Minimally invasive approaches for surfactant administration

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Abstract. Respiratory distress syndrome (RDS) is the most common respiratory morbidity in preterm infants. In addition to respiratory support, the current clinical treatment includes endotracheal intubation and rapid instillation of exogenous surfactant. However, this approach needs skilled operators and has been associated with complications such as hemodynamic instability and electroencephalogram abnormalities. New, less invasive methods for surfactant administration are needed. In this article, we reviewed the available non-invasive procedures for surfactant administration. In particular, we focused on aerosolized surfactant and surfactant administration through LMA. (www.actabiomedica.it)

Key words: aerosol, laryngeal mask airway, surfactant, respiratory distress syndrome

Introduction

Neonatal respiratory distress syndrome (RDS) is caused primarily by a deficiency in pulmonary surfactant. The current clinical treatment of infants with RDS includes endotracheal intubation and rapid intratracheal instillation of exogenous surfactant. Although this treatment reduces morbidity and mortality, intratracheal instillation of surfactant has been associated with adverse effects such as transient hypoxia, desaturation, hypercapnia and hemodynamic imbalance (1, 2), which might in turn cause fluctuations in cerebral blood flow and electroencephalogram abnormalities (1, 2).

There's a strong suggestion that an alternative method for surfactant administration would be helpful.

Non-invasive methods of surfactant administration could potentially reduce the need for intubation and the complications secondary to this procedure. A recent Cochrane review (3) reported the different methods to administer surfactant in addition to classic way:

1. intra-amniotic instillation (4);
2. pharyngeal instillation (5);
3. administration via laryngeal mask airway (LMA) (6);
4. administration via thin endotracheal catheter (7, 8);
5. nebulised surfactant administration in spontaneously breathing infants (9, 10).

The surfactant administration by non-invasive methods have not been methodologically codified. The aim of this review was to evaluate available non-invasive procedures for surfactant administration. In particular, we focused on aerosolized surfactant and surfactant administration through LMA.

Aerosolized surfactant

Aerosolized surfactant administration would not require infants to be intubated or disconnected from ventilatory support and would enhance the pulmonary distribution of the drug.

A recent animal study showed for the first time that a standard dose of surfactant for established RDS delivered as an aerosol could produce a similar response to rapid intratracheal bolus instillation of the same dose, in terms of gas exchange and pulmonary mechanics, and resulted in less lung damage (10). Moreover, surfactant aerosolization produced a more gradual and stable pattern in cerebral hemodynamics (10). These data are encouraging, but it is of note that the Authors used an inhalation catheter to administer intratracheal surfactant aerosols with animals paralysed, sedated and under cardiovascular management. So, this procedure included the laryngoscopy, that remains an invasive approach. Future studies focusing on administering aerosolized surfactant during non-invasive ventilatory support are needed.

Several factors complicate the aerosol treatment of preterm neonates with exogenous surfactant (low lung volumes, high respiratory rates, small airways, and high viscosity of surfactant, among others) (11), so it is understandably difficult to design a successful therapy. Of the clinical studies performed to date in preterm neonates (9, 12-14), only one has shown a moderate improvement in the arterial to alveolar oxygen tension ratio (9), while the other studies were inconclusive.

LMA for surfactant administration

A potential alternative strategy is to use a LMA as a conduit for surfactant delivery. This approach has the potential to reduce the need for tracheal intubation and, consequently, the invasiveness of the procedure. The LMA is a supraglottic airway device used to administer ventilation in adults, pediatric and neonatal patients (15). The LMA is shaped like a large endotracheal tube on the proximal end that connects to an elliptical mask on the distal end. It is designed to sit in the patient's hypopharynx and cover the supraglottic structures, thereby allowing relative isolation of the trachea. The two main advantages in the LMA use are reduced invasiveness and ease of placement (6).

In the last a few years, LMA is being proposed as an effective ad minimally invasive device to administer surfactant in premature infants with RDS. Only four studies have evaluated the administration of rescue surfactant by LMA to treat the respiratory distress syndrome. We identified one randomized controlled trial (16), and three case series (6, 17, 18).

