Surfactant administration during spontaneous breathing via a thin endotracheal catheter

S. Martinelli, I. Gatelli, A. Proto

Division of Neonatology and Neonatal Intensive Care Unit - Niguarda Ca' Granda Hospital, Milan Italy

Abstract. In the past two decades exogenous surfactant administration has been a cornerstone of therapy for preterm infants and is known to be effective either given prophylactically in the delivery room or later as selective therapy to infants with estabilished respiratory distress syndrome. Its introduction in neonatal practice in the early 90s was followed by a significant decrease in overall neonatal mortality. With the evolution and refinement of intensive care for preterm infants, the role of exogenous surfactant therapy is changing. The more widespread use of nasal continuous positive airway pressure (n-CPAP) as a primary mode of respiratory support means that many preterm infants now avoid intubation in the delivery room or in early post-natal life. Still, about 50% of them, will require intubation for surfactant delivery for evolving respiratory distress syndrome (RDS) during the course of hospitalization. In view of the difficulties and side effects that may be associated with intubation for surfactant delivery, less invasive ways of surfactant administration have been pursued. The rationale and the available evidences inherent the administration of surfactant via a thin endotracheal catheter during spontaneous breathing will be discussed. (www.actabiomedica.it)

Key words: respiratory distress syndrome, thin ednotracheal catheter, exogenous surfactant administration

Introduction

Respiratory distress syndrome (RDS) is the most common disease of very preterm infants and its estabilished treatment is the administration of exogenous surfactant. The results of many clinical trials published during the last 20 years suggest that early or "prophylactic" administration confers better results in terms of mortality and morbidity than late "rescue" therapy (1). As a consequence of this evidence it became a standard practice to electively intubate in the delivery room the majority of very preterm newborns at risk of RDS with the purpose to administer surfactant as soon as possible.

However, in some area of the world like Scandinavia, a strategy of stabilization of preterm infants with continuous positive airway pressure (n-CPAP) and surfactant administration as a rescue therapy has always remained the preferred approach to RDS of prematurity obtaining similar clinical outcome, if not better, than the intubation-mechanical ventilation plus surfactant administration strategy (2).

Since about 50% of the preterm newborns initially stabilized with n-CPAP may eventually end up to be intubated for evolving RDS and receive surfactant at a later stage of the disease, the InSurE procedure (Intubation for surfactant administration and rapid extubation to n-CPAP) was developed in Denmark in the 90's in order not to withhold surfactant in infants who are in need of it and , at the same time, restoring n-CPAP as soon as possible avoiding the prolongation of mechanical ventilation (MV) which is known to exert remarkable side effects to the lung structure (3).

This strategy gained a widespread diffusion in many NICUs around the world and confirmed in many clinical studies its efficacy compared to a strategy of lat-

er selective surfactant replacement and continued MV with extubation from low ventilator support (4).

This approach, however, still requires skill for intubation, has the potential for trauma to the glottis and airways and is usually undertaken after premedication, which may contribute to respiratory depression and a delay in extubation even after surfactant has been administered.

To incorporate the advantages of surfactant and to limit the complications that may be related to endotracheal intubation followed by short periods of positive pressure ventilation, other methods of surfactant administration, preferentially during spontaneous breathing, have been explored by neonatologists in the last few years.

Several techniques, collectively labelled with various acronimous like "LISA" (less invasive surfactant administration) or "MIST" (minimally invasive surfactant therapy) or "SWI" (surfactant without intubation) have been described and include the following: intra-amniotic instillation, pharyngeal instillation, administration via a laryngeal mask, surfactant nebulisation, administration via thin endotracheal catheter.

The latter, anedoctally introduced by Verder in a pilot study aimig to test the feasibility of the InSurE procedure, was implemented in the early 2000 in Cologne, Germany.

More in details the technique consists in delivering surfactant through a 3-5 F feeding tube previously inserted in the trachea using a Magill forceps under direct laryngoscopic visualization of the vocal cords in spontaneous breathing infants while receiving n-CPAP therapy. After its placement the catheter is maintained in position with two fingers at the infant lips and surfactant is administered in 1 or more boluses over a period of 1-3 minutes followed by immediate removal of the catheter.

The procedure was first described by Kribs et al in a feasibility trial including preterm infants of less than 27 weeks of gestational age. In this study the intervention data obtained during a 13 months observational period were compared with those of an 11 months historical control period. Reduced mortality (11.9% vs 35.3%, $P = 0.025$) and a reduced rate of severe IVH in survivors (5.1% vs 31.8%, $P = 0.01$) were observed in the intervention period (5).

Based on these results, the introducing center continued to use the method. During a 4 year observational period, the choice of n-CPAP as initial modality of respiratory support significantly increased from 69% to 91% compared with historical control ($P = 0.01$) with a rate of n-CPAP with surfactant administration of 75-86%. The increased use of n-CPAP with or without surfactant was accompanied by a significantly reduced need for MV during the initial respiratory illness (27% vs 63%, $P = 0.01$). In the group of infants initially stabilized with n-CPAP, meanly with surfactant, a lower mortality (7.7% vs 42%), BPD (7.1% vs 33.3%), severe IVH (5.2% vs 33.3%), pneumothorax (2.6% vs 6.7%) were recorded (6).

