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A small review on surfactant replacement therapy for neonates with respiratory distress syndrome

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Abstract

Since the early 1980s, surfactant replacement therapy (SRT) has revolutionized the treatment of neonatal respiratory distress syndrome (RDS) in premature infants, effectively addressing the surfactant deficiency associated with underdeveloped lungs. Surfactant therapy reduces alveolar surface tension, preventing lung collapse and optimizing gas exchange. Natural surfactants derived from animal sources have demonstrated superior efficacy over early protein-free synthetic surfactants, which are no longer widely available. Recent advancements include new-generation synthetic surfactants containing protein analogs that are undergoing clinical evaluation. The clinical administration of surfactants has shifted from standard endotracheal tube instillation to slightly invasive modes using thin catheters, falling the need for mechanical ventilation and related risks. Main components of surfactants, including dipalmitoylphosphatidylcholine (DPPC) and surfactant proteins (SP-A, SP-B, SP-C, SP-D), are crucial to its biophysical and immunological functions. Understanding the interaction between surfactant protein and surfactant is important for treatment of RDS. So in this mini review we have discussed about DPPC and surfactant protein interaction.

Keywords: Surfactant; neonates; Respiratory distress syndrome; Mechanical ventilation; Surfactant administration

1. Introduction

Since the early 1980s, surfactant replacement therapy (SRT) has revolutionized the treatment of neonatal respiratory distress syndrome (RDS) in premature infants, addressing their deficient surfactant production, which generally late arise in gestation [1]. Surfactant are compounds which reduce surface tension [2-6]. A loss of surfactant results in elevated surface tension, initiating the lungs to collapse and turn as stiff, making them tough to inflate. This condition, characterized via difficult breathing and hypoxemia, is known as neonatal respiratory distress syndrome (NRDS) or hyaline membrane disease. NRDS chance will increase with lowering gestational age, and it causes around 1% of all births, translating approximately 40,000 cases every year in the United States. Advances in SRT contributed crucially to decreasing NRDS mortality from 4,997 deaths in 1980 to 861 in 2005. SRT has additionally been explored in adults with acute respiratory distress syndrome (ARDS), where the surfactant system is compromised. Surfactants are compounds which contain hydrophobic and hydrophilic group in the same molecule [7-12]. Broadly surfactant can be divided in synthetic and natural surfactants [13]. For example, amino acid-based surfactants [14], which are derived from amino acids (building blocks of proteins) [15-19]. Further surfactants can be divided into anionic, cationic, amphoteric and zwitterionic surfactants [20]. Surfactant have many uses for example in agriculture, as nanotubes, in pharma industry, cosmetics and many more [21-25]. For neonates, exogenous surfactant stays a cornerstone of RDS treatment, optimizing gas exchange, lowering the risk of air leaks, and remarkably letting down mortality, its efficiency depends on factors such as timing of administration, surfactant formulation, and dosage regimen. Effective RDS management focus to deliver suitable respiratory care, minimize complications, and reduce the risk of bronchopulmonary dysplasia (BPD). Administering exogenous surfactant has been found to reduce the require for

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positive pressure ventilation, lower the trouble of pulmonary air leaks, and improve survival outcomes. Importantly, these benefits are achieved without an increase in adverse neurodevelopmental outcomes. However, several questions remain regarding the optimal use of surfactant, particularly in the context of advancements in neonatal care, including painless respiratory support after childbirth and modern way for deliver surfactant, a surface-active substance known as pulmonary surfactant coats The alveolar surfaces of vertebrate lungs, The function of PS can be generally categorized into two essential types: biophysical functions at the air-alveolar watery interactions and immunological protection opposed to infectious agents. These functions detail present in scientific reviews. To enhance the effectiveness of pulmonary surfactant formulations, particularly when they are inactivated by serum proteins like albumin, various additives have been explored. For instance, it has been shown that polymyxin B/PS mixture increase the resistance to inactivation result in substances such as meconium [26-30].