The studies suggest a marked heterogeneity in the following features:

Characteristics of participants (enrollment criteria and gestational age at treatment)

Attridge et al. (16) and Trevisanuto et al. (6) both enrolled infants with RDS, less than <72 hours, but weight and gestational age were significantly different. Attridge et al. (16) considered eligible for the study infants with birth weight > 1200 g, while Trevisanuto et al. (6) reported on a series of eight patients with birth weight > 800 g. Brimacombe et al. (17) recruited two infants of 1360 g – 30 weeks gestation and 3200 g – 37 weeks gestation. Micaglio et al. (18) reported three neonates of gestational age 37, 34, 32 and weight 3500, 2050 and 1530 g respectively.

The common criteria in all of the studies was that the infants were treated with nCPAP at a level of 5-6 $H_2 0$ for a clinically and radiographically confirmed respiratory distress syndrome.

Type of LMA used and air inflated in the cuff

Three studies were conducted with the size 1, classic LMA™ (Laryngeal Mask Co. Ltd, Jersey, UK) (6, 16, 17) and one study used the size 1 ProSeal LMA™ (Laryngeal Mask Co. Ltd, Jersey, UK) (18). Attridge et al. and Trevisanuto et al. (16, 6) inflated the cuff with 2 to 3 ml of air, while Micaglio et al. (18) did it to obtain a cuff pressure of about 60 $cmH_2 0$. This part of the procedure was not reported in the Brimacombe et al.'s study (17).

Type and volume of surfactant

Attridge et al. (16) used Calfactant (105 mg/kg = 3 ml/kg) administered in two to four aliquots, whereas Trevisanuto et al. and Micaglio et al. (6, 18) administered Curosurf (100 mg/kg = 1.25 ml/kg) instilled as a bolus. Brimacombe et al. (17) used Survanta in different doses (100 mg/kg = 4 ml/kg and 75 mg/kg = 3 ml/kg) administered as a bolus.

Timing of LMA surfactant administration

All the studies were conducted in patients with established RDS treated with nasal CPAP (rescue therapy).

Type of technique

Surfactant was instilled approximately midway down the airway lumen. In all the studies the instillation was followed by manual ventilation for 1-2 min to help drug dispersal. Attridge (16) and Brimacombe et al. (17) measured the volume of the stomach contents with an orogastric tube. Attridge et al. (16) reported only one infant in the LMA group who had greater than 25% of the surfactant volume when the stomach contents were aspirated following the procedure. All remaining infants had minimal gastric volumes when checked post-LMA surfactant administration.

In the first of two neonates by Brimacombe et al. (17) suctioning the airway tube, bowl and nasogastric tube yielded 1.7 ml of surfactant out of 5.0 ml administered, suggesting that 3.3 ml had entered the lung. Suctioning yielded no surfactant in the second one.

We treated 3 patients (not published) by using a gastric tube positioned above the distal part of the LMA main tube with aim to cross vocal cords. (Figure 1) The oxygenation did not improve by using this method. Subsequently, we positioned the tip of the gastric tube midway down the main LMA tube. This change allowed to improve oxygenation in all treatments. (6) (Figure 2)

Micaglio et al. (18) described very specifically the procedure: "in all the three neonates, an 8 Ch oral feeding catheter (OFC) was already positioned for enteral feeding. PLMA was inserted in each patient as following: after cutting the proximal side of the OFC, it was inserted into the distal orifice of the PLMA drainage tube. The device then was railroaded on the OFC with a gentle, continuos pushing maneuver" (18).

Type of supplemental sedation

Two out of four studies (6, 16) reported no use of supplemental sedation for the procedure. In the two patients treated by Brimacombe et al. (17) , the first one did not receive anesthesia for the procedure; instead, the second one required midazolam 2 mg in 0,5 increments until sedation. Micaglio et al. (18) reported the use of topical pharyngeal anesthesia with 2% lidocaine (3.5 mg/kg) in glucose 5% administered by allowing the patient to suck the glucose solution.

