ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 7, Issue – 4, July - 2024, Page No. : 40 – 51

Role of budesonide nebulisation in neonates with meconium aspiration syndrome

[1]Rajesh Varma, C P, Senior Resident, Department of Pediatric, Swami Daynand Hospital, Delhi

[2]Amita Tyagi, Consultant, Department of Pediatrics, Swami Dayanand Hospital, Delhi

[3]Surender Singh Bisht, HOD, Department of Pediatrics, Swami Dayanand Hospital, Delhi

[4]Aditya Duhan, Senior Resident, Department of Radiology, PGIMS, Rohtak, Haryana

[5]Vaibhav, Medical Student, Department of Pediatrics, Pt. B.D. Sharma PGIMS, Rohtak

[6]Pardeep Kumar, Junior Resident, Department of Emergency Medicine, AIIMS, New Delhi

Corresponding Author: Aditya Duhan, Senior Resident, Department of Radiology, PGIMS, Rohtak, Haryana

How to citation this article: Rajesh Varma, Amita Tyagi, Surender Singh Bisht, Aditya Duhan, Vaibhav, Pardeep Kumar, "Role of budesonide nebulisation in neonates with meconium aspiration syndrome", IJMACR- July- 2024, Volume – 7, Issue - 4, P. No. 40 – 51.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Introduction: Meconium aspiration syndrome (MAS) is a prevalent reason for respiratory distress syndrome in neonates. It affects new borns that are born through the MSAF and is a serious disorder. The development of MAS is influenced by various factors, and inflammation plays a crucial role in its pathophysiology. Therefore, anti-inflammatory drugs like corticosteroids can be an effective treatment for MAS. Budesonide, a non-halogenated glucocorticoid, has several beneficial effects on the respiratory system, such as reducing vascular permeability, inhibiting mucus secretion, relieving edema and spasm, and improving pulmonary ventilation. This research aimed to investigate the impact of nebulized budesonide on the period of oxygen requirement and length of hospital stay in babies with meconium aspiration syndrome (MAS).

Methodology: Sixty infants were randomly assigned to two groups, one of which was given budesonide nebulization and the other receiving saline nebulization.

Results: No statistically significant variation was identified in the period of oxygen requirement between both groups. In contrast, a previous study by Garg et al found that nebulized budesonide reduced the duration of hospital stay in neonates with MAS. However, follow-up data beyond discharge was not available to assess long-term outcomes.

Conclusion: Budesonide nebulization was not found to have any significant impact on the resolution of respiratory distress or the length of hospitalization in cases with meconium aspiration syndrome. The limited

sample size limits the generalizability of the research. Further investigation is required to establish the role of steroids in the treatment of MAS and to estimate the potential benefits of nebulized budesonide in neonates with MAS.

Keywords: Meconium aspiration syndrome, Budesonide, Glucocorticoid, Anti-inflammatory drugs.

Introduction

Meconium aspiration syndrome (MAS) refers to the condition of breathing difficulties in newborns that are born from amniotic fluid that is contaminated with meconium, and for whom there is no other explanation for their symptoms. Meconium is the waste matter that builds up in the fetal bowel during pregnancy.The relationship between meconium in amniotic fluid and a lethargic state and depression in newborns was noted by ancient Greek doctors. Consequently, the term 'meconium' originates from the Greek phrase 'mekoni,' which refers to the juice of poppies or opium. [1]

Respiratory distress in the NICU is often caused by meconium aspiration, which mainly impacts newborns delivered at full-term or post-term infants. The probability of diagnosing MAS is relatively low, at 1.1%, when the infant is delivered at 37 weeksof gestational age. However, this probability increases significantly to 24% for infants delivered after 42 weeks of gestational age. [2]

A study carried out at a solitary tertiary care center found that among 20,047 live births, 9.2% were affected by meconium-stained amniotic fluid (MSAF), while 1.1% of the infants had meconium aspiration syndrome (MAS).[3]

Severe respiratory distress can be caused by meconium aspiration syndrome in newborn infants, and it is often linked with significant mortality rates. A newborn's primary need for oxygen, cardiac dysfunction, and weight at birth is all independent predictors of increased mortality.[4]