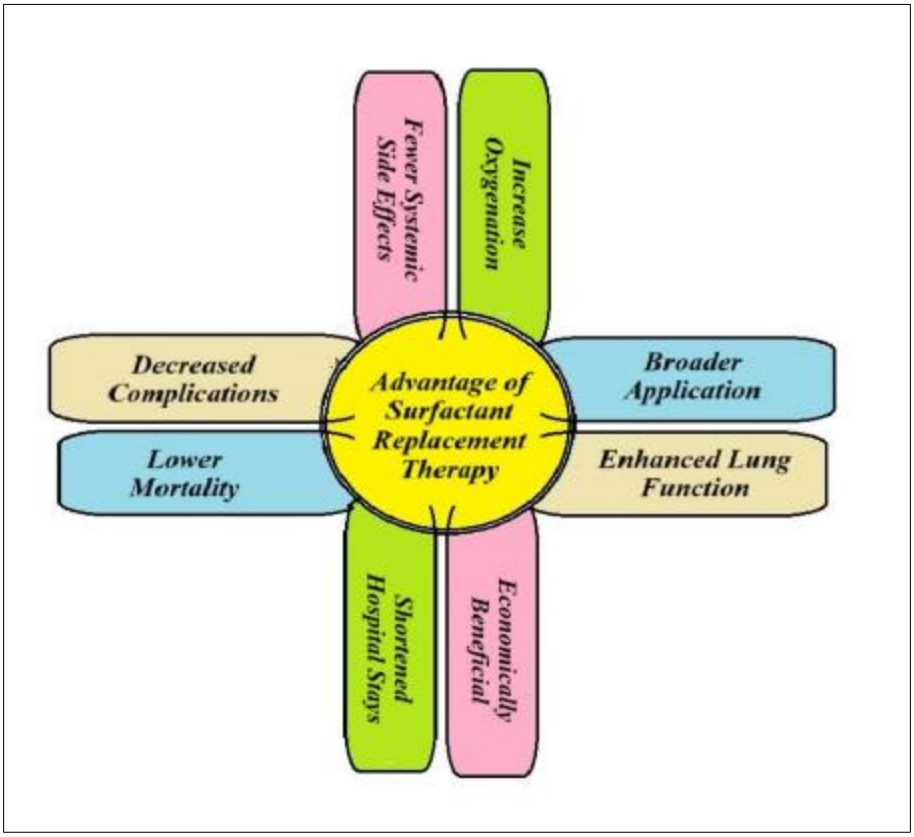

Figure 1 Advantage of surfactant replacement therapy

1.1. Surfactant Preparation

Certain surfactant preparations are approved for treating neonatal respiratory distress syndrome (RDS), though their availability varies globally. These preparations are classified as either synthetic (lab-manufactured) or natural (derived from animal lungs). Early synthetic surfactants lacked proteins, making them less effective and slower-acting than natural surfactants. Meta-analyses of clinical trials have shown that natural surfactants yield better outcomes in preterm infants with RDS, including lower rates of pneumothorax (collapsed lung) and reduced mortality. Consequently, Europe has discontinued protein-free synthetic surfactants, leaving three natural preparations in use: the bovine-derived beractant and bovactant, and the porcine-derived poractant alfa. Natural surfactants vary in efficacy. Short-term trials comparing beractant and poractant alfa as rescue treatments indicate that poractant alfa leads to faster oxygenation improvement and a trend toward lower mortality. Specifically, an initial poractant alfa dose of 200 mg/kg is associated with significantly lower mortality and reduced need for re-dosing compared to 100 mg/kg doses of either beractant or poractant alfa. However, whether these differences result from the surfactant type or dosing regimen remains unclear. Recent advancements have led to the development of next-generation synthetic surfactants containing synthetic analogs of surfactant proteins. These newer formulations outperform earlier synthetic versions. For example, lucinactant has been approved in the United States for RDS prevention, and clinical trials are ongoing for other synthetic surfactants. Surfactants primarily consist of phospholipids (90%) and proteins (10%). The predominant phospholipid is phosphatidylcholine (PC), with dipalmitoylphosphatidylcholine (DPPC) being the most abundant variant. A DPPC monolayer is essential for maintaining near-zero surface tension during alveolar compression. Four key surfactant

proteins—SP-A, SP-B, SP-C, and SP-D—play critical roles in surfactant stability and function, despite constituting only a small fraction of the molecule. In their absence, DPPC tends to form partially crystalline domains during exhalation. The large hydrophilic lectin proteins SP-A and SP-D are essential for pulmonary defense. They bind apoptotic cells in a calcium-dependent manner, enhance alveolar macrophage phagocytosis, and stimulate the production of reactive oxygen and nitrogen species to combat infections [31-36].

1.1.1. Indications for Use

- **Primary Indication**: - Surfactant replacement therapy is primarily indicated for infants diagnosed with RDS due to surfactant deficiency.
- **Other Conditions**: -It may also be used in other conditions such as:
  - Meconium aspiration syndrome
  - Acute respiratory distress syndrome (ARDS) in elderly children and adults (though this is less common).

