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Clinical Pearl: Inhaled Budesonide with Surfactant Decreases BPD Rates Without Affecting Neurodevelopmental Outcomes

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Since Bronchopulmonary Dysplasia (BPD) was first described over 50 years ago, we have made significant progress in understanding its pathophysiology, risk factors, prevention, and management. Nevertheless, BPD remains one of the most common and devastating chronic medical conditions faced by premature infants, with incidence rates ranging between 15-35% among infants born before 32 weeks gestation (1).

Recently, the use of budesonide with surfactant has been shown to decrease BPD rates and severity (2). It has been suggested that surfactant administration facilitates the delivery of other medications, including budesonide (3). However, budesonide has been detected at high levels in plasma within 15 minutes of intratracheal administration in preterm sheep, with levels gradually decreasing but still detectable by 24 hours after administration (4). Studies on human infants have also shown that inhaled budesonide is absorbed into the circulation, with an estimated elimination half-life of 4 hours. (3) Given that steroid use in premature infants has a well-known association with adverse neurodevelopmental outcomes, it is crucial to evaluate the long-term, systemic effects of inhaled corticosteroids in this group of patients. Outcome data was evaluated in a recent observational study by Anderson et al. (5).

The authors analyzed data from the neonatal intensive care unit at the Saint Louis University and SSM Health Cardinal Glennon Children's Hospital after a clinical practice change in 2016, administering intratracheal budesonide combined with pulmonary surfactant in all infants born at birth weight at or below 1,250g who failed an initial CPAP trial within the first 24 hours of postnatal life or were intubated in the delivery room. The authors compared the infants who received the combination of surfactant and budesonide between 2016-2018 to a historical cohort of infants who received surfactant alone between 2013-2016, looking into data of 470 infants. There was statistically less severe type 2 and 3 BPD in the surfactant and budesonide group ($p < 0.03$ and $p < 0.02$, respectively (5). The patients were monitored in the outpatient setting and evaluated with the Peabody Developmental Motor Scales II at 4-6 months corrected age and Bayley Scales of Infant and Toddler development III at 18-22 months corrected age. The comparison of results revealed no significant differences between the two groups. Additionally, the number of hospitalizations and emergency room visits were similar, with less use of nebulized albuterol in patients who received surfactant and budesonide.

What is worth noting, both BPD and the use of postnatal steroids carry the risk of adverse neurological outcomes (6). Therefore, one could argue that using corticosteroids in patients with more severe RDS appears to have a more reasonable risk-to-benefit ratio. The authors cite data by Yeh et al., who demonstrated a significant decrease in BPD rates from 50% to 29% using budesonide and surfactant, and did not show significant differences in neurodevelopmental outcomes when comparing to infants treated with surfactant alone (3). The data presented by Anderson et al. provide additional value as the cohort of infants included in their study had less severe RDS, potentially advocating for inhaled corticosteroids with surfactant in premature infants regardless of RDS severity.

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More data is still needed to help develop specific guidelines regarding this mode of therapy, and, as the authors point out, large, randomized trials are underway (7,8). However, the data presented by Anderson et al. are certainly very encouraging from a safety perspective. Combined with the available studies on the impact of budesonide/surfactant therapy on rates of BPD, we will hopefully be able to implement this promising treatment as a standard of care across the country, pending larger clinical trial results.

References:

1. *Bonadies L, Zaramella P, Porzionato A, Perilongo G, Muraca M, Baraldi E. Present and Future of Bronchopulmonary Dysplasia. J Clin Med. 2020;9(5):1539. Published 2020 May 20. doi:10.3390/jcm9051539*
2. *Kothe TB, Sadiq FH, Burleyson N, Williams HL et al. Surfactant and budesonide for respiratory distress syndrome: An observational study. Pediatr Res 2020;87: 940-945.*
3. *Yeh TF, Chen CM, Wu SY, Husan Z, Li TC, Hsieh WS, et al. Intratracheal administration of budesonide/surfactant to prevent bronchopulmonary dysplasia. Am J Respir Crit Care Med. 2016;193:86–95.*
4. *Kothe TB, Royse E, Kemp MW, Schmidt A, Salomone F, Saito M, Usuda H, Watanabe S, Musk GC, Jobe AH, Hillman NH. Effects of budesonide and surfactant in preterm fetal sheep. Am J Physiol Lung Cell Mol Physiol. 2018 Aug*

1;315(2):L193-L201. doi: 10.1152/ajplung.00528.2017. Epub 2018 Apr 19. PMID: 29671605; PMCID: PMC6139660.

5. *Anderson CD, Kothe TB, Josephsen JB, Sadiq FH, Burleyson N, Williams HL, Hillman NH. Budesonide mixed with surfactant did not affect neurodevelopmental outcomes at 6 or 18 months corrected age in observational cohorts. J Perinatol. 2021 Jul;41(7):1681-1689. doi: 10.1038/s41372-021-01066-x. Epub 2021 May 13. PMID: 33986470; PMCID: PMC8117121.*
6. *Doyle LW, Cheong JL, Ehrenkranz RA, Halliday HL. Early (< 8 days) systemic postnatal corticosteroids for prevention of bronchopulmonary dysplasia in preterm infants. Cochrane Database Syst Rev. 2017;10:CD001146.*
7. *NICHD Bude- sonide in Babies (BiB) trial (NCT04545866)*
8. *Preventing Chronic Lung Disease in Extremely Preterm Infants Using Surfactant + Steroid (PLUSS) (ACTRB12617000322)*

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