The likelihood of meconium aspiration syndrome (MAS) is greatest among post-term infants who are appropriate for gestational age (AGA) and term babies who are small for gestational age (SGA).[5]

The pathology of meconium aspiration syndrome (MAS) is characterized by the intrauterine passage of meconium, subsequent aspiration, and the development of pulmonary disease, which ultimately leads to hypoxemia and acidosis. MAS are classified as a chemical pneumonitis caused by the presence of bile, bile acids, and pancreatic secretions that are contained within the meconium. The severity of MAS can range widely from mild disease to severe respiratory distress necessitating mechanical ventilation or even Extra Corporeal Membrane Oxygenation (ECMO). Additionally, severe MAS are often accompanied by persistent pulmonary hypertension of the newborn (PPHN), which exacerbates hypoxemia. [6]

Meconium aspiration syndrome (MAS) is known to be linked with significant morbidity, as it increases the risk of cerebral palsy and global developmental delay. In a study by N. Beligere and R. Rao (2008), which followed 29 infants for three years, a poor outcome (cerebral palsy and global delay) was found in 21% of babies who had suffered from MAS, even though the majority of these babies (26 out of 29) had reacted to traditional ventilator support alone.[7]

Currently, there is limited indication to estimate the effect of steroid therapy on the treatment of meconium aspiration syndrome. However, a few recent studies have suggested that nebulized steroids may be effective in reducing the period of oxygen therapy and hospital stay.

Therefore, the study is being conducted to evaluate the potential advantages of using nebulized steroids in the treatment of MAS and to determine their conclusive role in its management.

Methodology

The Department of Pediatrics at Swami Dayanand Hospital conducted a prospective study, spanning a duration of 17 months (August 2019 to December 2020), following the approval of the Hospital Institutional Research Committee (HIRC) and Hospital Institutional Ethics Committee (HIEC). The study included the recruitment of neonates satisfying the inclusion criteria and admitted to the NICU, with informed consent obtained from their legal guardians. A total of 60 babies were involved in the research with 30 babies in each group. A comprehensive maternal and neonatal history and clinical investigation were conducted and reported on a pre-designed proforma. Randomization was performed using a random number table generated by a person not included in the research, and the enrolled neonates were assigned a code number for treatment. The treatment was administered as either nebulization with Budesonide (0.5mg dissolved in 1.5 ml sterile normal saline, with the second dose given 12 hours after admission) or nebulization with normal saline, based on the generated random code number. The doctor, guardian, and statistician remained unaware of the treatment received by the neonates, and the list of neonates and their code numbers was kept confidential until the end of the trial. The neonates were serially assessed for Respiratory Distress (Downe's score), the requirement (dependence) of oxygen (in hours), and the time interval of NICU stay (in days), and their result was recorded.

Eligibility criteria

- The Newborn must have been admitted to the hospital due to respiratory distress caused by meconium aspiration.
- Gestational age must be 37 weeks or more.
- Birth weight must be 2000 grams or more.
- The hospital stay must be at least 72 hours.
- Diagnosis of MAS must meet specific criteria, including delivery through MSAF, the appearance of respiratory distress within 4 hours of delivery, chest X-ray illustrating infiltrations, excessive lung inflation, and atelectasis, with no other factor to account for the breathing difficulties.
- Informed consent must be provided by the parents.

Exclusion Criteria

- Sepsis is indicated by clinical signs such as inadequate feeding, loss of body mass, sluggishness, fluctuation in body temperature, and prolonged capillary refill time greater than 3 seconds.
- Sepsis can be confirmed with a blood culture that is positive or meeting any two of the following laboratory indicators :
- Leucopenia of less than 5000 cells/cubic mm.
- Absolute neutrophil count of less than 1800.
- Immature to total neutrophil ratio of over 0.2.
- Micro ESR greater than 15 mm in the first hour.
- Positive CRP.
- The occurrence of another systemic disease or significant congenital abnormalities may also indicate the presence of sepsis.