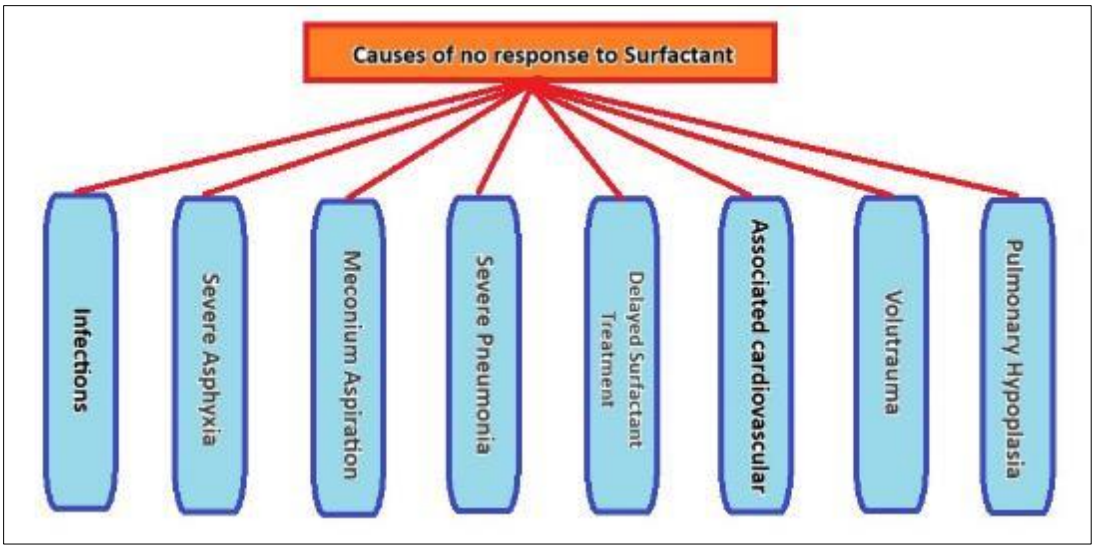

Figure 2 Diagram showing causes of no response to surfactants

1.2. Clinical practice

New modes of surfactant administration gone on examined regarding to influence on mechanical properties of the lung and gas conversation. instillation via the endotracheal tube (ETT) is the standard method to administer surfactant in the mechanically ventilated newborn with RDS. instillation via the endotracheal tube permit fast surfactant bolus application, ensuing normally in a greater homogenous surfactant circulation, as compared to gradual infusion of surfactant, as evidenced from animal studies. Surfactant Administration via a thin catheter rather than an endotracheal tube (ETT) can also integrate the avoidance of mechanical air flow with the assistances of early surfactant. The development of SRT has revolutionized neonatal care, significantly improving outcomes for infants diagnosed with RDS. The therapy involves the administration of exogenous surfactant, which can be derived from animal sources (natural surfactants) or synthesized in the laboratory (synthetic surfactants).

2. Conclusion

In conclusion, surfactant replacement therapy (SRT) has profoundly transformed the management of neonatal respiratory distress syndrome (RDS), offering a lifesaving intervention for preterm infants. Both natural and synthetic surfactant formulations have demonstrated effectiveness, with natural preparations showing superior outcomes in early studies and new-generation synthetic surfactants providing promising advancements. The therapy not only optimizes lung function but also reduces mortality and minimizes complications such as bronchopulmonary dysplasia (BPD). Additionally, novel administration techniques, including minimally invasive methods, further enhance its clinical utility. As research continues to refine surfactant compositions and delivery methods, the potential for improved respiratory care outcomes in both neonates and older patients with acute respiratory conditions continues to grow, underscoring the indispensable role of SRT in modern medicine.

References

[1] Sweet, D. G. et al. European consensus guidelines on the management of respiratory distress syndrome- 2016 update. Neonatology 111, 107–125 (2017).

[2] Rui A. Gonçalves, Krister Holmberg, Björn Lindman, Cationic surfactants: A review,Journal of Molecular Liquids,Volume 375, 2023, 121335, ISSN 0167-7322, https://doi.org/10.1016/j.molliq.2023.121335.

