



## EFFICACY OF SURFACTANT ADMINISTRATION TO PRETERM INFANTS VIA THIN CATHETER VERSUS INSURE TECHNIQUE.

Mayda Riaz<sup>1</sup>, Shakila Asmat<sup>2</sup>, Fouzia Shaukat<sup>3</sup>, Muhammad Aslam<sup>4</sup>, Muhammad Tahir Majeed<sup>5</sup>, Sajjad Rafique<sup>6</sup>

1. MBBS, FCPS  
Senior Registrar and Fellow in Neonatology,  
Hameed Latif Hospital, Lahore.
2. MBBS, FCPS  
Senior Registrar Paediatrics,  
Sandeman Provincial Hospital,  
Quetta.
3. MBBS, DCH, MCPS, FCPS  
Professor Paediatrics,  
Shaikh Zayed Hospital, Lahore.
4. MBBS, DCH (Glasgow), MRCPCH (London), MRCP (UK)  
Professor & HOD Paediatrics,  
Shaikh Zayed Hospital, Lahore
5. MBBS, MPhil  
Professor Pathology,  
CMH Multan Institute of Medical Sciences, Multan
6. MBBS, MRCP (London) MRCPCH (UK), DRCPCH (UK)  
Consultant Paediatrician & Neonatologist,  
Hameed Latif Hospital, Lahore.

**Correspondence Address:**  
Dr. Mayda Riaz  
Senior Registrar and Fellow in Neonatology,  
Hameed Latif Hospital, Lahore.  
dr.maydariaz@gmail.com

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### INTRODUCTION

Respiratory distress syndrome (RDS) is a common respiratory disease occurring in 37.28% of premature infants and 0.11% of term infants.<sup>1</sup> It is caused by deficiency of surfactant leading to microatelectasis and decrease in lung volume.<sup>2</sup> Prematurity is the commonest risk factor<sup>3,4</sup> followed by white ethnicity, male gender, maternal diabetes, Caesarean section, chorioamnionitis, low birth weight, birth asphyxia, lung infections and meconium aspiration syndrome.<sup>4</sup> The disease has mortality rate as high as 43.61%.<sup>1</sup> Antenatal steroids and prophylactic surfactant therapy have significantly reduced the incidence of RDS and its associated mortality and morbidity.<sup>5</sup> Diagnosis of RDS can be interpreted on the basis of clinical findings of tachypnea, grunting, chest retractions,

**ABSTRACT... Objectives:** To compare the efficacy of administering surfactant to preterm infants using thin catheter and Intubate-Surfactant-Extubate (InSurE) techniques in terms of need of mechanical ventilation within 1<sup>st</sup> 72 hours of life. **Study Design:** Randomized controlled trial. **Setting:** Neonatal intensive care unit (NICU), Federal Postgraduate Medical Institute and Shaikh Zayed Hospital (FPGMI and SZH), Lahore. **Period:** From November 2014 to April 2015. **Material & Methods:** A total of one hundred preterm infants who developed respiratory distress syndrome (RDS) and fulfilled the inclusion criteria were enrolled in the study. The enrolled infants were randomly divided into two groups each comprising fifty infants. The infants in Group A were administered surfactant via thin catheter technique, whereas those in Group B by InSurE technique. The infants were monitored by clinical and laboratory parameters for the need of mechanical ventilation within 1<sup>st</sup> 72 hours of life. Descriptive statistical analyses were performed. **Results:** Majority of the preterm infants in Group A (54%) and Group B (56%) were born through Caesarean section. Group A constituted 58% (n=29) males and 42% (n=21) female infants, while Group B constituted 52% (n=26) males and 48% (n=24) females. Mean gestational age in Group A and Group B was found to be 29.43±4.24 weeks and 28.54±3.87 weeks, respectively. Mean birth weight in Group A and Group B was found to be 1375.87+143.36 and 1392.87+129.27 grams, respectively. Efficacy of surfactant was recorded as 64% (n=32) in group A and 44% (n=22) in group B (p=0.04). **Conclusion:** Surfactant administration using thin catheter is significantly more efficacious than InSurE in respect of the need of mechanical ventilation during 1<sup>st</sup> 72 hours of life.