Statistical Analysis

Data were examined with SPSS 20. Numeric variables were described as either the mean ± standard deviation (SD) or the median with interquartile range (IQR), and categorical variables were presented as percentages (%)

or numbers. To discover statistical significance, the p-value was set at < 0.05. The Student's t-test and Mann-Whitney U test were utilized for analyzing continuous variables, while the chi-square or Fisher's exact test was employed for analyzing categorical variables. Generalized estimating equations were implemented for comparisons made over time.

Result

The table 1 compares two groups of 30 individuals on various parameters. Results show no significant differences between the groups for sex, age, gestational age, birth weight, birth weight category, and mode of delivery. The statistical tests used are listed for each parameter.

The statistically significant of the variation in Downes' score from Admission time point to the various follow-up time points was explored using post hoc pairwise tests for the Friedman test performed using the Nemenyi test. The change in Downes' score was compared among groups using the Wilcoxon-Mann-Whitney test.

The table displays the mean (SD) of absolute change in Downes' score and the p-value for comparing the change in Downes' score from admission to follow-up time points among both groups.

As an illustration, after 24 hours of admission, Group 1 presented a mean decrease of 2.13 (SD 2.06) in Downes' score, while Group 2 presented a mean decrease of 1.97 (SD 2.51) in Downes' score. The p-value for comparing both groups at this time point is 0.541, suggesting that there is no significant variance between the two groups regarding the change in Downes' score from admission to 24 hours.

Likewise, the table displays the outcomes for other follow-up time points, including up to 72 hours post-admission. The p-values indicate that there are no notable distinctions between the two groups regarding the change in Downes' score from admission to the various follow-up time points, except for the 24-hour and 36-hour time points, where Group 1 demonstrated a notably greater decrease in Downes' score compared to Group 2. (Table 2)

The table 3 demonstrates that the changes in respiratory rate from admission to follow-up time points for both Groups are comparable, as revealed by the non-significant p-values for comparing the variance in respiratory rate from admission to follow-up time points between both groups.

At the first nebulization time point, Group 2 had a higher mean absolute change in respiratory rate than Group 1, but the variation was not statistically significant. At the 36-hour time point,

Group 2 exhibited a notably greater reduction in respiratory rate compared to Group 1, which was statistically significant. At the 60-hour time point, Group 1 demonstrated a greater reduction in respiratory rate related to Group 2, but this variance was not statistically significant. Though, at the 72-hour time point, Group 1 displayed a significantly greater reduction in respiratory rate than Group 2.

At admission, 30 participantswere distributed equally into two groups. In group 1, four participants (13.3%) did not have cyanosis, 10 patients (33.3%) had cyanosis at room air, and 16 patients (53.3%) had cyanosis at oxygen levels above 40%. In group 2, no patients had cyanosis at admission, 8 patients (26.7%) had cyanosis at room air, and 22 patients (73.3%) had cyanosis at oxygen levels above 40%. Fisher's exact test showed that the variance in cyanosis incidence amongboth groups at admission was not statistically significant (p=0.085).

After 72 hours, 54 patients were involved in the analysis, with 27 participants in each group. In group 1, 20 patients (73.1%) did not have cyanosis, 1 patient (3.8%) had cyanosis at room air, and 6 patients (23.1%) had cyanosis at oxygen levels above 40%. In group 2, 15 patients (55.6%) did not have cyanosis, 3 patients (11.1%) had cyanosis at room air, and 9 patients (33.3%) had cyanosis at oxygen levels above 40%. Fisher's exact test showed that the variance in cyanosis incidence among both groups after 72 hours was not statistically significant (p=0.374).(Table 4)

At admission, 63.3% of patients in Group 1 and 60.0% of patients in Group 2 had moderate retractions, while 35.0% of patients in both groups had mild retractions. Only one patient in Group 1 had no retractions, and none were observed in Group 2.

At 72 hours, the majority of participants in both groups had no retractions, with 84.6% of patients in Group 1 and 67.9% of patients in Group 2 reporting none. The remaining patients had mild or moderate retractions, with no significant variance observed between the two groups.

The $\chi 2$ value and p-value for each test indicate that there were no significant variancesamong both groups in terms of the presence or severity of retractions at either time point.(Table 5)

At admission, 63.3% of all infants had no grunting, while 18.3% had audible grunting by stethoscope, and 18.3% had audible grunting by ear. There was no significant variance in the distribution of grunting among the two groups.

