**ORIGINAL ARTICLE**

# PAIN SCORE IN NEONATES WHILE ADMINISTERING SURFACTANT VIA LISA METHOD WITH AND WITHOUT PREMEDICATION WITH OPIOID AND ATROPINE

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## ABSTRACT

**Objective:** To determine the Pain score in neonates while administering surfactant via LISA method with and without premedication with opioid and atropine. Quasi ex perimental study. This quasi experimental study was conducted in neonatology unit of CMH Quetta from Feb 2024 to Dec 2024.

**Method:** Inclusion criteria was spontaneously breathing preterm neonates who were ≤35 weeks of gestation diagnosed as RDS within first 48 hours of life. Premedication with nalbuphine at 0.05mg/kg and atropine 20microg/kg was used in intervention group. The surfactant Curosurf (200 mg/kg body weight) was instilled intratracheally via the feeding tube. Pain score was assessed by NIPS (neonate infant pain score)

**Results:** Total 50 preterm neonates were included. Out of these 25 patients were given LISA with premedication and 25 were given LISA without any premedication. There were 26 (52%) male neonates and female neonates. The mean gestational age at birth was 30.68 ± 3.67 weeks. Mean pain score in group A was 2.90 ± 2.09 before LISA and after medication it reduced to 2.04 ± 1.64 (p value 0.001) while mean pain score in group B was 1.92 ± 1.08 which increased to 3.00 ± 1.61 after LISA.

**Conclusion:** Nalbuphine and atropine in low dose is effective in managing pain and discomfort during LISA in pre term neonates with less post procedural complications**.**

**Key Words:** lisa, opioid, pain score, surfactant

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## INTRODUCTION

Respiratory distress syndrome is one of the leading cause of death in pre term infants by causing a decrease in adequate levels of surfactant causing respiratory discomfort and patient ultimately requires respiratory support.[1] In last few decades instillation of exogenous surfactant has been considered as most accepted treatment for RDS.[2] Surfactant instillation to deal with premature lungs is very important in every neonatal unit. It provides necessary respiratory assistance to premature lungs thus reducing the respiratory system related complications and eventually decreasing mortality. The method of administering a surfactant has evolved over the last few years i-e from ETT and mechanical ventilation to a less invasive method like less invasive surfactant administration (LISA) in a spontaeously breathing infant which has less documented

complications like reduced risk of interventricular hemmorhage , bronchopulmonary dysplasia thus associated with low mortality rate.[2]

Neonatologists are searching for better ways to treat RDS in newborns since long. In early 1980s CPAP was introduced as a part of minimal handling of neonates to deal with RDS[4]. Swede lors Victorian was the first to use CPAP with surfactant instillation.[3] Henrick verder moved ahead and use small bore gastric tube for surfactant instillation in 1992 in a spontaneously breathing individual thus introducing LISA.[3] Neonates treated by LISA had better survival rate and decreased need of mechanical ventilation.[5] European consensus guidelines in 2019 has declared LISA as recomended treatment for surfactant instillation.[6] Initially surfactant was introduced using ETT under sedation and analgesia however use of analgesia with LISA is still debatable as some authors support use of analgesia because it leads to less cardiovascular response and low incidence of interventricular hemmorhage. Seeing the other side of the picture good analgesia with sedation leads to less respiratory drive which is very important for surfactant instillation via LISA.[3] So an ideal drug should provide good ease with minimal disturbance of respiratory system. Still there is lack of consensus concerning premedication prior to the LISA. A variety of medications like opioids, ketamine lidocaine spray and atropine are being used by different neonatologist before LISA procedure.[7]

Pain is declared as fifth vital sign by some authors and pain management is very important during any procedure as it will lead to less post procedural compliactions.[8,9] To our knowledge there is no study available in Pakistan which has compared pain score with and without premedication during LISA. We have conucted this study to measure pain score in neonates during LISA with and without premedication with opioid(nalbuphine) and atropine.

