GŁOSKOWSKA, Julia, FRAŃCZUK, Agata, KULETA, Katarzyna, DYL, Tomasz, KRUK, Adrian, GRUSZCZYŃSKA, Hanna, SZPULAK, Angelika, KOPCZYŃSKA, Ewelina, MAKŁOWICZ, Aleksandra and PEREGRYM, Michał. Methods of surfactant administration in newborn. Literature review. Quality in Sport. 2024;22:54692. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.22.54692
https://apcz.umk.pl/QS/article/view/54692

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 27.08.2024. Revised: 19.09.2024. Accepted: 20.09.2024. Published: 23.09.2024.

Short article

Methods of surfactant administration in newborn. Literature review

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Abstract:
The most common cause of respiratory distress syndrome (RDS) in neonates born prematurely is surfactant deficiency. Surfactant administration has been the method of choice for the treatment of RDS since the 1990s, only the method of delivery is changing with the use of increasingly less invasive methods of respiratory support in neonatal respiratory failure. For many years, the standard method was the administration of surfactant after intubation through an endotracheal tube during artificial ventilation. Gradually, new methods were introduced to reduce or avoid the use of ventilation (INSURE), followed by methods that bypass intubation (LISA). The latest SALSA technique made it possible to omit the use of a laryngoscope and the need for intubation. The new methods of surfactant administration can be used successfully in newborns requiring only non-invasive respiratory support, in neonatal centers in regions with limited access to specialized medical care.

Shorts:
INSURE - INtubation, SURfactant administration and Extubation to CPAP
LISA/ LIST: Less Invasive Surfactant Administration/ Less invasive surfactant therapies
SALSA: Surfactant Administration through Laryngeal or Supraglottic Airways

Keywords: Preterm infant, surfactant, respiratory distress syndrome, noninvasive respiratory support, insure, lisa, salsa

Introduction:
Respiratory distress syndrome (RDS) is an important and most frequently diagnosed disease in preterm infants [1]. It is caused by surfactant deficiency, a fundamental substance in lung mechanics, responsible for reducing surface tension and preventing alveolar collapse during expiration. Surfactant replacement therapy plays an essential role in treatment of RDS and was established as an effective and safe therapy for immaturity-related surfactant deficiency by the early 1990s [2, 3]. The respiratory management of preterm infants with or at risk for RDS has evolved in neonatal intensive care units (NICUs) over the past decade.

Nowadays, the primary strategy to manage RDS in preterm infants relies on the application of noninvasive support, primarily nasal continuous positive airway pressure (nCPAP) and current guidelines for management of RDS recommend CPAP as the primary mode of respiratory support even in the most premature neonates [4]. However, many infants will develop RDS and require surfactant treatment. Combining a noninvasive ventilation approach with a strategy for surfactant administration is important to ensure optimal outcome, but questions remain about the optimal timing, mode of delivery and value of predictive tests for surfactant deficiency. Surfactant has traditionally been administered through an endotracheal tube as bolus. Invasive methods with airway manipulation by laryngoscopy and placement of an endotracheal tube have been performed for decades for surfactant administration.

While the strategy to intubate, give surfactant, and extubate has been widely accepted in clinical practice, newer methods of noninvasive surfactant administration, using thin catheter or laryngeal mask airway are being adopted or investigated [5,6,7] Several techniques of minimally invasive surfactant therapy have been described.

Methodology:

An electronic search was completed in PubMed database. Recommendations were extracted from the identified articles and collated as themes.

Discusson

1.INSURE: INtubation, SURfactant administration and Extubation to CPAP

It involves a combination of early surfactant supply, a short period of ventilation, followed by the use of n-CPAP as a method of respiratory support. This method has been found to reduce the need for mechanical ventilation, the duration of respiratory support, and the need for surfactant in preterm infants with respiratory distress syndrome (RDS). A meta-analysis of the results of randomized trials showed that in children requiring n-CPAP respiratory support who were intubated and given surfactant and then, after a period of brief 3-5 minutes of mechanical ventilation with a self-expanding bag, reconnected to n-CPAP, the need for mechanical ventilation was significantly less frequent compared to patients who were not given surfactant [8].