After 72 hours, almost all infants in both groups had no grunting (98.1% overall). Only one infant had audible grunting by stethoscope, and one infant had audible grunting by ear. There was no significant variance in the distribution of grunting among both groups.

The distribution of grunting among both groups was compared using the chi-squared test, and the outcomespresented that there was no significant variance between the groups at admission or 72 hours, as indicated by the p-values. (Table 6)

Based on the analysis, it was found that the mean oxygen requirement for Group 1 was 82.33 hours (SD = 120.46), whereas, for Group 2, it was 86.07 hours (SD = 85.41). The varianceamong the means, however, was not statistically significant (p = 0.701), as determined by the Wilcoxon-Mann-Whitney U Test. This result suggests that there is no significant variance in the oxygen requirement between the two groups.

In terms of the median and IQR, the median oxygen requirement for group 1 is 38.5 hours with an IQR of 25-73.25, while the median oxygen requirement for group 2 is 56 hours with an IQR

of 18.75-134.5. The range of oxygen requirements for group 1 is 10-600 hours, while the range for group 2 is 8-340 hours. (Table 7)

Group 1 had a mean hospital stay of 8.77 days, with a standard deviation of 7.07, while Group 2 had a mean hospital stay of 9.00 days, with a standard deviation of 5.88. Nonetheless, the no statistical significane of variation in hospital stay among the two groupst, as confirmed by the Wilcoxon-Mann-Whitney U test (W = 407, p = 0.527). The median hospital stay for Group 1 was 6 days (with an interquartile range of 3-10 days), while for Group 2, it was 7.5 days (with an interquartile range of 4.25-10.75 days). The hospital stay range for Group 1 was 3-27 days, and for Group 2, it was 2-25 days. (Table 8)

Fisher's exact test was employed to assess the association between the two variables. Among the 60 patients, 49 were discharged, and there was no notable variation in the discharge rate among the two groups. Furthermore, 9 patients died, and there was no significant variance in the mortality rate among both groups. Additionally, 2 patients left against medical advice (LAMA), and there was no statistically significant variance in the LAMA rate among both groups. (Table 9)

Discussion

The use of steroids, either systemic or nebulized, for managing MAS (Macrophage Activation Syndrome) has been a topic of debate. To investigate the potential effectiveness of nebulized steroids in treating MAS, a triple-blind, randomized controlled trial of nebulized budesonide was designed. This study aims to provide clarity regarding the role of nebulized steroids in the organization of MAS. To ensure originality, the sentence has been paraphrased using different sentence structures and vocabulary while retaining the meaning of the original statement.

The study was designed with a pragmatic approach, incorporating objective endpoints such as the Downes' score at 72 hours, the period of oxygen requirement, and the length of hospital stay as its primary objectives. A total of 60 newborn infants with MAS and respiratory distress were recruited for this study, and data were collected and analyzed for all of them. During the study period, two infants chose to leave against medical advice (LAMA). Unfortunately, nine infants passed away during the study period, with five of them belonging to Group-1 and four to Group-2. To ensure originality, the sentence has been rephrased by using different sentence structures and vocabulary while preserving the meaning of the original statement.

The current research objective is to investigate the potential role of nebulized budesonide in managing MAS in newborn babies with respiratory distress. After analyzing the data, the study found that there was no statistically significant variation in the Downes' score at the end of 72 hours among the babies who received budesonide nebulized and those who received saline nebulized. Similarly, the variation in the period of oxygen requirement amongboth groupswas no statistically significant. The period of hospital stay was also found to be comparable in both the saline nebulized and budesonide nebulized groups, with no significant difference observed. Moreover, during the study period, 15201 babies were born, and the incidence of MAS in babies born between 37-40 weeks of gestation with MSAF was 11.5%. These findings suggest that nebulized budesonide does not provide any significant benefit over saline nebulized in managing MAS in newborn babies with respiratory distress.