Type of outcome measures

The outcome was considerably different in all of the studies. Attridge et al. (16), the only randomized controlled trial (RCT), considered as primary outcome the decrease in oxygen requirement after the LMA therapy (FIO2 intermittently measured). Otherwise, Trevisanuto et al. (6) reported the increase in the arterial-to-alveolar oxygen tension ratio (a/APO_2) (baseline and 3 h after therapy) as the major accomplishment. Brimacombe et al. (17) just observed an improvement of the gas exchange in two neonates (three occasions within 3-6 h). Micaglio et al. (18) didn't want to advocate PLMA utilization for surfactant administration but, rather, to report improved first attempt success rate of PLMA insertion using a guide inside the drain tube.

Efficacy

In the only RCT (16), infants enrolled in the treatment group had a sustained decrease in oxygen require-

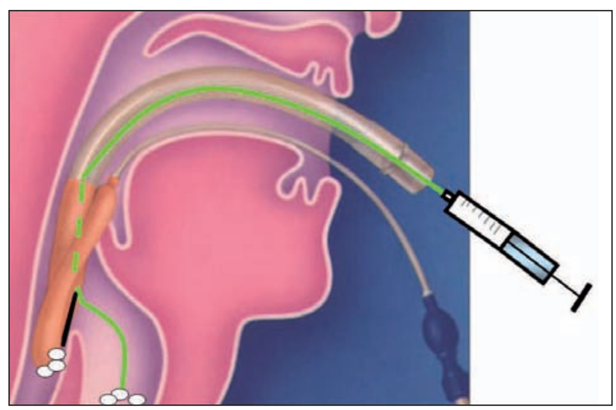

Figure 1. Figure shows the tip of the oral feeding catheter beyond the distal part of the LMA main tube (trachea or esophagus ?). No improvement in patients' oxygenation was obtained suggesting an unsatisfactory surfactant administration.

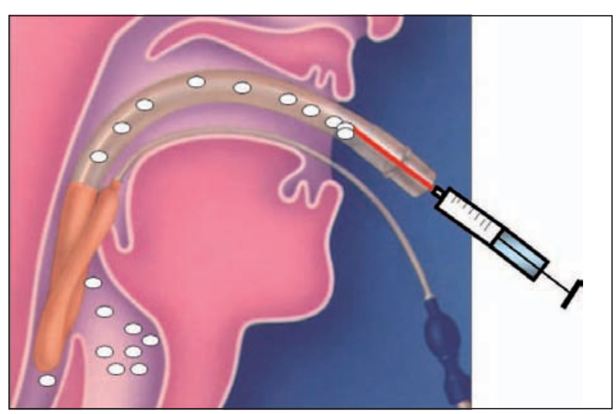

Figure2. Figure shows the tip of the oral feeding catheter in the middle of the LMA main tube. This change allowed a good oxygenation response in all treated patients suggesting a good surfactant administration.

ment after LMA surfactant therapy (FIO2 at 1 h: LMA 0.21-0.27 vs. Controls 0.34-0.40; p<0.0001). Trevisanuto et al. (6) reported a mean a/APO2 significantly increased (0.13 ± 0.04 to 0.34 ± 0.11; p<0.01) while Brimacombe et al. (17) noted a considerable improvement in gas exchange (3 occasions within 3-6h) .

Micaglio et al. (18) reported a successful use of an OFC to guide insertion of PLMA in all cases (improved first attempt success rate of PLMA insertion using a guide inside the drain tube).

Adverse effects

No study reported adverse events associated to the procedure.

Conclusions

Non-invasive methods of surfactant administration re have the advantage to avoid intubation and, consequently, may potentially reduce complications secondary to this procedure. Animal studies and small observational experiences in humans showed that surfactant administration through a LMA is safe and effective. A prospective randomized trial is needed to evaluate this non-invasive approach in neonates with RDS.

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