## METHOD

This quasi experimental study was conducted in neonatology unit of Combined Military Hospital Quetta from Feb 2024 to Dec 2024 after getting formal permission from hospital ethical committee. A written informed consent form was taken from parents before participation in the study. Sample size was estimated by using WHO calculator by keeping 95% confidence level , 5% Margin of error with revised PIPP score i-e 9 in opioid group vs 12 in non opioid group[10]. Inclusion criteria was spontaneously breathing preterm neonates who were $\leq$35 weeks of gestation diagnosed as RDS who were on CPAP @6 L of oxygen and FIO2 $\geq$ 0.3 within first 48 hours of life. Exclusion criteria was neonates with congenital anatomical abnormalities like abnormalities of upper airway, major congenital abnormalities, congenital diaphragmatic hernia, tracheoesophageal fistula, choanal atresia, cleft palate, poor respiratory effort, neonates requiring intubation and invasive ventilation due to hemodynamic instability, Or FIO2 requirement $\geq$0.6. RDS was diagnosed on clinical features i-e need for supplemental oxygen or respiratory support, tachypnea, grunting and intercostal retractions and typical chest radiograph suggestive of RDS (bilateral reticulogranular pattern of the lung parenchyma, air bronchograms and low lung volume) by a consultant neonatologist. Detailed antenatal history like use of antenatal steroids, diabetes, hypertension and chorioamnionitis was taken and clinical examination was done to rule out anatomical abnormalities of the upper airway before including a neonate in study. Preterm neonates with RDS were initially stabilized on non-invasive ventilation (NIV) in the form of nCPAP. Surfactant was given if respiratory distress increased on NIV and two or more of the following criteria were met: silverman–andersen respiratory severity score (SAS) $\geq$4 , CPAP pressure $\geq$6 ,$FIO_2$ requirement >0.3. Neonates divided in 2 groups using lottery method. Premedication with nalbuphine at 0.05mg/kg and atropine 20microg/kg was used in intervention group and no medication was used in control group. For spontaneously breathing infants on NIV , a 8 fr feeding tube was measured by formula (weight in kg plus 6) and placed in the trachea 1–2cm beyond vocal cords by directly visualizing the cords with a laryngoscope.. The surfactant Curosurf (200 mg/kg body weight) was instilled intratracheally via the feeding tube. Surfactant was delivered within 3 to 5 minutes in 4 aliquots with gaps of 30 seconds to avoid surfactant coming back up, while the infant continues to breath with nCPAP during the procedure. When catheterization was not possible in 20-30 seconds, the procedure was discontinued and was attempted when the baby was stable. Feeding tube was removed immediately after the procedure. Infant's heart rate and $SPO_2$ were monitored during the procedure via pulse oximetry. $FIO_2$ was adjusted to attain a target $SPO_2$ $\geq$92%. Subsequent dose of surfactant was given if the neonate met the inclusion criteria again in 6-12Hrs hours after the first dose. The procedure was performed by neonatologists trained for delivery of surfactant by LISA. A second person observed the procedure to look for any adverse events, such as apnea or bradycardia and for the assessment of pain score. Pain score was assessed by NIPS (neonate infant pain score). Infants in either group were intubated and mechanically ventilated if they developed any complication like severe respiratory distress with SAS $\geq$7, $FIO_2$ requirement $\geq$0.6 on NIV, ph <7.2, $pCO_2$ $\geq$60mmhg or significant apnea. In both groups all other

treatments including ventilator settings were according to unit protocols.

Data was analyzed through SPSS version 25. Mean and standard deviation were calculated for numerical variables while frequencies and percentages were calculated for categorical variables. Chi-square was applied to determine the association between various variables. P-value ≤ 0.05 was considered significant.

## RESULTS

Total 96 preterm neonates were born between Feb 2024 to Dec 2024. Out of these 50 were eligible for LISA. Out of these 25 patients were given LISA with premedication and 25 were given LISA without any premedication. There were 26 (52%) male neonates and female neonates. The mean gestational age at birth was 30.68 ± 3.67 weeks. The mean wight at birth was 1715.60 ± 550.68 gms. 31 (62%) neonates have no maternal risk factor while 19 (38%) patients had associated maternal risk factor like polyhydrominos, PPROM, GDM and APH. Demographics of the patients are mentioned in table 1.

