**IAP - IJPP CME 2018**

# SURFACTANT THERAPY- EVOLUTION AND NEWER TRENDS

*Giridhar Sethuraman
**Sasi Bhushan Gottimukkala

**Abstract:** *Respiratory distress syndrome is an important cause of mortality in preterm babies and surfactant replacement therapy forms an important part of its treatment. However, recent studies have shown that very early administration of continuous positive airway pressure and selective rescue surfactant administration, in extremely preterm infants, increases survival and reduces bronchopulmonary dysplasia, when compared to early intubation and surfactant administration. Less invasive methods of surfactant instillation in spontaneously breathing infants, avoiding intubation and mechanical ventilation are being explored. Also newer synthetic surfactants and surfactant-drug combinations are being studied to improve efficacy and reduce bronchopulmonary dysplasia.*

**Keywords:** *Surfactant, Respiratory distress syndrome, Preterm, Bronchopulmonary dysplasia.*

* Associate Professor of Neonatology

** DM Postgraduate - Neonatology,
Chettinad Hospital and Research Institute,
Kanchipuram, Tamil Nadu.

email: giridharsethu@gmail.com

## Points to Remember

- ***Surfactant replacement therapy should be considered for all preterm infants with RDS.***
- ***Natural surfactant preparations are preferred over synthetic preparations.***
- ***Early rescue surfactant therapy should be considered for babies <26 weeks' gestation when $FiO_2$ requirements >0.3 and >26 weeks' when $FiO_2$ requirements >0.4.***
- ***Newer surfactant administration methods (LISA/ MIST) may be preferred over INSURE for surfactant administration. However the best minimally invasive method of surfactant administration is yet to be identified.***
- ***Antenatal steroids work additively with postnatal surfactant and is recommended in all pregnancies with threatened preterm labour <34 weeks' gestation.***

## References

1. Gruenwald P. Surface tension as a factor in the resistance of neonatal lungs to aeration. Am J Obstet Gynecol 1947; 53:996-1007.
2. Pattle RE. Properties, function and origin of the alveolar lining layer. Nature 1955; 175: 1125-1126.
3. Clements JA, Brown ES, Johnson RP. Pulmonary surface tension and the mucus lining of the lungs: some theoretical considerations. J Appl Physiol 1958; 12:262-268.
4. Avery ME, Mead J. Surface properties in relation to atelectasis and hyaline membrane disease. AMA J Dis Child 1959; 97:517-523.
5. Enhorning G, Robertson B. Lung expansion in the premature rabbit fetus after tracheal deposition of surfactant. Pediatrics 1972; 50:58-66.
6. Jobe A, Ikegami M, Glatz T, Yoshida Y, Diakomanolis E, Padbury J. Duration and characteristics of treatment of premature lambs with natural surfactant. J Clin Invest 1981; 67:370-375.
7. Fujiwara T, Maeta H, Chida S, Morita T, Watabe Y, Abe T. Artificial surfactant therapy in hyaline-membrane disease. Lancet 1980; 1:55-59.

