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MISA (Minimally Invasive Surfactant Administration) Versus Insure (Intubation, Surfactant, Extubation) In Preterms Less Than 34 Weeks With RDS

Mohamed I. Garib*, Wafaa Moustafa M. Abo El-Fotoh, Mohamad A. Ramadan
Department of Pediatrics, Faculty of Medicine, Menoufia University, Egypt
***Corresponding author:** Mohamed Garib, **Mobile:** (+20) 01010688218, **E-Mail:** mhmdghreeb@yahoo.com

ABSTRACT

Background: Newborn Respiratory Distress Syndrome (RDS) or what is known as surfactant deficiency disorder is a syndrome that affects premature infants who are born prematurely and is caused by a developmental deficiency in the production of pulmonary surfactant or as it is called immature formation of the lungs, or as a result of a defect in the protein gene that forms pulmonary surfactant. Non-invasive positive pressure ventilation (NIPPV) is the first technique for respiratory therapy while MISA and InSurE are both the most commonly used in RDS.

Objective: To compare the use of the MISA method and the InSurE method in the treatment of premature infants less than 34 weeks of gestational age with respiratory distress syndrome (RDS).

Patients and methods: The sample size was 70 infants with gestational age less than 34 weeks with RDS. 35 newborn were enrolled in each group. First group received surfactant via MIST technique and the other 35 newborn received it via InSurE technique. Infants in the InSurE group required intubation, according to previous collected data from the neonatal intensive care unit (NICU) center.

Results: After the injection of surfactant, the 13 (37%) infants needed another dose in the MIST group, while only 3 (8.57%) infants in the InSurE group needed a second dose of the same substance. Accordingly, the response of the MIST group was shown to be a less improvement than the InSurE group in the child's breathing methods.

Conclusion: The MIST method was the most successful with a rate of 96.5% in terms of time and the child's response to treatment, and the researcher recommended that the reasons for the effectiveness of MISA in treating RDS should be studied. However duration of invasive mechanical ventilation were higher in MIST group than InSurE group.

Keywords: ICU, InSurE, MIST, RDS.

INTRODUCTION

The respiratory Distress Syndrome (RDS) is a common syndrome between premature who are 34 weeks gestation or younger. RDS symptoms almost appear within minutes of birth. However, they may not be observed for several hours. Newborn respiratory distress syndrome has surfactant deficiency lung disease. This surfactant is made by the cells in the airways of lung and its structure content is phospholipids and protein [(1)].

Surfactant is discovered in the amniotic fluid. Most babies will have acquired appropriate quantities of surfactant by the time they reach 35 weeks of pregnancy. Surfactant deficiency causes breathing complications in which less oxygen is provided and more carbon dioxide accumulates in the blood. There are several techniques and medication that used for RD syndrome treatment. Treatment will depend on how ill the newborn is [(2)].

Non-invasive positive pressure ventilation (NIPPV) is considered as the first technique in respiratory treatment, minimally-invasive surfactant administration (MISA) and the Intubation Surfactant Extubating (InSurE) techniques are the most common treatment for improving the oxygenation function of the lung. Non-invasive ventilation is needed for surfactant administration. Surfactant is administered as a liquid phase by tube that is an endotracheal tube in a suitable dose. Strategies that are used in minimally invasive technique for surfactant therapy (MIST) show good helpful results in preterm infants' treatment [(3)].

Nasal continuous positive airway pressure (NCPAP) is a common treatment for neonatal, which helps maintain the airways open by forcing air into the nose. It can be administered by a ventilator (while the baby is breathing on his or her own) or a separate CPAP device, which is monitored by InSurE. Nasal intermittent positive pressure ventilation (NIPPV) is considered as a better alternative for the primary respiratory support because its rate of respiratory failure is lower and also it can deliver time-cycled positive pressure ventilation more than positive end expiratory pressure (PEEP) level in the endotracheal tube absence [(4)].

In our research we wanted to compare between two techniques to give surfactant for the new born. The first technique is minimal invasive surfactant administration (MISA) which can be done by tube inserting without intubation and other technique is InSurE, which is intubation then giving surfactant then extubation. This research aims to discover the effects of MISA versus InSurE in preterm less than 34 weeks with RDS.

PATIENTS AND METHODS

The number of preterm infants at the beginning of the study was 89, 19 preterm infants were excluded due to the lack of study conditions such as: 6 infants were not in need for surfactant, 5 infants were intubated at birth, 4 infants had congenital anomaly, and 4 infants were given surfactant after 6 hours of birth. The study was

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conducted at the Pediatrics Department, Menoufia Hospital.