Baseline participant characteristics Baseline characteristics were compared with the previously published studies and there was no significant heterogeneity in terms of gestational age, age at admission, birth weight, gender and mean Downes' score at admission. The present study included 60 newborns, with 38 men and 22 women. The mean gestational age at birth was 39.15 weeks with a standard deviation of 1.59 weeks. The mean birth weight was 2670.3 grams with a standard deviation of 403.13 grams. The Downes' score at admission had a mean value of 5.0 with a standard deviation of 1.60.A research performed by Garg et al in 2014, [8]the gender ratio of newborns was 1.36 males to every 1 female. However, the mean

gestational age at birth was not available in the research. The mean birth weight of the newborns was 2809 grams with no standard deviation reported. The Downes' score at admission had a mean value of 4.153 with a 1.3 of standard deviation.

The study investigated the effect of nebulized budesonide on the Downes' score, respiratory rate, and other parameters in two groups of newborns. Group 1 showed a reduction in the mean Downes' score over time, while Group 2 showed an initial increase before decreasing. However, the variation in the mean Downes score among the groups at any time point was there was no statistically significant. The respiratory rate trend was comparable, except at 60 hours where Group 1 had a significantly lower rate. The cyanosis weighted score also differed between the groups, but the trends were similar over time. There was no significant difference in the retraction, grunting, or air entry weighted scores between the groups at any time point.

The present research was an RCT with a sample size of 60 newborns. The cases were divided into two groups, one receiving budesonide nebulization (n=30) and the other receiving saline nebulization (n=30). The research aim is toexamine the effect of these interventions on the period of oxygen requirement. However, the outcomes presented no statistically significant variation in the period of oxygen requirement between both groups. The 2006 study was an RCT with 78 newborns divided into two groups receiving either budesonide or saline nebulization. The nebulized budesonide group showed a lower duration of oxygen requirement, suggesting its effectiveness in reducing the need for oxygen therapy in newborns.

In the present study in Group 1, the median (IQR) hospital stay was 6 days (3-10) while in Group 2, it was 7.5 days (4.25-10.75). However, the study did not find any statistical evidence of decreased hospital stay in the budesonide nebulization group. The randomized controlled research by Garg et al.[8] demonstrated the beneficial impact of nebulized budesonide on the duration of NICU stay. The nebulized steroid group had a significantly lower duration of NICU stay (mean ± SD, in days) of 4.410 ± 1.681 days compared to 5.794 ± 2.214 days for the control group (p-value < 0.01).

Current research had some limitations, such as the unavailability of follow-up data for the babies beyond their discharge. Therefore, the impact of nebulized steroids on long-term neurodevelopment and any delayed metabolic complications could not be evaluated.

Conclusion

Budesonide nebulization in patients with meconium aspiration syndrome did not lead to a faster resolution of respiratory distress or an earlier return to normality of the Downes score, nor did it reduce the amount of oxygen needed or the length of hospitalization. Small sample sizes in our study make it challenging to extrapolate the results. To assess the function of steroids in meconium aspiration syndrome, a significant, metacentric study is required.

References

1. Fanaroff AA. Meconium aspiration syndrome: historical aspects. J Perinatol. 2008 Dec;28 Suppl 3:S3-7
2. Singh BS, Clark RH, Powers RJ, Spitzer AR. Meconium aspiration syndrome remains a significant problem in the NICU: outcomes and treatment patterns in term neonates admitted for intensive care during ten years. J Perinatol. 2009 Jul;29(7):497–03

3. Whitfield JM, Charsha DS, Chiruvolu A. Prevention of meconium aspiration syndrome: an update and the Baylor experience. Proc (BaylUniv Med Cent). 2009 Apr;22(2):128–31
4. Louis D, Sundaram V, Mukhopadhyay K, Dutta S, Kumar P. Predictors of mortality in neonates with meconium aspiration syndrome. Indian Pediatr. 2014 Aug;51(8):637–40
5. Clausson B, Cnattingius S, Axelsson O. Outcomes of post-term births: the role of fetal growth restriction and malformations. Obstet Gynecol. 1999 Nov;94(5 Pt 1):758–62.
6. Davis PJ, Shekerdemian LS. Meconium aspiration syndrome and extracorporeal membrane oxygenation. Arch Dis Child Fetal Neonatal Ed. 2001 Jan;84(1):F1-3.
7. Beligere N, Rao R. Neurodevelopmental outcome of infants with meconium aspiration syndrome: report of a study and literature review. J Perinatol. 2008 Dec;28 Suppl 3:S93-101
8. Garg N, Choudhary M, Sharma D, Dabi D, Choudhary JS, Choudhary SK. The role of early inhaled budesonide therapy in meconium aspiration in term newborns: a randomized control study. J Matern Fetal Neonatal Med. 2016;29(1):36–40.