Following the promising results deriving from a single center experience a randomized controlled trial of surfactant administration with this technique (the AMV trial-avoiding mechanical ventilation) was conducted in 12 German NICUs. Infants with a gestational age of $26\text{-}28^{+6}$ weeks were enrolled if they were being managed on n-CPAP and required an $FiO_2 \leq 0.30$ in the first 12 hours of life. Randomization was to receive surfactant via a thin feeding catheter (the intervention group, n = 108), or to continue on n-CPAP (n = 112). All infants were subsequently managed with n-CPAP unless intubation criteria were reached. The main trial results was that infants in the intervention group had a lower rate of MV during the first 72 hours of life (28% vs 46%) and less need of supplemental oxygen at 28 days of age (7).

Recently a modified version of this technique named "the Hobart method" has been described and implemented in Australia; instead of the flexible feeding catheter that may be difficult to insert through the vocal cords with the use of a Magill's forceps, especially for those neonatologists who may be unfamiliar with this technique because they solely practice oral intubation, a semi-rigid 16 gauge vascular catheter (Angiocath) that can be guided through the vocal cords without a throcar or forceps has been used.

A 2 site feasibility study of the Hobart method including 61 preterm infants with a gestational age of 25-32 weeks has been recently published. This group received surfactant during spontaneous breathing if they were treated with n-CPAP as initial respiratory support, were younger than 24 hours of age, required

a CPAP pressure ≥ 7 cm/H_20 and an FiO_2 ≥ 0.30 (25-28 weeks gestation) or ≥ 0.35 (29-32 weeks' gestation). Compared to historical controls achieving the same CPAP and FiO_2 thresholds, surfactant treated infants show a reduction in need for intubation ≤ 72 hours and a shorter duration of oxygen therapy (8).

Another interesting study (single center RCT) aiming to describe the feasibility of early administration of surfactant via a thin feeding tube during spontaneous breathing (Take Care procedure) and to compare early MV requirement with the InSurE procedure has recently been published. A population of 200 preterm infants with a GA ≤ 32 weeks who suffered from RDS and on n-CPAP as primary respiratory support, were randomized to receive surfactant treatment either by the Take Care or InSurE procedure. The results indicate that the Take Care technique was feasible and successfully reduced the MV requirement in the first 72 hours of life, shortened MV duration and resulted in a lower BPD rate when compared with the InSurE technique (9).

Noteworthy all available evidence suggests that both techniques of surfactant instillation by brief tracheal catheterization, either using a feeding or vascular catheter, are safe and relatively well tolerated.

Definitive data inherent the safety and efficacy of this apparently less invasive way of surfactant delivery will hopefully come from the results of 2 ongoing prospective multicenter RCT's in Germany and Australia.

The first one (NINSAPP-trial ISRCTN 64011614) aims to investigate the efficacy of surfactant administration during spontaneous breathing with n-CPAP or during MV in the therapy of RDS in premature infants ≤ 27 weeks of GA; the primary outcome is survival without BPD at 36 weeks PMA.

The second one (OPTIMIST-A trial ACTRN 12611000917932) will compare, in a population of 25-28 GA weeks preterm infants, the Hobart method of surfactant administration during n-CPAP treatment with standard care (continuation of n-CPAP); the primary outcome is death or physiologic BPD at 36 weeks PMA. A peculiarity of this study is that the intervention will be masked from the duty clinicians by involvement of a treatment team not directly involved in the clinical care of that infant.

References

1. Soll RF, Morley CJ. Prophylactic versus selective use of surfactant in preventing morbidity and mortality in preterm infants. Cochrane Database Syst Rev 2001; 2: CD000510.
2. Jònsson B, Katz-Salamon M, Faxelius G, et al. Neonatal care of very-low-birthweight infants in special-care units and neonatal intensive-care units in Stockolm. Early nasal continuous positive airway pressure versus mechanical ventilation: gain and losses. Acta Paediatr Suppl 1997; 419: 4-10.
3. Verder H, Albertsen P, Ebbesen F, et al. Nasal continuous positive airway pressure and early surfactant therapy for respiratory distress syndrome in newborns of less than 30 weeks gestation. Pediatrics 1999; 103(2): E24
4. Stevens TP, Harrington EW, Blennow M, et al. Early surfactant administration with brief ventilation vs selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome. Cochrane Database Syst Rev 2007; 4:CD003063.
5. Kribs A, Pillekamp F, Hunseler C et al. Early administration of surfactant in spontaneous breathing with nCPAP: feasibility and outcome in extremely premature infants (postmenstrual age ≤ 27 weeks). Paediatr Anaesth 2007; 17: 364-9
6. Kribs A, Vierzig A, Hunseler C, et al. Early surfactant in spontaneous breathing with nCPAP in ELBW infants-a single center four year experience. Acta Paediatr 2008; 97: 293-8
7. Gopel W, Kribs A, Ziegler A, et al. Avoidance of mechanical ventilation by surfactant treatment of spontaneously breathing preterm infants (AMV): an open-label, randomized, controlled trial. Lancet 2011; 378: 1627-34
8. Dargaville PA, Aiyappan A, De Paoli AG; et al. Minimally-invasive surfactant therapy in preterm infants on continuous positive airway pressure. Arch Dis Child Fetal Neonatal Ed 2013; 98: F122-F126.
9. Gozde Kanmaz H, Erdeve O, Emre Canpolat F, et al. Surfactant administration via thin catheter during spontaneous breathing: randomized controlled trial. Pediatrics 2013; 131 (2):E502-E509

Correspondence
Stefano Martinelli
Piazza Ospedale Maggiore 3
20162 Milano, Italy
Tel. +39 02 64442742
E-mail: stefano.martinelli@ospedaleniguarda.it