Sample size:

The sample size was 70 infants with age less than 34 weeks with RDS. They were divided into 2 equal groups; 35 newborn received surfactant via MIST technique and the other 35 newborn received it via InSurE technique. Infants in the InSurE group required intubation, according to previous collected data from the neonatal intensive care unit (NICU) center. The time of need for surfactant from birth was 3 hours. The duration that is recorded of surfactant administration was observed to be 193 seconds.

Randomization:

Done by computer, which generate random and different sequence and continuous numbers. To ascertain the principle of the treatment that is being employed, which is absolutely unknown, no intervention was carried out at any point of the trial, from intervention to outcome assessment and data collected analysis [(5)].

Intervention:

The Drager baby log 8000 plus ventilator was used to achieve 90 to 95% of saturation with oxygen in all newborn with RDS that approved in the NICU. All clinical team who are responsible for continuous follow up of newborns in the NICU describe RDS according to infants' oxygen requirement. Primary conditions for NIPPV included a peak inspiratory pressure (PIP) of 13–16 cm of H_2O, a PEEP of 5–6 cm of H_2O, a rate of 40 minutes, and a percentage of oxygen of 35% [(6)].
Patients who needed more than 30% FiO_2 on (NIPPV) technique to maintain oxygen saturation between 92 and 96 percent in the first 7 hours of birth that were assigned in a random way to receive the surfactant by MIST or InSurE.

Table (1): MIST and InSurE procedures.

MIST procedure	InSurE procedure
The procedure was done in NICU.	The procedure was done by the team in the NICU.
The clinical team tried hard to see the true length of the tube that feeding babies.	Newborns were intubated with particular size of endotracheal tube by using InSurE technique.
To make the baby more comfortable, swaddle and nesting were used.	No anesthesia was used, but nesting and swaddling were done.
Protectant alpha was used as a replacement for surfactant.	Protectant alpha was considered as a suitable surfactant.
When babies show an observed decrement in the RDS, they were weaned to nasal positive airway pressure.	Pressure of breathing and independent flatting resuscitation bag of the particular size.
	After half hour of surfactant administration, the infants were extubated and put back on NIPPV.

Ethical approval:

The study was approved by the Ethical Committee of the Faculty of Medicine, Menoufia University. Informed written consent was obtained from parents of all participant newborns before recruitment in the study, after explaining the objectives of the work. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Quantitative data were presented as means and standard deviation (SD) and were compared by independent t-test. Qualitative date were presented as number and percentage and were compared by Fisher's exact test or Pearson's chi-square test. $P < 0.05$ was statistical significance level for all comparisons.

RESULTS

The difference between the 2 studied groups was insignificant as regard gestational age, sex, and birth weight (Table 2)

Table (2): Demographic characteristics of gestational age, sex and birth weight

Variables			MIST (n=35)	InSurE (n=35)	P Value
Gestational Age		Mean	28.09	27.32	0.97
		S. D	1.52	1.78	
Sex	Male	N	18	20	1.00
		%	51.14	57.14	
	Female	N	17	15	
		%	48.57	42.85	
Birth Weight	< 2.7 Kg	N	20	19	0.94
		%	57.1	54.3	
	2.71: 4 Kg	N	8	12	
		%	22.8	34.3	
	> 4 Kg	N	7	4	
		%	20	11.4	

Table 3 shows that the need and duration of invasive mechanical ventilation were higher in MIST group than InSurE group.

Table (3): Comparison of the studied groups as regard the techniques' parameters

Variable Results		MIST (n=35)	InSurE (n=35)	P Value
Duration of NIPPV (Days)	Mean	6.1	4.4	0.062
	S.D.	1.23	1.54	
Need of Invasive MV	Mean	3.23	2.43	0.024
	S.D.	1.98	2.44	
Duration of Invasive MV (Days)	Mean	4.3	2.34	0.043
	S.D.	1.32	1.33	
Cases received INO	Mean	9.3	10.32	0.060
	S.D.	3.43	5.36	
Evidence of PPH	Mean	23.3	22.5	0.071
	S.D.	5.21	4.98	
Evidence of air leaks	Mean	10.3	9.54	0.056
	S.D.	3.98	3.52	

NPPV: (Non-invasive positive pressure ventilation), MV: (Mechanical Ventilation)
INO: (Inhaled Nitric Oxide), PPH: (Persistent Pulmonary Hypertension)

The number of infants who needed second dose was significantly higher in the MIST group than that in the InSurE group (Table 4).