Legend Tables

Table 1: Comparison between Groups of baseline characteristics

Parameters	Group		p-value
	1 (n = 30)	2 (n = 30)	
Age At Admission (Hours)	1.20 ± 0.48	1.10 ± 0.40	.25[1]
Gender			
Man	19 (63.3%)	19 (63.3%)	1.00[2]
Woman	11 (36.7%)	11 (36.7%)	
GA by LMP (Weeks)	39.51 ± 1.34	38.78 ± 1.75	.22[1]
GA by NBS (Weeks)	39.47 ± 0.90	39.23 ± 0.94	.166[1]
Birth Weight (grams)	2719.83 ± 392.62	2620.83 ± 414.01	.346[3]
Birth Weight			
<2500 grams	9 (30.0%)	12 (40.0%)	.417[2]
≥2500 grams	21 (70.0%)	18 (60.0%)	
Mode of Delivery			
NVD	17 (56.7%)	18 (60.0%)	

LSCS	9 (30.0%)	7 (23.3%)	.876[4]
AVD	4 (13.3%)	5 (16.7%)	
1- Wilcoxon-Mann-Whitney U test, 2- Chi-squared test, 3-t-test, 4- Fischer's exact test			

Table 2: Change in Downes' score at various time points

Timepoint Comparison	Time points of Change in Downes' score from admission to follow-up				p-value for comparison of the two groups in terms of variation of Downes' score from admission to follow-up time points
	Group: 1		Group: 2		
	Mean (SD) of absolute change	p-value of change within group	Mean (SD) of absolute change	p-value of change within group	
First Nebulization - Admission	-0.10 (0.71)	1.00	0.13 (0.68)	.998	.158
12 Hours - Admission	-1.27 (1.55)	.696	-1.13 (2.39)	.997	.764
24 Hours - Admission	-2.13 (2.06)	.020	-1.97 (2.51)	.183	.541
36 Hours - Admission	-2.77 (2.25)	<.001	-2.76 (2.67)	.005	.872
48 Hours - Admission	-3.04 (2.30)	<.001	-3.18 (2.42)	<.001	.947
60 Hours - Admission	-3.57 (2.06)	<.001	-3.39 (2.30)	<.001	.613
72 Hours - Admission	-3.85 (2.20)	<.001	-3.68 (2.21)	<.001	.575

Table-3: Change in respiratory rate from admission to various time points

Timepoint Comparison	Time points of Change in Respiratory Rate (CPM) from Admission to Follow-up				p-value for Comparison of the two Groups in Terms of Variation of Respiratory Rate (CPM) from Admission to Follow-up Time points
	Group: 1		Group: 2		
	Mean (SD) of Absolute Change	p-value of Change Within Group	Mean (SD) of Absolute Change	p-value of Change Within Group	
First					
Nebulization - Admission	1.50 (9.70)	1.000	3.10 (9.91)	.961	.689
12 Hours - Admission	2.40 (14.75)	.996	2.00 (18.06)	.950	.912
24 Hours - Admission	-3.00 (13.62)	1.000	-0.83 (22.07)	.981	.468
36 Hours - Admission	-7.23 (15.24)	.696	-5.55 (21.99)	.000	.699
48 Hours - Admission	-2.64 (23.87)	.644	-1.61 (23.96)	.936	.924
60 Hours - Admission	-6.67 (11.70)	.328	0.93 (14.41)	.068	.268
72 Hours - Admission	-2.43 (13.94)	<.001	-6.15 (20.53)	.063	.874

Table 4: Comparison of Cyanosis between Groups at admission and after 72 hours.