**Key words:** InSurE, Respiratory Distress Syndrome, Surfactant, Thin Catheter.

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nasal flaring, chest radiograph and arterial blood gases.<sup>6</sup>

Conventionally, surfactant is administered via endotracheal tube followed by positive pressure ventilation.<sup>7</sup> Endotracheal intubation is invasive procedure and positive pressure ventilation increases the likelihood of Broncho pulmonary dysplasia.<sup>8</sup> Even short time exposure to excessive delivered tidal volume during ventilation can exacerbate lung injury and compromise the therapeutic effect of surfactant therapy.<sup>9</sup> The method being an expensive modality is hard to afford in low income countries. Hence, there has been a great endeavour to create alternative ways of surfactant administration.

Surfactant therapy with nasal continuous positive airway pressure (nCPAP) was found to be successful in establishing and managing the functional residual capacity of premature lungs.<sup>10</sup> Consequently, various less invasive methods of surfactant administration like InSurE and minimally invasive surfactant therapy (MIST) were devised and many are still under trials.

In InSurE technique the infants are intubated, given surfactant followed by brief period positive pressure ventilation, extubated and then placed on nCPAP. Modification of InSurE led to invent of MIST comprising four methods of surfactant administration i.e. intrapharyngeal, thin catheter, laryngeal mask and nebulization.<sup>11</sup> Out of these, thin catheter was found to be an effective method as it reduced the need for mechanical ventilation especially during 1<sup>st</sup> 72 hours of life.<sup>12,13,14</sup>

Pakistan stands 4<sup>th</sup> amongst countries with highest rate of preterm births.<sup>15</sup> Consequential increase in the incidence of RDS is demanding of specialized NICUs and proper guidelines for surfactant administration. The situation also advocates an extreme need for practicing cost effective and non invasive method of surfactant therapy. So far, very few studies have been carried out in Pakistan to assess the effectiveness of such methods. This study aims at evaluating the benefits of surfactant administration using thin catheter and InSurE techniques in our setup.

## MATERIALS AND METHODS

A randomized control trial was conducted from November 2014 to April 2015 in NICU of a university teaching, tertiary care, FPGMI and SZH, Lahore. Approval from Institutional ethical committee and written informed consent was obtained from parents of preterm infants. Preterm infants who met inclusion criteria as given below were included in the study:

1. Preterm infants both males and females, born in Gynae and Obstetrics unit of Shaikh Zayed Hospital Lahore, at less than 32 weeks of gestation.
2. The preterm infants born through SVD or caesarean section.
3. The preterm infants who developed RDS

within two hours of birth.

Preterm neonates who met exclusion criteria as given below were excluded from the study:

1. The preterm infants born with major congenital anomalies e.g. Atrial septal defect, Ventricular septal defect, Tetralogy of Fallot etc. as diagnosed on clinical examination, chest radiograph and Echocardiography.
2. The preterm infants whose parents did not give consent.
3. The preterm infants who underwent positive pressure ventilation with or without intubation in delivery room.

Respiratory distress syndrome was diagnosed clinically on manifestation of tachypnea, grunting, intercostal recessions, need for oxygen supplementation and reduced air entry on auscultation. Diagnosis was confirmed by chest radiograph and arterial blood gases (ABGs).

A total of 100 preterm infants were enrolled in the study and their data was entered in a predesigned proforma. All these infants were started nCPAP therapy with initial settings of fraction of inspired oxygen (FiO<sub>2</sub>) 60%, and positive end expiratory pressure of 6cm H<sub>2</sub>O. Pulse oximeter was attached for monitoring of their oxygen saturation.

Group allocation was concealed in an opaque envelope. Envelope, selected through lottery method was opened and patient was assigned to a specific group i.e. Thin catheter group (Group A) and InSurE group (Group B).

Exogenous surfactant was administered to infants in Group A through a 5Fr flexible sterile nasogastric tube (NG tube). The NG tube was introduced in infant's trachea 1cm below the level of vocal cords by using a laryngoscope. Surfactant was given at a dose of 4ml/kg in small portions within 1-3 minutes while the infant continued spontaneous breathing on nCPAP during the procedure. The infant's oxygen saturation was continuously monitored by pulse oximeter throughout the procedure. After surfactant administration the catheter was removed.

