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Literature Review: Role of Budesonide with Surfactant on Preterm Infants

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Abstract

This review analyzes the advocacy of budesonide-booster and surfactant in treating respiratory disorders in preterm neonates. Premature labor leads to respiratory distress syndrome [RDS] because of inadequate surfactant production and immature lungs, which in turn raises the probability of chronic lung disorders like BPD. However, while promoting lung function and oxygenation as provided in exogenous surfactant therapy is effective, it does not meet the processes causing inflammation to reduce pulmonary complications in the long run. Budesonide, a highly selective anti-inflammatory glucocorticosteroid, can be used as an adjuvant to surfactant treatment because of its ability to act on the lungs with minimal systemic effects directly. Studies from PubMed and Embase also show that when combined, budesonide and surfactant have beneficial effects in decreasing the severity of RDS, enhancing lung function, and reducing the prevalence of BPD in premature infants. However, these promising results should be further investigated in terms of the determination of optimal dosing, administration time, and therapeutic application concerning safety issues in the long term. This combined strategy has valuable prospects for enhancing the respiratory prognosis in premature newborns.

Keywords: Budesonide; surfactant therapy; respiratory distress syndrome; preterm infants; bronchopulmonary dysplasia; inflammation.

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1. Introduction

Preterm birth, which is birth before 37 completed weeks of pregnancy, is a significant source of neonatal morbidity and mortality all over the world. One of the most severe concomitants of preterm birth is respiratory distress syndrome [RDS] due to surfactant deficiency and immaturity of the lungs, alveolar collapse, impaired gas exchange, as well as hypoxemia. Exogenous surfactant therapy started in the 1980s and has significantly impacted newborns' health by improving lung elasticity and oxygenation [1]. Nonetheless, surfactant therapy fails to treat inflammation arising from MV, oxidative stress, and infection associated with chronic lung disorders such as bronchopulmonary dysplasia [BPD]. Budesonide is a synthetic corticosteroid with a strong anti-inflammatory effect, and it is beneficial as an adjuvant treatment when used with a surfactant [2]. Intratracheally administered, budesonide reduces total body exposure but reduces inflammation in the lungs. This combination therapy is expected to enhance respiratory parameters and decrease the incidence of BPD, thus becoming an area of interest.

2. Literature Review

2.1 Surfactant Therapy in Preterm Infants

Surfactant therapy has been an important therapeutic modality in the management of respiratory distress syndrome [RDS] in preterm neonates since the 1980s. Intratracheal exogenous surfactant role is to decrease the surface tension in the alveoli, thus preventing their collapse and ensuring uniform lung inflation [3]. Due to its lipid-protein feature, it can effectively distribute across alveolar surfaces in NICU neonates with immature lungs, enhancing lung compliance and oxygenation [4]. The clinical analyses show that the surfactant treatment decreases neonatal and pediatric mortality and the rate of mechanical ventilation, thus leading to better short-term outcomes [4]. However, surfactants are less effective in inflammation and oxidative stress elicited by MV, oxygen toxicity, and infection [5]. Surfactant molecules are subjected to proteolytic enzymes and reactive oxygen species' actions that reduce their effectiveness and overall beneficial results [6]. Furthermore, surfactants fail to capture the inflammogenic or initiating factor pivotal to developing chronic lung conditions such as BPD.

Although the mortality rate in premature infants has declined through improved neonatal intensive care, chronic lung disease remains a constant challenge, thus demanding the use of add-on therapies for inflammation. Surfactant therapy, while stabilizing the lungs, does not limit principally the voloturated-induced lung injury/ systemic inflammatory response syndrome [7]. Nevertheless, the offered limitations underscore the necessity of new approaches that will integrate surfactants for their biophysical properties, along with active drugs to address inflammation. The synergy of the surfactant along with budesonide is a landmark innovation that targets both architectural and inflammatory issues in preterm lungs [8].

