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Original Research Article

Study of usefulness of budesonide nebulization in oxygen dependent preterm newborns in NICU

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ABSTRACT

Background: Increased duration of neonatal intensive care unit (NICU) stay of preterm neonates have becoming an emotional and financial burden to parents leading to very high chances of parents discontinuing the treatment and thus increased morbidity and mortality of neonates. Oxygen dependency is the major cause of the prolonged NICU stay for the neonates having respiratory illness like respiratory distress syndrome (RDS), meconium aspiration syndrome (MAS), and pneumonia. Inhaled budesonide being a safe immunosuppressor has shown the promising result in the treatment of these immune system activated respiratory disorders of neonate and thus reduction of oxygen dependency and later reducing the hospital stay duration. The intent of this study is to evaluate the usefulness of inhaled budesonide in such respiratory disorders of neonate.
Methods: A randomized controlled trial involving 60 oxygen dependent neonates in NICU was conducted from July 2021 to March 2023.
Results: Budesonide nebulization decreased the duration of oxygen dependency of neonates and thus reduced NICU stay.
Conclusions: Budesonide nebulization is associated with improvements in respiratory parameters in neonates with RDS, MAS, Pneumonia leading to early oxygen weaning and early discharge.

Keywords: Respiratory distress, Budesonide, Inhaled, Neonate, Meconium aspiration syndrome

INTRODUCTION

Modern lifestyle changes of women have increased the prevalence of obesity, poly cystic ovarian disease and other lifestyle problems which has led to gestational diabetes, infertility and other ailments which further have increased prevalence of intrauterine growth restriction (IUGR), premature births, twin gestation, meconium aspiration syndrome.

And all these neonates need prolonged NICU stay. Respiratory issues associated with these like respiratory distress syndrome, meconium aspiration syndrome, Pneumonia are the commonest cause of prolonged oxygen dependency and thus prolonged stay.

Respiratory distress syndrome

Respiratory distress syndrome (RDS) is very common disorder in premature neonates.[1,2] RDS is caused by surfactant deficiency due to immaturity of type II pneumocytes leading to alveolar collapse and thus defective gas exchange.[3-6] RDS can be prevented by administration of antenatal steroids to mothers and

exogenous surfactant to the premature neonates.[7,8]

Neonatal RDS is an inflammatory process in the immature neonatal lung, inflammatory injury to the alveoli leads to leakage of serum proteins which cause surfactant inactivation.[9,10] According to many studies the inflammatory process is the main cause of pathogenesis in respiratory distress syndrome.[11] Inflammatory cytokines play an important role in lung damage.[12] The inflammatory process leads to apoptotic process in epithelial cells causing lung damage in neonatal RDS.[13]

Anti-inflammatory agents like corticosteroids interfere with the inflammatory processes in the neonatal lungs and thus have a beneficial role in the management of neonatal RDS.[14,15] But systemic corticosteroids have many adverse effects like intestinal bleeding and growth failure.[16,17] Inhaled corticosteroids like budesonide have local action and might reduce lung inflammation and thus improvement in the severity of neonatal RDS but less adverse effects, compared with systemic corticosteroids.[18,19]

So, this study wants to know the effect of inhaled budesonide on neonatal respiratory distress syndrome.

Meconium aspiration syndrome

Meconium aspiration syndrome is one of the most common causes of respiratory distress in neonates. Neonates born through MSAF have 100 times more risk of developing respiratory distress. MSAF is caused by fetal distress due to placental dysfunction, post mature or small for date babies and antepartum hemorrhage.

The pathophysiology of MAS is complex. Meconium in airway causes obstructive emphysema. Meconium particles create direct irritation and toxicity which causes marked alveolar and parenchymal inflammation and edema and leakage of proteins into airways. Cytokine and other inflammatory mediators are released and causes vascular leakage and causes injury pattern similar to respiratory distress syndrome.[20,21]

So thus, there will be chance of usefulness of inhaled corticosteroids which has less side effects.

Pneumonia

Respiratory infections are the most common respiratory issues in neonates in NICU. They are either due to maternal cause and iatrogenic due to cross infections in NICU during regular care or during mechanical ventilation. ventilator associated pneumonia is one of the major causes for the extension of length of hospital stay, increased use of antibacterial drugs and expense increase.[22] Pathogens causes secretion of mucus, increasing edema, spasm and thus decreasing pulmonary ventilation. Budesonide, an inhaled glucocorticoid can reduce vascular permeability, inhibit secretion of mucus, and relieve edema, spasm and pulmonary ventilation. And is highly effective to local inflammation; hence, it has been applied in the clinical treatment of bronchopneumonia and bronchial asthma.[23-25]

METHODS

Study type

It was a prospective randomized controlled trial.