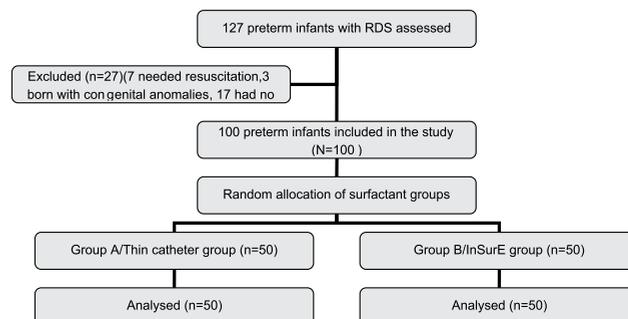
Surfactant was administered to infants in Group B by disconnecting nCPAP and passing a 2.5Fr endotracheal tube (ETT) in trachea, using laryngoscope. Depth of ETT insertion was calculated by using formula (weight in kg+6cm) and it was adjusted according to the weight of the infant. Surfactant was given through ETT at dose of 4ml/kg in two halves and the infant received positive pressure ventilation (PPV) by ambu bag. After 10-15 minutes of PPV, ETT was removed. Oxygen saturation of the infant was monitored throughout the procedure.

This procedure in both groups was followed by placement of infants on nCPAP. The infants were then monitored by chest radiograph, oxygen saturation and ABGs after two hours of surfactant administration. Thereafter the monitoring was carried out by ABGs and oxygen saturation on 8 hourly basis till 72 hrs of life. Surfactant administration was defined to be effective if it prevented mechanical ventilation in 1<sup>st</sup> 72 hrs of life and improved clinical condition of the infant.

Data was analyzed using statistical package for social sciences (SPSS) version 17.0. Descriptive statistical analyses were performed. Quantitative data like gestational age and weight was described by mean and standard deviation (SD). Qualitative data like efficacy, gender, and mode of delivery viz. spontaneous vaginal delivery (SVD) or Caesarean section (C section) was presented by frequency and percentage. The difference in efficacy in two groups was calculated using Chi square test and p value of <0.05 was considered significant.

## RESULTS

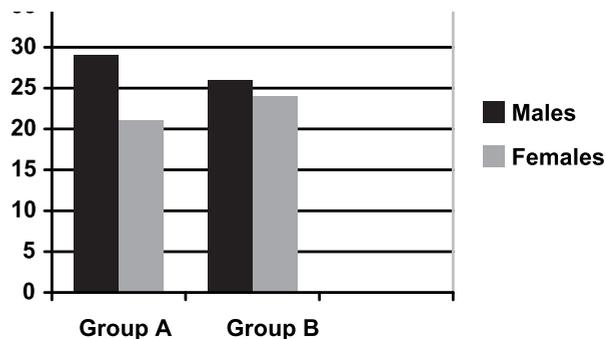
During the study period 127 preterm infants born at SZH, Lahore were assessed for inclusion in the study. Out of these, 7 infants needed resuscitation at birth, 3 had congenital anomalies while 17 infants' parents did not give consent and were excluded from the study. Remaining 100 (N=100) preterm infants fulfilled the criteria and were included in the study (Figure-1).



**Figure-1. Flow diagram showing distribution of preterm infants in the study.**

The infants were divided into two groups i.e. Group A (n=50) and Group B (n=50) using randomized selection as mentioned previously. In Group A, 54% (n=27) and 46% (n=23), while in Group B, 56% (n=28) and 44% (n=22) of the infants were born through C section and SVD respectively.

Gender distribution revealed that Group A comprised of 58% (n=29) males and 42% (n=21) females, whereas in Group B, 52% (n=26) of the preterm infants were males and 48% (n=24) were females (Figure-2).



**Figure-2. Gender breakdown of preterm babies in Group A and Group B.**

Among patients in Group A, 46% (n=23) of preterm babies were born at 25-28 weeks of gestation and 54% (n=27) were born at 29-32 weeks. Whereas in Group B, 52% (n=26) were born at 25-28 weeks and 48% (n=24) were born at 29-32 weeks of gestation. Mean gestational age in Group A and Group B was found to be 29.43±4.24 weeks and 28.54±3.87 weeks, respectively.

In Group A, 50% (n=25) of preterm babies weighed <1200 grams and 50% (n=25)

weighed between 1200-1500 grams. Similarly, in Group B, 58% (n=29) of the premature infants weighed <1200 grams and 42% (n= 21) of them weighed between 1200-1500 grams. Mean birth weight was calculated as 1375.87+143.36 and 1392.87+129.27 gram in Group-A and B, respectively.

Statistical analysis showed no significant difference in demographic data of patients in both groups (Table-I).