[3] Nafseen Ahmed, Ansari, N.H., Ali, M.S. et al. Interaction of DL-Valine/DL-Serine with Cationic and Anionic Surfactants in Aqueous Media: Volumetric, UV-visible Spectroscopic, and Conductometric Studies. Colloid J 86, 588–609 (2024). https://doi.org/10.1134/S1061933X2460009X

[4] Ali, Anwar, Ansari, Nizamul Haque, Farooq, Ummer, Tasneem, Shadma and Nabi, Firdosa. "Study of Intermolecular Interactions of CTAB with Amino Acids at Different Temperatures: A Multi Technique Approach" Zeitschrift für Physikalische Chemie, vol. 233, no. 2, 2019, pp. 167-182. https://doi.org/10.1515/zpch-2017-1070

[5] Ansari, N.H., Khan, A.A., Iqubal, S.M.S. et al. Review on conductometric, volumetric and computational studies on surfactants-amino acids interactions. J.Umm Al-Qura Univ. Appll. Sci. 10, 593–602 (2024). https://doi.org/10.1007/s43994-024-00125-1

[6] Ali, A., Ansari, N.H. Studies on the Effect of Amino Acids/Peptide on Micellization of SDS at Different Temperatures. J Surfact Deterg 13, 441–449 (2010). https://doi.org/10.1007/s11743-010-1221-8

[7] Johnson, P., Trybala, A., Starov, V., & Pinfield, V. J. (2021). Effect of synthetic surfactants on the environment and the potential for substitution by biosurfactants. Advances in colloid and interface science, 288, 102340. https://doi.org/10.1016/j.cis.2020.102340

[8] Shingda, S.R., Ali, P.S., Gandhare, N.V., Pathan, N.B., and Ansari, N.H. (2021). Investigation of mechanistic interactions between Rifampicin and bovine serium albumin in the presence of different surfactants. Journal of dispersion science and technology, 44 (6), 1075-1084. https://doi.org/10.1080/01932691.2021.1997759

[9] Ali, Anwar, Itoo, Firdoos Ahmad and Ansari, Nizamul Haque. "Interaction of Some Amino Acids with Sodium Dodecyl Sulphate in Aqueous Solution at Different Temperatures" Zeitschrift für Naturforschung A, vol. 66, no. 5, 2011, pp. 345-352. https://doi.org/10.1515/zna-2011-0511

[10] Ali, A., Ansari, N.H., Farooq, U. et al. Interaction of Glycylglycine with Cationic Surfactants—Cetylpyridinium Chloride and Cetylpyridinium Bromide: A Volumetric, Ultrasonic and Conductometric Study. Int J Thermophys 39, 107 (2018). https://doi.org/10.1007/s10765-018-2426-8

[11] Ali, A., Shahjahan & Ansari, N.H. Density and viscosity of α-amino acids in aqueous solutions of cetyltrimethylammonium bromide. Russ Chem Bull 59, 1999–2004 (2010). https://doi.org/10.1007/s11172-010-0346-2

[12] Badmus SO, Amusa HK, Oyehan TA, Saleh TA. Environmental risks and toxicity of surfactants: overview of analysis, assessment, and remediation techniques. Environ Sci Pollut Res Int. 2021 Nov;28(44):62085-62104. doi: 10.1007/s11356-021-16483-w. Epub 2021 Sep 29. PMID: 34590224; PMCID: PMC8480275.

[13] Nizamul Haque Ansari, Shahid, S., Khan, M.S. et al. Amino Acid-Based Biosurfactants: Promising and Ecofriendly Biomolecules for Attaining Sustainable Agriculture and Environmental Safety. Colloid J (2025). https://doi.org/10.1134/S1061933X24601021.

[14] María Rosa Infante, Lourdes Pérez, Aurora Pinazo, Pere Clapés, María Carmen Morán, Marta Angelet, María Teresa García, María Pilar Vinardell, Amino acid-based surfactants, Comptes Rendus Chimie, Volume 7, Issues 6–7, 2004, Pages 583-592, ISSN 1631-0748, https://doi.org/10.1016/j.crci.2004.02.009.

[15] Ling, ZN., Jiang, YF., Ru, JN. et al. Amino acid metabolism in health and disease. Sig Transduct Target Ther 8, 345 (2023). https://doi.org/10.1038/s41392-023-01569-3

[16] Ali, A., Patel, R., Shahjahan, Bhushan, V., & Haque Ansari, N. (2012). Physical Chemistry-Volumetric, viscometric and refractometric studies of glycine, alanine, valine and glycylglycine in aquo-sucrose solution at different temperatures. Journal of the Indian Chemical Society, 89(10), 1335.