Study place

The study was conducted in the NICU of Vinayaka Hospital, Tumkur.

Study period

Study period was from July 2021 to March 2023.

Selection criteria

60 preterm (28-36 weeks) neonates with respiratory illness who or on nasal cannula oxygen and who doesn't require CPAP or mechanical ventilation were included in the study.

Exclusion criteria

Extremely premature <8 weeks neonates and term neonates were excluded from study.

Procedure

Study size was 60. Over the study period, neonates included in this study were divided into 2 groups: group 1 (the budesonide nebulization group) consisted of 30 neonates who received budesonide nebulization, and group 2 (the placebo group) consisted of 30 neonates who received placebo. Group 1 received budesonide nebulization (2.5 ml, 0.5 mg/ml) (Cipla), twice daily for 5 days. Group 2 received humidified distilled sterile water (2 ml).

Statistical analysis

Statistical package for the social sciences (SPSS) 20 Software was used for data analysis.

RESULTS

In group 1, 13 neonates were male and 17 were female and in group 2, 14 neonates were male and 16 were female (Table 1).

Table 1: Gender distribution among study groups.

Gender	Group 1 (budesonide) n=30	Group 2 (placebo) n=30
Male	13	14
Female	17	16

In group 1, 9 neonates were 28-30 weeks, 11 were 30-34 weeks, 10 was of 34-37 weeks of age and in group 2, 8 neonates were 28-30 weeks, 12 were 30-34 weeks, and 10 was of 34-37 weeks of age (Table 2).

Table 2: Gestational age distribution among study groups.

Gestational age (weeks)	Group 1 (budesonide) n=30	Group 2 (placebo) n=30
28-30	9	8
30-34	11	12
34-37	10	10

In group 1, 5 neonates were <1000 g, 8 was 1000-1500 g, 10 was 1500-2500 g and 7 were >2500 g of weight and in group 2, 4 neonates were <1000 g, 7 were 1000-1500 g, 11 were 1500-2500 g and 8 were >2500 g of weight.

Table 3: Distribution of birth weight among study groups.

Birth weight (g)	Group 1 (budesonide) n=30	Group 2 (placebo) n=30
<1000	5	4
1000-1500	8	7
1500-2500	10	11
>2500	7	8

In group 1, 15 neonates were having RDS,8 were having MAS, 7 were having pneumonia, in group 2, 14 neonates were having RDS,7 were having MAS, 9 were having pneumonia (Table 4).

Table 4: Respiratory illness among study groups.

Respiratory illness	Group 1 (budesonide) n=30	Group 2 (placebo) n=30
Respiratory distress syndrome	15	14
Meconium aspiration syndrome	8	7
Pneumonia	7	9

Table 5: Duration of oxygen requirement.

Respiratory illness	Group 1 (budesonide) n=30	Group 2 (placebo) n=30
	Average duration of O_2 requirement (days)	
Respiratory distress syndrome	6	13
Meconium aspiration syndrome	3	5
Pneumonia	4	7

Average duration of oxygen requirement in group 1 was 6, 3, 4 days for RDS, MAS, pneumonia respectively. Average duration of oxygen requirement in group 2 was 13, 5, 7 days for RDS, MAS, pneumonia respectively.

DISCUSSION

In this study, inhaled budesonide treated neonates with all the three respiratory illness had a shorter oxygen requirement duration than the neonates in the placebo group of similar illness. This is in similar with other studies that reported budesonide inhalation in neonates with RDS is associated with a decreased hospital stay and complications.[26]

In the study by Tripati et al the duration of oxygen requirement was significantly less in the steroid-treated group compared to controls.[19] The duration of oxygen requirement was also less in the interventional group compared to controls, which can be explained by the anti-inflammatory effect of steroids leading to improvement in lung inflammatory changes, thus reducing the duration of oxygen dependence.[27-29]

Metanalysis by Shinwell et al concluded that very preterm infants appeared to benefit from inhaled corticosteroids with reduced risk for BPD and no effect on death, other morbidities or adverse events.[30]

As several studies have showed budesonide inhalation improves neonatal pulmonary functions with very less adverse effects. Many studies have already proved the clinical efficacy and safety of budesonide inhalation a well-known anti-inflammatory drug already in use for prevention and treatment of several pulmonary diseases.

CONCLUSION

Inhaled budesonide is the effective way of reduction of duration of various neonatal respiratory illness and thus decreasing the oxygen requirement duration and thus duration of NICU stay and thus decreasing financial and emotional burden of the parents.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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