Table (4): Comparison of the studied groups as regard reintubation/invasive mechanical ventilation risk or hemodynamically significant patent ductus arteriosus, and second dose of surfactant

Variable Results		MIST (n=35)	InSurE (n=35)	P Value
Reintubation/ Invasive mechanical ventilation	N	4	8	0.04
	%	11.42	22.86	
Hemodynamically significant patent ductus arteriosus	N	8	10	0.68
	%	22.86	28.57	
Intraventricular hemorrhage	N	0	2	0.88
	%	0	5.71	
Second dose of surfactant	N	13	3	0.04
	%	37.41	8.57	

DISCUSSION

Our study aims to compare the efficacy of the techniques MIST and InSurE in RDS infants who are aged less than 34 weeks, and were utilizing NIPPV as the first respiratory support in this randomized controlled experiment. When NIPPV is employed in preterm RDS, we found no difference in the total duration of NIPPV in MIST versus InSurE. There was also no change in the BPD/mortality composite outcome [(7)]. In our study we found that the MIST group had a more need for IMV than the InSurE group.

The difference is statistically significant also in the total duration of hospital stay which is more in the MIST group than the InSurE group. In another study **Bugter *et al.*** [(8)] the introduction of MIST was associated with significantly fewer diagnostic and therapeutic procedures in the first week of life which emphasizes the beneficial effects of MIST.

Respiratory distress syndrome in newborns occurs as a result of less surfactant in the lung than normal, the surfactant in the lung (phospholipid) is a substance that allows air to enter the alveoli, surfactant is formed in fetuses at 24 weeks of pregnancy. Its quantity increases with progress in pregnancy, and therefore the most vulnerable children to respiratory distress syndrome are premature babies born before 37 weeks of pregnancy, especially those born by caesarean section, as well as children born to a mother with gestational diabetes [(9)].

NIPPV was employed as the predominant form of respiratory support, whereas NCPAP had been the first device being used for respiratory support in previous MIST procedure. This could have low the requirements of IMV in the research groups. Non-invasive ventilation, which has previously been indicated as being preferred for premature neonates undergoing MIST, can be used to counteract the negative effects of MIST linked to limited air flow and airway resistance [(10)]. Even in physiological research, NIPPV has been demonstrated to be effective in preventing leaks and tracheal blockage caused by MIST catheterization [(5)].

In various studies, when surfactant is administrated through a tube that is tracheal feeding tube were found in 10% to > 30% of MIST attempts [(11)]. Previous studies had problems with NCPAP being interrupted throughout the operation; they retained continuous NIPPV support using an adequate nasal interface during the MIST procedure [(12)].

In the current study, the initial attempt at introducing a feeding tube in the MIST technique was successful 96.5 percent of the time, compared to 75 percent in a previous study. The high success rate in our study could be attributed to neonatologists being trained in the MIST approach prior to study enrolment [(10)].

In the current study, the need for a second dosage of surfactant was observed more in MIST group Surfactant reflux was also very rare (less than ten percent),during the MIST technique.

In previous study by **Mosayebi *et al.*** [(4)], the MIST group required more second dose surfactant than the InSurE group (35.6 percent vs 6.5 percent, p = 0.003), presumably due to the MIST method using a lower amount of surfactant (100 mg/kg) than the InSurE treatment (200 mg/kg). In the current trial, both groups received a similar dose of surfactant therapy.

Increasing the rate of surfactant retreatment in MIST was done to aid surfactant distribution, whereas InSurE it didn't. However, during investigation, continuous NIPPV administration during MIST may have more pressure effect and reducing the need for surfactant retreatment in some cases. This result is well recognized for its great unpredictability, and it was not a trial-predetermined conclusion. Many other factors play a role, including complications like sepsis, and

feeding issues that arise during the NICU stay, public health considerations such as availability of beds and existence of back transfer protocols [13].

Surfactant retreatment, can be done almost between 2–6 hours after the first dosage, according to clinical studies and published instructions, and this has been our NICU routine [14].

Our study showed that the newborn group of the MIST stayed in the hospital for longer duration than the InSurE group. This statistical difference which is significant has high social and economic effects especially in the low socioeconomic communities. We can take in consideration other factors occurring during the NICU admission like infections, nutritional and feeding issues and other public health factors like level of hospitals and availability of places in the NICUs.

CONCLUSION

The MIST method was the most successful with a rate of 96.5% in terms of time and the child's response to treatment, and the researcher recommended that the reasons for the effectiveness of MISA in treating RDS should be studied. However duration of invasive mechanical ventilation were higher in MIST group than InSurE group.

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