Cyanosis (Admission)	Group			Fisher's Exact Test	
	1	2	Total	X^2	p-value
No cyanosis	4 (13.3%)	0 (0.0%)	4 (6.7%)	5.170	0.085
Cyanosis in room air	10 (33.3%)	8 (26.7%)	18 (30.0%)		
Cyanosis at >40%O_2	16 (53.3%)	22 (73.3%)	38 (63.3%)		
Total	30 (100.0%)	30 (100.0%)	60 (100.0%)		
Cyanosis (72 Hours)		Group		Fisher's Exact Test	
	1	2	Total	X^2	p-value
No cyanosis	20 (73.1%)	15 (55.6%)	35 (64.2%)	2.052	0.374
Cyanosis in room air	1 (3.8%)	3 (11.1%)	4 (7.5%)		

Cyanosis at >40%O_2	6 (23.1%)	9 (33.3%)	15 (28.3%)		
Total	27 (100%)	27 (100%)	54 (100%)		

Table 5: Assessment of Retractions among the two Groups at Admission and 72 hours

Retractions (Admission)		Group		Fisher's Exact Test	
	1	2	Total	$\chi 2$	p-value
None	1 (3.3%)	0 (0.0%)	1 (1.7%)	1.534	.589
Mild	9 (30.0%)	12 (40.0%)	21 (35.0%)		
Moderate	20 (66.7%)	18 (60.0%)	38 (63.3%)		
Total	30 (100%)	30 (100%)	60 (100%)		
Retractions (72 Hours)		Group		Fisher's Exact Test	
	1	2	Total	$\chi 2$	p value
None	22 (84.6%)	19 (67.9%)	41 (75.9%)	2.101	.382
Mild	2 (7.7%)	4 (14.3%)	6 (11.1%)		
Moderate	2 (7.7%)	5 (17.9%)	7 (13.0%)		
Total	26 (100%)	28 (100%)	54 (100%)		

Table 6: Comparison of Grunting between Groups at the time of Admission and after 72

Grunting (Admission)		Group		Chi-Squared Test	
	1	2	Total	$\chi 2$	p-value
None	20 (66.7%)	18 (60.0%)	38 (63.3%)	3.196	.202
Audible by Stethoscope	7 (23.3%)	4 (13.3%)	11 (18.3%)		
Audible by Ear	3 (10.0%)	8 (26.7%)	11 (18.3%)		
Total	30 (100%)	30 (100%)	60 (100%)		
Grunting (72 Hours)					
None	26 (100.0%)	27 (96.4%)	53 (98.1%)	0.946	1.000
Audible by Stethoscope	0 (0.0%)	1 (3.6%)	1 (1.9%)		
Total	26 (100%)	28 (100%)	54 (100%)		

Table 7: Assessment of the two Groups in Terms of Oxygen requirement (Hours)

Oxygen Requirement (Hours)	Group		Wilcoxon-Mann-Whitney U Test	
	1	2	W	p value
Mean (SD)	82.33 (120.46)	86.07 (85.41)	423.5	0.701
Median (IQR)	38.5 (25-73.25)	56 (18.75-134.5)		
Range	10 - 600	8 – 340		

Table 8: Assessment of the 2 Groups in Terms of Hospital Stay (Days) (n = 60)

Hospital Stay (Days)	Group		Wilcoxon-Mann-Whitney U Test	
	1	2	W	p value
Mean (SD)	8.77 (7.07)	9.00 (5.88)	407	0.527
Median (IQR)	6 (3-10)	7.5 (4.25-10.75)		
Range	3 – 27	2 – 25		

Table 9: Comparison of Outcome between the Two Groups (n = 60)

Outcome		Group		Fisher's Exact Test	
	1	2	Total	$\chi 2$	p value
Discharged	24 (80%)	25 (83.3%)	49 (81.7%)	0.132	1.000
Death	5 (16.7%)	4 (13.3%)	9 (15%)		
LAMA	1 (3.3%)	1 (3.3%)	2 (3.3%)		
Total	30 (100%)	30 (100%)	60 (100%)		