8. Soll RF, Blanco F. Natural surfactant extract versus synthetic surfactant for neonatal respiratory distress syndrome. Cochrane Database Syst Rev. 2001; (2):CD000144.
9. Sinha SK, Lacaze-Masmonteil T, Valls i Soler A, Wiswell TE, Gadzinowski J, Hajdu J, et al; Surfaxin Therapy Against Respiratory Distress Syndrome Collaborative Group. A multicenter, randomized, controlled trial of lucinactant versus poractant alfa among very premature infants at high risk for respiratory distress syndrome. Pediatrics. 2005; 115(4):1030-1038.
10. Moya F, Sinha S, Gadzinowski J, D'Agostino R, Segal R, Guardia C, et al; SELECT and STAR Study Investigators. One year follow-up of very preterm infants who received lucinactant for prevention of respiratory distress syndrome: results from 2 multicenter randomized, controlled trials. Pediatrics 2007; 119(6)%: e1361-70. Epub 2007 May 28.
11. Ricci F, Murgia X, Razzetti R, Pelizzi N, Salomone F. In vitro and in vivo comparison between poractant alfa and the new generation synthetic surfactant CHF5633. Pediatr Res. 2017 Feb; 81(2):369-375.
12. Ramanathan R, Rasmussen MR, Gerstmann DR, Finer N, Sekar K, North American Study G. A randomized, multicenter masked comparison trial of poractant alfa (Curosurf) versus beractant (Survanta) in the treatment of respiratory distress syndrome in preterm infants. Am J Perinatol 2004; 21:109-119.
13. Ardell S, Pfister RH, Soll R. Animal derived surfactant extract versus protein free synthetic surfactant for the prevention and treatment of respiratory distress syndrome. Cochrane Database Syst Rev 2015; 8:CD000144.
14. Soll R, Ozek E. Multiple versus single doses of exogenous surfactant for the prevention or treatment of neonatal respiratory distress syndrome. Cochrane Database Syst Rev 2009; (1):CD000141.
15. Robillard E, Alarie Y, Dagenais-Perusse P, Baril E, Guilbeault A. Microaerosol administration of synthetic beta-gammadipalmitoyl- L-alpha-lecithin in the respiratory distress syndrome: a preliminary report. Can Med Assoc J 1964; 90:55-57.
16. Verder H, Robertson B, Greisen G, Ebbesen F, Albertsen P, Lundstrom K, et al. Surfactant therapy and nasal continuous positive airway pressure for newborns with respiratory distress syndrome. Danish-Swedish Multicenter Study Group. N Engl J Med 1994; 331:1051-1055.
17. Dunn MS, Kaempf J, de Klerk A, de Klerk R, Reilly M, Howard D, et al; Vermont Oxford Network DRM Study Group: Randomized trial comparing 3 approaches to the initial respiratory management of preterm neonates. Pediatrics 2011; 128:e1069-e1076.
18. Rojas MA, Lozano JM, Rojas MX, Laughon M, Bose CL, Rondon MA, Charry L, et al; Colombian Neonatal Research Network: Very early surfactant without mandatory ventilation in premature infants treated with early continuous positive airway pressure: a randomized, controlled trial. Pediatrics 2009; 123:137-142.
19. Sandri F, Plavka R, Ancora G, Simeoni U, Stranak Z, Martinelli, et al. Prophylactic or early selective surfactant combined with nCPAP in very preterm infants. Pediatrics 2010; 125:e1402-e1409.
20. Isayama T, Chai-Adisaksopha C, McDonald SD. Noninvasive ventilation with vs without early surfactant to prevent chronic lung disease in preterm infants: a systematic review and meta-analysis. JAMA Pediatr 2015; 169:731-739.
21. Kribs A, Pillekamp F, Hunseler C, Vierzig A, Roth B: Early administration of surfactant in spontaneous breathing with nCPAP: feasibility and outcome in extremely premature infants (postmenstrual age d"27 weeks). PaediatrAnaest 2007; 17:364-369.
22. Dargaville PA, Aiyappan A, Cornelius A, Williams C, De Paoli AG: Preliminary evaluation of a new technique of minimally invasive surfactant therapy. Arch Dis Child Fetal Neonatal Ed 2011; 96:F243-F248.
23. Kanmaz HG, Erdeve O, Canpolat FE, Mutlu B, Dilmen U. Surfactant administration via thin catheter during spontaneous breathing: randomized controlled trial. Pediatrics 2013; 131(2):e502-e509.
24. Aguar M, Cernada M, Brugada M, Gimeno A, Gutierrez A, Vento M. Minimally invasive surfactant therapy with a gastric tube is as effective as the intubation, surfactant, and extubation technique in preterm babies. Acta Paediatr 2014; 103:e229–e233.
25. Aldana-Aguirre JC, Pinto M, Featherstone RM, Kumar M: Less invasive surfactant administration versus intubation for surfactant delivery in preterm infants with respiratory distress syndrome: a systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed 2017; 102:F17-F23.
26. Rigo V, Lefebvre C, Broux I: Surfactant instillation in spontaneously breathing preterm infants: a systematic review and meta-analysis. Eur J Pediatr 2016; 175:1933-1942.
27. Isayama T, Chai-Adisaksopha C, McDonald SD Noninvasive Ventilation With vs Without Early Surfactant to Prevent Chronic Lung Disease in Preterm Infants: A Systematic Review and Meta-analysis. JAMA Pediatr. 2015; 169(8):731-739.
28. Gopel W, Kribs A, Ziegler A, Laux R, Hoehn T, Wieg C, et al. Avoidance of mechanical ventilation by surfactant treatment of spontaneously breathing preterm infants (AMV): an openlabel, randomised, controlled trial. Lancet 2011; 378:1627-1634.
29. Kribs A, Hartel C, Kattner E, Vochem M, Kuster H, Moller J, et al. Surfactant without intubation in preterm infants with respiratory distress: First multi-center data. Klin Padiatr 2010; 222:13-17.

