximise their efficacy. Among the challenges that can boost the effect of surfactants are new materials, spacing, dosage, ways of administration, and adjustment for various gestational age groups.[1,2] Surfactants are organic compounds that lower the surface tension of a liquid lining the alveoli.[2] Surfactants decrease the surface tension of the fluid by adsorbing the liquid-gas interface.[3] A surface-active lipoprotein complex (phospho lipoprotein) produced by type II alveolar cells is a pulmonary surfactant. The key lipid surfactant portion, dipalmitoyl phosphatidylcholine (DPPC), decreases surface tension by adsorbing alveoli to the air-water interface with the hydrophilic head groups in the water and the hydrophobic tails facing the air.[4]

Surfactant Functions

- To improve pulmonary compliance.
- Atelectasis (collapse of the lung) can be

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avoided at the end of expiration.

- In order to promote the recruiting of collapsed airways.

Benefits of Surfactant Replacement Therapy in RDS

The occurrence of acute respiratory failure with disrupted gas exchange in a preterm baby with a normal clinical course or x-ray (ground glass presentation, air bronchograms and reduced lung volume) is typically described by RDS.[5] The lungs of preterm infants with RDS are both anatomically and biochemically immature; they do not synthesise or secrete RDS. Surfactant usually lines the alveolar surfaces of the lung, thus decreasing surface stress and avoiding atelectasis.[5] Surfactant replacement therapy decreases death and morbidity of babies with RDS, either as a rescue procedure or as a prophylactic natural surfactant therapy.[6,7] These morbidities include oxygenation defects, the occurrence of leakage of pulmonary air (pneumothorax and interstitial pulmonary emphysema) and the length of ventilatory assistance. Replacement of surfactants improves the chance of survival without bronchopulmonary dysplasia (BPD, also referred to as chronic lung disease) mainly by improving survival rather than the occurrence of BPD. Compared to randomised placebo children without surfactants, babies administered with surfactants had shorter hospital stays and reduced costs of intensive care treatment.[8] The rise in longevity is done without a rise of adverse neurodevelopmental results.[9]

Risks of Exogenous Surfactant Therapy

Bradycardia and hypoxemia during instillation as well as endotracheal tube blockage are short-term risks of surfactant replacement therapy.[10] There can also be a rise in pulmonary haemorrhage after surfactant therapy; however, mortality associated with pulmonary haemorrhage is not increased and total mortality is lower after surfactant therapy.[11] In surfactant-treated children that are deficient in surfactants, there is also a very fast increase in gas exchange.[12] Natural surfactants include proteins (surfactant protein-A, surfactant protein-B) from bovine or porcine origins and concerns about the immunological consequences have been raised.[13] To date, there is no proof that there are immunological improvements of therapeutic concern.[14] Babies with RDS have observable circulating immune complexes targeted at proteins of surfactants, but these do not seem to be more common in surfactant-treated babies.[15] One study found a lower occurrence of protein-A and anti surfactant protein Banti surfactants in surfactant-treated babies compared to controls.[16,17]

Which is Better: Natural or Synthetic Surfactants?

A total of 11 randomised trials were subject to systematic analysis comparing natural and synthetic surfactants for babies with RDS.[10] The study found that overall mortality is decreased relative and synthetic surfactants due to the use of natural surfactants. In babies treated with natural surfactants, pulmonary air leak syndrome is less frequent. In babies given natural or synthetic surfactants, the occurrence of BPD is not different, but since mortality is minimised in babies given natural surfactants, the cumulative result of death or BPD is decreased. Natural surfactants thus enhance longevity without BPD and with a lower rate of air leakage and should be favoured to synthetic surfactants.[18]

Surfactants Prescribed as Prophylaxis or Rescue Therapy for Preterm Babies with RDS-

Multiple trials have examined whether surfactants should be prescribed to all babies at serious risk of developing RDS or only after RDS development. Seven RCTs in prophylactic versus rescue treatment were analysed by Soll and Morley.[19] These were both experiments that used natural surfactants. Six of the RCTs enrolled children less than 30 weeks gestational and one enrolled children 29 to 32 weeks gestational. Prophylactic surfactant therapy reduced mortality both before 28 days and before hospital discharge. The occurrence of RDS, pneumothorax and pulmonary interstitial emphysema all decreased in babies treated prophylactically. There was no difference in the occurrence of BPD.[19] With the existing mortality rates at tertiary centres, prophylactically providing surfactant to all babies less than 26 weeks gestation and to all 26 to 27 weeks gestation who did not benefit from antenatal steroids would be a fair choice. hInfants at serious risk of RDS should undergo prophylactic natural surfactant therapy as soon as they are stable within a few minutes after intubation.[19]