Table 1: Demographics of patients

| Variable | | n (%) |
|---|---|---|
| Gestational age at birth (weeks) | | 30.68 ± 3.67 |
| Gender | Males | 26 (52%) |
| | Females | 24 (48%) |
| Weight at birth (grams) | | 1715.60 ± 550.68 |
| Age at LISA (days) | | 1.12 ± 0.47 |
| Maternal risk factors | Yes | 19 (38%) |
| | No | 31 (62%) |

Patients were segregated into two groups i-e group A in which premedication with nalbuphine 0.05mg/kg and atropine 20microg/kg was given and group B in which no medication was given. Mean pain score in group A was 2.90 ± 2.09 before LISA and after medication it reduced to 2.04 ± 1.64 while mean pain score in group B was 1.92 ± 1.08 which increased to 3.00 ± 1.61 after LISA. Comparison of p values with different variables in both groups is mentioned in table 2.

Table 2: Comparison of variables in both groups.

| Variable | Pain score before LISA | Pain score after LISA | p value |
|---|---|---|---|
| Group A Medication (n=22) | 2.90 ± 2.09 | 2.04 ± 1.64 | <0.001 |
| Group B No Medication (n=28) | 1.92 ± 1.08 | 3.00 ± 1.61 | 0.932 |

Statistically significant correlation was observed in pain score in group A before and after LISA (p value 0.001).

## DISCUSSION

American academy of peadiatrics and Italian neonatologists suggest to use sedation and analgesia before intubation in all non-emergency situations.[11] In neonates when awake laryngoscopy is performed it is associated with tachycardia, increased catacholamines release, pulmonary hypertension and apnea[10]. If neonate cries during lyrngoscopy there is chance that he may develop raised intracranial pressure or intraventricular hemmorhage if no sedation is given before hand.[10]

To our knowledge this is the first study conducted in Pakistan to determine the effects of opioids and atropine before LISA. In our study less pain is seen in patients who were given opioid and atropine before the procedure as compare to patients in which no drug was given. These findings are consistent with the results shared by Dekker J *et al* and Bourgoin L *et al* in two different studies.[12,13] Barois J *et al* also shared the similar results that use of analgesia before LISA is associated with low pain scores and more hemodynamic stability.[14] De luca *et al* also cocluded in their study that analgesia before LISA causes less pain and easy management of neonates as compare to nenonates in which no analgesia was given.[15] Reynolds P *et al* also suggested in their study that neonates were more comfortable after LISA in which analgesia was given before the procedure.[16]

Literature suggests that pain in neonatal period leads to cognitive, social and neurosensory impairment while high dose of analgesia in this period leads to decrese cerebellar volume and poor motor functions.[17,18] In our study we used Premedication with nalbuphine at 0.05mg/kg and atropine 20microg/kg which decreases the pain of LISA but may later associated with some coginitive impairment which can be studied in new upcoming studies. In our study premedication with opioid is associated with more chances of successful intubation as compare to non medication group. These results are similar to results shared by DE Kort E *et al* in their study that without sedation there are more chances of unsuccessful intubation. Many studies shows that opioids are associated with more chance of apnea which later may require ventilatory support but in our study only one neonate required ventilatory support suggesting that opioids at low dose are more safe to address necessary analgesia and sedation leading to decrease complications. The limitation of this study is that it is a single center study corelating only pain after LISA after using nalbuphine and atropine however more studies are required by keeping more variables like hemodynamic status and to calculate the safer dose of nalbuphine which is necessary to decrease short and long term complications like post procedure apnea and sensorymotor dysfunctions.

## CONCLUSION

Nalbuphine and atropine in low dose is effective in managing pain and discomfort during LISA in pre term neonates with less post procedural complications**.**

## ETHICAL APPROVAL

Ethical approval of article was granted by the Institutional Ethical Review Board of CMH Quetta vide reference No CMH QTA-IERB /30/2024 dated 05 August, 2024.

## CONFLICT OF INTEREST

Authors declare no conflict of interest.

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## AUTHOR'S CONTRIBUTIONS

AA: Manuscript writing, data collection
HB: Critical Reviwing, data analysis
HM: Manuscript writing, statistical analysis
MSA: Research supervisor, critical reviwing
SY, HA: Data collection, data analysis
All Authors: Approval of the final version of the manuscript to be published

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