30. Minocchieri S, Berry CA, Pillow JJ; CureNeb Study Team. Nebulised surfactant to reduce severity of respiratory distress: a blinded, parallel, randomised controlled trial. Arch Dis Child Fetal Neonatal Ed. 2018 Jul 26. [Epub ahead of print]
31. Abdel-Latif ME, Osborn DA, Pharyngeal instillation of surfactant before the first breath for prevention of morbidity and mortality in preterm infants at risk of respiratory distress syndrome. Cochrane Database Syst Rev. 2011 Mar 16; (3):CD008311.
32. Brimacombe J, Gandini D, Keller C: The laryngeal mask airway for administration of surfactant in two neonates with respiratory distress syndrome. PaediatrAnaes 2004; 14:188-190.
33. Pinheiro JM, Santana-Rivas Q, Pezzano C: Randomized trial of laryngeal mask airway versus endotracheal intubation for surfactant delivery. J Perinatol 2016; 36: 196-201.
34. Vannozzi I, Ciantelli M, Moscuzza F, Scaramuzzo RT, Panizza D, Sigali E, Boldrini A, Cuttano A. Catheter and Laryngeal Mask Endotracheal Surfactant Therapy: the CALMEST approach as a novel MIST technique. J Matern Fetal Neonatal Med. 2017 Oct; 30(19):2375-2377.
35. 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.
36. Morley CJ, Davis PG, Doyle LW, Brion LP, Hascoet JM, Carlin JB, Investigators CT: Nasal CPAP or intubation at birth for very preterm infants. N Engl J Med 2008; 358:700-708.
37. SUPPORT Study Group of the Eunice Shriver NICHD Neonatal Research Network: Early CPAP versus surfactant in extremely preterm infants. N Engl J Med 2010; 362:1970-1979.
38. Rojas-Reyes MX, Morley CJ, Soll R. Prophylactic versus selective use of surfactant in preventing morbidity and mortality in preterm infants. Cochrane Database Syst Rev 2012; 3(3):CD000510.
39. Bahadue FL, Soll R. Early versus delayed selective surfactant treatment for neonatal respiratory distress syndrome. Cochrane Database Syst Rev 2012; 11(11):CD001456.
40. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Plavka R, et al. European consensus guidelines on the management of respiratory distress syndrome – 2016 update. Neonatology 2017; 111:107-125.
41. Venkataraman R, Kamaluddeen M, Hasan SU, Robertson HL, Lodha A. Intratracheal Administration of Budesonide - Surfactant in Prevention of Bronchopulmonary Dysplasia in Very Low Birth Weight Infants: A Systematic Review and Meta-Analysis. Pediatr Pulmonol 2017; 52(7):968-975.
42. El Shahed AI, Dargaville PA, Ohlsson A, Soll R. Surfactant for meconium aspiration syndrome in term and late preterm infants. Cochrane Database Syst Rev 2014 Dec 14; (12):CD002054.
43. Hahn S, Choi HJ, Soll R, Dargaville PA. Lung lavage for meconium aspiration syndrome in newborn infants. Cochrane Database Syst Rev. 2013 Apr 30; (4):CD003486.
44. Choi HJ, Hahn S, Lee J, Park BJ, Lee SM, Kim HS, Bae CW. Surfactant lavage therapy for meconium aspiration syndrome: a systematic review and meta-analysis. Neonatology. 2012; 101(3):183-191
45. Bandiya P, Nangia S, Saili A.Surfactant Lung Lavage vs. Standard Care in the Treatment of Meconium Aspiration Syndrome-A Randomized Trial. J Trop Pediatr. 2018 Jun 6. [Epub ahead of print].