Surfactant was given to patients in Group A by thin catheter and to patients in Group B by endotracheal tube. The infants were monitored

for the need of mechanical ventilation within 1<sup>st</sup> 72 hours of life. Among the patients in Group A, 36 % (n=18), needed mechanical ventilation whereas 64% (n=32) succeeded to avoid mechanical ventilation. On the other hand, in Group B, 56% (n=28) needed mechanical ventilation and 44% (n=22) succeeded in avoiding mechanical ventilation within 1<sup>st</sup> 72hrs of life. Statistical analysis showed significant difference (p=0.04) in efficacy of surfactant administration among both groups (Table-II). Surfactant administration via thin catheter proved to be better method of surfactant administration than InSurE technique, in avoiding mechanical ventilation in 1<sup>st</sup> 72hrs of life of preterm infants.

		Thin Catheter Group Group A ( n=50)	InSurE Group Group B (n=50)	P-Value
Mode of delivery	C section (n%)	27 (54%)	28 (56%)	0.840
	SVD (n%)	23 (46%)	22 (44%)	
Gender	Males n (%)	29 (58%)	26 (52%)	0.546
	Females n (%)	21 (42%)	24 (48%)	
Gestational age (weeks)	25-28	23 (46%)	26 (52%)	0.548
	29-32	27(54%)	24 (48%)	
Birth weight (grams)	<1200	25 (50%)	29 (58%)	0.422
	>1200-1500	25 (50%)	21 (42%)	

**Table-I. Demographic and clinical characteristics of both groups.**

Efficacy	Thin Catheter Group Group A (n=50)	InSurE Group Group B (n=50)	P-Value
Yes	32 (64%)	22 (44%)	0.04
No	18 (36%)	28 (56%)	
Total	50 (100%)	50 (100%)	

**Table-II. Comparison of efficacy of surfactant between both groups.**

## DISCUSSION

Our study concluded that surfactant administration via thin catheter is significantly effective in reducing the need for mechanical ventilation in 1st 72 hrs of life, as compared to the conventional method (InSurE) of surfactant administration. This result is comparable to those given by Alia et al<sup>16</sup> and Lau et al.<sup>17</sup> In contrast to our results, Mohammad izadeh et al<sup>18</sup> concluded no difference in need for mechanical ventilation among both methods.

In the study, we found no significant difference in demographic data (gestational age, birth weight, gender, mode of delivery) among both groups of preterm infants offered surfactant administration,

which is comparable to results given by other studies.<sup>18,19</sup>

Surfactant administration through thin catheter has few advantages over InSurE technique. Thin catheter provides surfactant while the infant is breathing spontaneously, thus avoids use of positive pressure ventilation. It also allows infants to maintain function of the glottis and continue spontaneous breathing. On the other hand, InSurE technique is associated with sedation or analgesia, regular intubation and a short period of positive pressure ventilation.<sup>20</sup>

According to Rigo et al<sup>21</sup>, the risk of early CPAP failure, BPD and death has been reduced by use of thin catheter, when compared to InSurE technique. Studies<sup>22</sup> also show, that preterm survival rate is improved when surfactant administration via thin catheter technique is used in combination with CPAP.

Further trials need to be conducted in other neonatal units of Pakistan on a larger scale, so as to establish the efficacy of surfactant administration through thin catheter. A good follow up of these patients needs to be maintained for assessing long term outcomes. It is imperative to generate proper institutional guidelines for surfactant administration to preterm infants along with use of noninvasive ventilation techniques to attain a better outcome in these patients.

With the use of thin catheter in preterm infants with RDS, the survival rate can be improved and short and long term complications associated with positive pressure ventilation can be prevented, that will ultimately improve the preterm survival rate in our country.

## CONCLUSION

We concluded that administration of surfactant to preterm babies using thin catheter is significantly effective when compared to InSurE technique as far as requirement of mechanical ventilation in 1<sup>st</sup> 72 hrs of life is considered. The technique is cost effective, easy to perform and can be carried out in less equipped neonatal setups.

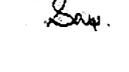
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### AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Mayda Riaz	Proposed topic, basic study design, methodology and manuscript writing.	
2	Shakila Asmat	Data collection, statistical analysis and interpretation of results.	
3	Fouzia Shaukat	Data collection, statistical analysis and interpretation of results.	
4	Muhammad Aslam	Literature review and referencing & quality insure	
5	Muhammad Tahir Majeed	Proposed topic, basic study design, methodology and manuscript writing.	
6	Sajjad Rafique	Literature review and referencing and quality insurer.	