2.2 Budesonide: Mechanism and Role in Neonatal Care

Budesonide is a corticosteroid drug whose primary mechanism is asthma and COPD. It reduces the activity of moieties such as NF-κB, which controls the outputs of inflammation mediators and cytokines [9]. Furthermore, budesonide reduces lung inflammation by stabilizing the cell membrane, decreases vascular permeability, and uncovers the property of preventing pulmonary edema [10]. While budesonide delivered intratracheally affects

many tissues in the body, including those outside the lungs, only pulmonary tissues are targeted and modified by budesonide, making intratracheal budesonide efficient in controlling inflammation with minimal adverse consequences [11]. This kind of delivery is especially beneficial in Pthag, explained by the high sensitivity of preterm to systemic CST, which can cause adrenal suppression, growth retardation, and neurodevelopmental delays [11].

Interest has been placed on budesonide in neonatal care since it can prevent chronic disease that entails arrested lung growth accompanied by inflammation [12]. In particular, the inhaled application of budesonide had a therapeutic and preventative effect on inflammatory injury and respiratory outcome measures [13]. Specifically, there are clinical and preclinical reports on its capacity to suppress cytokine release, decrease indices of lung damage, and promote alveolarization in preterm neonates. Despite BPD prevention potential, side effects of systemic corticosteroids have been a concern. Thus, a localized therapy of intratracheal budesonide is a safer approach [14].

2.3 Theoretical Rationale for Combining Budesonide with Surfactant

This combination therapy solely relies on the synergistic effect of budesonide and surfactant in treating RDS's structural and inflammatory features. Surfactant reduces alveolar surface tension to promote lung expansion, enhance oxygenation, and decrease the composition of pulmonary oxygen index and inspiratory-to-expiratory pressure ratio besides mean airway pressure, while budesonide inhibits inflammatory cytokines involved in VILI and BPD development [15]. This strategy helps the clinicians get maximal advantages from the surfactant treatment with minimal harm from residual inflammation, which is a significant drawback of surfactant-alone treatment [16]. Intratracheal administration of budesonide and surfactant was shown through previous preclinical models to decrease inflammatory biomarkers, improve lung function, and increase mortality rates versus surfactant alone [17]. In humans, clinical trial studies have found that this combination enhances oxygenation, decreases the duration of ventilation, and decreases the odds of BPD in preterm infants. A study conducted a large sample randomized controlled trial and found that budesonide–surfactant prevented BPD, reducing its risk factors while being safe for preterm neonates [18]. However, the study design, sample size, and dosing regimen are diverse, and further research is needed to optimize this therapy and prove its effectiveness.

2.4 Clinical Evidence and Safety Considerations

Clinical trials regarding the concurrent use of budesonide and surfactant in preterm infants have not been discouraging. The meta-analyses have strong evidence to support that this approach decreases the time on MV, oxygen needs, and BPD rates [19]. Enhancing efficiency in the basic human need for oxygen and general lung functionality, such as results, further endorses combining therapy, especially within the neonatal intensive care unit [20]. Notably, budesonide targeting the lungs and other parts of the airway receives limited systemic absorption, thereby being safer in causing effects such as adrenal suppression, growth impairment, and neurodevelopmental delays [21]. Nevertheless, optimizing safety considerations could be a challenging task in which these promising findings might be helpful. Although short-term effects seem beneficial, the impact of intratracheal budesonide on growth, immunity, and the endocrine system, in the long run, remains uncertain [22].

Subgroup analyses are needed to examine overall developmental progress in survivors since preterm infants are susceptible to systemic corticosteroids' adverse effects. Also, differences in dose, timing of intervention administration, and patient inclusion lead to the requirement for more extensive, multisite trials for better standardization of protocol and generalization of outcomes [23].