[17] Ali, A., Patel, R., Shahjahan et al. Physicochemical Behavior of Some Amino Acids/Glycylglycine in Aqueous D-Galactose Solutions at Different Temperatures. Int J Thermophys 31, 572–584 (2010). https://doi.org/10.1007/s10765-010-0742-8

[18] Nizamul Haque Ansari, Significance of amino acids as plant bio-stimulant, Agro Science Today, 5 (6), 0902 – 0908, 2024.

[19] Zhang, S., Zeng, X., Ren, M. et al. Novel metabolic and physiological functions of branched chain amino acids: a review. J Animal Sci Biotechnol 8, 10 (2017). https://doi.org/10.1186/s40104-016-0139-z

[20] Shumaila Shahid, Nizamul Haque Ansari, Farah Akhtar Khan, Mohd Shoeb Khan and Navaid Zafar Rizvi, Surfactants as adjuvants in agriculture, Food and Scientific Reports, 6(1): 51-54, 2025.

[21] Sam Maher, Caroline Geoghegan, David J. Brayden, Safety of surfactant excipients in oral drug formulations, Advanced Drug Delivery Reviews, Volume 202, 2023, 115086, ISSN 0169-409X, https://doi.org/10.1016/j.addr.2023.115086.

[22] Shumaila Shahid, Brij Bihari, Akil Ahmed Khan and Nizamul Haque Ansari, Management of plant diseases by surfactants, International Journal of tropical Agriculture, Vol. No.41, 1-2, 121-127, 2023.

[23] Nizamul Haque Ansari, Role of Surfactant in Dispersion of Carbon Nano Tubes to Use as Reinforcing Material for Biodegradable Nano Composites, Physical Science and Biophysics Journal, 7 (2), 2023, DOI: 10.23880/psbj-16000254.(Editorial)

[24] Nizamul Haque Ansari, Shumaila Shahid, Mohd Shoeb Khan, Organosilicone Compounds in Agriculture, Sun. Agri., e- Newsletter, 4(12), 10-13, 2024.

[25] Kumar, N.; Tyagi, R. Dimeric Surfactants: Promising Ingredients of Cosmetics and Toiletries. Cosmetics 2014, 1, 3-13. https://doi.org/10.3390/cosmetics1010003

[26] Perez-Gil,J.; Keough,K.M.W.Biochim.Biophys.Acta1998,1408,203–217.

[27] Batenburg, J. J.; Haagsman, H. P. Prog. Lipid Res. 1998, 37, 235–276.

[28] Cochrane, C. G. Am. J. Physiol. 2005, 288, L608–L609.

[29] Perez-Gil, J. Biochim. Biophys. Acta 2008, 1778, 1676–1695.

[30] Notter, R. H. Lung surfactants: Basic science and clinical applications, 149th ed.; Marcel Dekker, Inc.: New York, 2000; pp 1-444.

[31] Soll RF, Blanco F. Natural surfactant extract versus synthetic surfactant for neonatal respiratory distress syndrome. Cochrane Database Syst Rev 2001;2:CD000144.

[32] Speer CP, Sweet DG. Surfactant replacement: present and future. In: Bancalari E, ed. The Newborn Lung. 2nd ed. Philadelphia, PA: Elsevier Saunders; 2012:283–99.

[33] Jordan BK, Donn SM. Lucinactant for the prevention of respiratory distress syndrome in premature infants. Expert Rev Clin Pharmacol 2013;6:115–21.

[34] Seurynck-Servoss SL, Brown NJ, Dohm MT, Wu CW, Barron AE. Lipid composition greatly affects the in vitro surface activity of lung surfactant protein mimics. Colloids Surf B Biointerfaces. 2007; 57:37–55. doi: 10.1016/j.colsurfb.2007.01.001. [DOI] [PubMed] [Google Scholar]

[35] Gerber F, Krafft MP, Vandamme TF, Goldmann M, Fontaine P. Potential use of fluorocarbons in lung surfactant therapy. Artif Cells Blood Substit Immobil Biotechnol. 2007;35:211–20. doi: 10.1080/10731190601188307. [DOI] [PubMed] [Google Scholar]

[36] Sano H, Kuroki Y. The lung collectins, SP-A and SP-D, modulate pulmonary innate immunity. Mol Immunol. 2005;42:279–87. doi: 10.1016/j.molimm.2004.07.014. [DOI] [PubMed] [Google Scholar]