2.LISA/LIST: Less Invasive Surfactant Administration/ Less invasive surfactant therapies

A less invasive method of surfactant delivery involving the insertion of a thin catheter into the trachea under visual guidance with a laryngoscope, using Magill forceps.

Surfactant is administered to the neonate while remaining on non-invasive respiratory support, allowing treatment to be carried out without the need for intubation and mechanical ventilation. A randomized, controlled, multicenter study was conducted in 2011. where the control group was neonates with CPAP breathing support who, due to increasing symptoms of respiratory failure in the course of RDS, received surfactant therapeutically after intubation, and the study group was neonates, with CPAP breathing support, in case of an increase in oxygen demand above 30% ($FiO2 > 0.3$), received exogenous surfactant during spontaneous breathing via a thin catheter. The study showed that the use of exogenous surfactant without intubation during nCPAP significantly reduced the number of newborns requiring mechanical ventilation on postnatal day 2-3 (28% in the study group vs. 46% in the control group; $p = 0.008$). Also reduced need for mechanical ventilation: fewer neonates in the study group needed mechanical ventilation compared to the control group (33% vs 73%; $p < 0.0001$). In addition, mechanical ventilation time was reduced: Newborns in the study group were treated for a shorter time with mechanic ventilation [9]. In other randomised controlled trial (RCT) has been investigated outcomes for preterm infants with respiratory distress syndrome treated with LIST rather than administration of surfactant through an endotracheal tube. Compared to InSurE, LIST decreased the risks of bronchopulmonary dysplasia (BPD) or death and of early CPAP failure [10,11].

3.SALSA: Surfactant Administration through Laryngeal or Supraglottic Airways

In 2013, the laryngeal mask airway (LMA) has emerged as an effective method for surfactant delivery, showcasing a significantly reduces the need for intubation and mechanical ventilation in premature infants with moderate respiratory distress syndrome [13,14]. The SALSA technique differs from traditional intubation, INSURE or LISA so that there is no insertion of the tube or catheter through the vocal cords, therefore, no use of a laryngoscope. The technique involves instead a placement of a laryngeal mask into the posterior pharynx without the need of laryngoscopy. Proper placement is indicated by listening for bilateral breath sounds and, if available, color change on a carbon dioxide detector. A piece of tubing connected to the surfactant syringe is then placed into the lumen of the laryngeal mask to deliver the surfactant in aliquots just above the vocal cords. The device is simple and since it is placed without use of a laryngoscope, placement does not require a skilled health care provider. [12]. This, in turn, reduces the necessity for sedative medications. Furthermore, SALSA presents minimal contraindications, which primarily encompass maxillofacial, tracheal, or established pulmonary malformations [13].

A randomized controlled trials including infants diagnosed with RDS shows that surfactant therapy via laryngeal mask was noninferior to administration via endotracheal tube and it decreased early failures, possibly by avoiding adverse effects of premedication, laryngoscopy, and intubation. [15,16,17]

Summary: The administration of surfactant through an endotracheal tube in the treatment of respiratory distress syndrome has been the standard of care for decades. Methods of administration continue to evolve. Each of the techniques discussed in this review has safety and efficacy. However the surfactant administration procedure such as SALSA which does not require advanced skills can save lives, reduce disparities in care, and contribute to more uniform neonatal survival rates worldwide.

Disclosures

Author's contribution: Conceptualization, JG, KK; methodology, AF, AS,HG; software, EK, AM;check, AD, AK and MP; formal analysis, KK, MG, AF; investigation, AS, AK; resources, JG; data curation, AM ; writing-rough preparation, MP, AF, KK; writing-review and editing, JG, KK, HG ; visualization, EK, TD; supervision, JG; project administration, TD; receiving funding, (-). All authors have read and agreed with the published version of the manuscript.

Funding Statement

This study received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Acknowledgments

No acknowledgements.

Conflicts of Interest

The authors declare no conflict of interest.

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