3. Results

The research investigated the results of adding intratracheal budesonide to surfactant treatment in preterm newborns with RDS. Studies showed better short-term lung function and body physiology alongside longer-term clinical outcomes than aerosolized surfactant alone. Oxygenation escalations were facilitated after the treatment, showing improved arterial oxygen levels and reduced oxygen dependence. Combined therapy was also applied in the infants, who, compared to all other groups, had significantly reduced time on mechanical ventilation and lower demand for supplemental oxygen, reflecting improved lung compliance and adequate gas exchange. Concerning chronic lung disease, there was an impressive reduction in bronchopulmonary dysplasia [BPD] among the babies receiving budesonide-surfactant. This result indicates that the synergistic effect of the combined therapy in preventing inflammation-related lung injury, one of the primary causes of BPD, is applicable [16]. Biomarker analysis also read that the IF-IT study confirmed that infants treated with budesonide-surfactant tended to have a lower concentration of pro-inflammatory cytokines, including the IL-6 and TNF-α, than the control.

Similar safety evaluation studies revealed minimal risk attributed to intratracheal budesonide administration. Systemic corticosteroid adverse effects, including adrenal suppression or growth retardation, had no statistically meaningful differences between the treated and placebo groups [7]. Subsequent data on neurodevelopmental outcomes did not demonstrate any difference in the development of developmental delays in infants who took the combined therapy. Furthermore, the study also showed how important timing was in the administration process in determining the best results. The advantage of starting the budesonide-surfactant regimen shortly after birth, within the first hours of life, was greater effectiveness in terms of respiratory stabilization and lower rates of ventilator dependence for more extended periods [14].

4. Discussion

Pulmonary surfactant and budesonide treatment are attractive management approaches in the prevention of respiratory morbidity in preterm infants with RDS. This dual approach utilizes the biophysical properties of surfactant for alveolar mechanical stability and addresses a chief factor causing chronic lung injury [24]. The results prove the proposal that if this combined therapy is initiated early, BPD, one of the most frequent postnatal complications in premature infants, is minimized. It reduces inflammatory cytokine production, inhibiting the side effects of mechanical ventilation and oxygen toxicity that tend to aggravate lung injury and development. The effectiveness of this combination therapy results from the combined effect of both agents in the mechanism described above. While surfactant raises the alveolar surface tension and increases oxygenation, budesonide inhibits IL-6 and TNF-α, reduces the action of free radicals, and supports tissue repair [25]. Intratracheal delivery of budesonide has an advantage in that only the drug is delivered to the lung site, reducing the overall inhalation of systemic corticosteroids and their side effects. This targeted delivery minimizes risks such as adrenal

suppression, growth inhibition, and immune suppression, which are inconveniences associated with systemic steroids.

Thus, the efficacy of the combined therapy has been confirmed in clinical practice by the decrease in MV and oxygen dependence, which are critical measures of the patient's pulmonary performance. However, the identified lower frequency of BPD means that this approach will significantly decrease the prevalence of chronic respiratory diseases in preterm infants [18]. However, differences in study designs, dosing regimens, and sample sizes underscore the cruciality of standard operating procedures for enhancing treatment effects. Nevertheless, an important issue is the safety of this approach, which needs long-term outcome follow-up. No adverse effects were reported in current investigations, but further investigation of short- and long-term effects on neurodevelopment, endocrine function, and growth is warranted. Further, the period at which budesonide must be given and the dose that must be given at that remarkable period are critical to helping patients get the most out of budesonide without side effects.

5. Conclusion

In conclusion, the combination of budesonide and surfactant therapy presents a promising approach to improving respiratory outcomes in preterm infants with respiratory distress syndrome [RDS]. This dual therapy targets both structural and inflammatory aspects of lung damage, decreasing the risk of BPD and improving short-term pulmonary outcomes. Clinical trials also put it to work effectively: effects increase oxygenation, decrease the duration of mechanical ventilation, and reduce oxygen dependence. Further, due to the local delivery of budesonide, the systemic exposition of corticosteroids is reduced, and a comparatively safer method than conventional methods is available. However, these positive findings call for better studies to determine the optimal dosing regimen, the best time for administration, and long-term adverse effects. The synergy of budesonide and surfactant can transform the management of preterm new-borns born with BPD and enhance their lifespan and quality of life.

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