Surfactant Replacement Therapy Procedure

Surfactant was instilled through the endotracheal tube in liquid form for all surfactant replacement therapy trials.[17] Some studies instilled all the surfactant at once, while othergave in small parts.[18] Just one very small trial compared a slow infusion with bolus surfactant administration. It concluded that slow infusion was at least as effective as bolus therapy.[20] There is no evidence to support the practise of putting the baby in several different positions during surfactant administration.[20]

Dosage of Surfactant

In the various clinical trials, dosages ranged from 25 mg to 200 mg phospholipids/kg body weight as single doses. At a dosage of 120 mg/kg, Surfactant-TA (a natural bovine surfactant) was more effective than 60 mg/kg.[20] At 200 mg/kg, Curosurf (a natural porcine surfactant) was more acutely effective than 100 mg/kg.[21] Lower doses may well be ideal for prophylaxis, although higher doses may be needed for the treatment of known RDS when antisurfactant proteins are present in the airspace. Therefore, improvements in results tend to be seen up to a dose of approximately 120 mg phospholipids/kg body wt for first dose, first larger doses do not cause improvement in outcome.

Requirements for Retreatment and Timing

Retreatment should be considered when there is a requirement of 30 percent or more for chronic or repeated oxygen and can be administered as early as 2 h after the initial dose or, more generally, 4 h to 6 h after the initial dose.[22]

Ventilatory Management After Surfactant Therapy

Due to the rapid changes in lung mechanics and the ventilation/perfusion matching that occurs after rescue surfactant therapy and the avoidance of serious lung disease by the prophylactic use of natural surfactants, many infants can be very easily weaned and extubated to nasal continuous positive airway pressure (CPAP) within 1 hour of intubation and surfactant therapy.[17] To do this, only a brief period of respiratory distress should be triggered by the premedication used for intubation and personnel must be educated and certified in rapid ventilator weaning. Such weaning is sometimes carried out with little to no blood gases, depending instead on the clinical state of the baby and spontaneous respiratory effort and taking into account the criteria for oxygen as determined from pulse oximetry and also using measurements of transcutaneous carbon dioxide. There is currently no evidence that, compared with the more conventional weaning approach, a fast weaning and extubation approach enhances long-term performance. Such an approach resulted in a decrease in the need for more than 1 h of mechanical ventilation in two small randomised trials.[21]

Surfactant therapy V/S antenatal steroids- A single course of steroids should be offered to expectant mothers with threatened preterm labour, according to current guidelines. Wide cohort studies suggest that surfactant and steroid combinations are more effective than surfactant alone, which is exogenous. A secondary analysis of evidence from surfactant research also suggests a decline in the incidence of disease in infants receiving antenatal steroids. Two additional RCTs have shown that prenatal steroids appear to minimise the risk of bad outcomes even in centres where surfactants are available; one has shown a decrease in RDS and an increase in survival without ventilatory assistance, and both have shown a substantial decrease in extreme intraventricular haemorrhage.[23]

Conclusion

The therapy of exogenous surfactants is safe and has important benefits in the treatment of many neonatal respiratory diseases. Excellent quality RCTs have been well studied and have clearly reported that their administration should be normal in the treatment of RDS and as prophylaxis in identified preterm baby classes. In other infant respiratory disorders, data continues to be gathered for its use. The following guidelines are provided by the Canadian Paediatric Society:-

- Antenatal steroids should be prescribed to mothers at risk of delivering babies less than 34 weeks gestation, in compliance with established guidelines, regardless of the availability of postnatal surfactant therapy.
- Exogenous surfactant therapy should be offered to intubated infants with RDS.
- As soon as they are healthy within a few minutes of intubation, infants who are at high risk for RDS should receive prophylactic natural surfactant care.
- Repeated doses of surfactants should be given to infants with RDS who have chronic or recurrent oxygen and ventilatory requirements during the first 72 h of life. It has not been shown that administering more than three doses has a benefit.
- Retreatment may be considered when an oxygen demand of 30 percent or more is persistent or chronic, and can be administered as early as 2 h after the initial dose or, more generally, 4 h to 6 h after the initial dose.
- Ventilatory management options to be considered following prophylactic surfactant therapy include very rapid weaning and extubation within 1 h of CPAP.
- If at all necessary, mothers with a threatened delivery before 32 weeks of gestation should be moved to a tertiary centre.
- Infants that have been gestated for less than 29 weeks outside the tertiary centre should

be recommended for immediate intubation followed by the administration of surfactants until stabilisation, provided that qualified personnel are available.

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