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COMPARISON OUTCOME OF SURFACTANT ADMINISTRATION VIA TRACHEAL CATHETERIZATION DURING SPONTANEOUS BREATHING WITH INSURE

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SUMMARY: Surfactant administration via thin endotracheal catheter (Tec) seems to be less invasive than InSurE method .We analyzed data obtained from multicenter hospitals.

This multi center randomized clinical trial study was conducted concomitant within NICU of three university hospitals of Tabriz, Isfahan and Mashhad for a period of 20 months on neonates with gestational age of 27-32 weeks. All infants received nCPAP before administration of surfactant. If we required fio2> 30%to maintain spo2 >85% then surfactant was administered. A 5f vascular catheter was placed through 1 to 2 cm below the vocal cords and surfactant was administrated slowly.

Mean gestational age in TEC was 29.6 weeks and in InSurE was the same. Mean weight in TEC was 1339 grams and in InSurE was 1304 gram. Surfactant was administered to 66 preterm via TEC method and to 70 infant via InSurE. Mortality in TEC group was significantly lower than InSurE. P< 0.01RR= 0.56, CI, 95(0.42-0.76). NEC reduced in TEC. CPAP duration decreased in two centers, p<.05 but increased in another center. Fio2 decreased rapidly and HCO3 increased 2 hours after surfactant P< 0.03 in TEC. The average mean of Oxygen supplementation, BPD, Mechanical ventilation between two groups was not statistically significant.

TEC method was effective in treating RDS. Mortality was significantly decreased in TEC group. As TEC procedure is a new method of surfactant administration and there are few studies about it, so it is too early to be certain about all aspects of this procedure.

Key words: Preterm, respiratory distress syndrome, surfactant without intubation, bronchopulmonarydysplasia.

INTRODUCTION

Neonatal respiratory distress syndrome in premature newborns is the most common cause of morbidity. None of the interventions made in the past twenty years in order to manage this disease, were as effective as surfactant replacement. Administration of surfactant is accompanied by an undeniable increase in lung volume

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stability of FRC, improving ventilation/perfusion ratio, improved oxygenation and reduction in the incidence of Air leak. Although this approach has so far is failed to reduce the incidence of BPD significantly (1). Animal studies show that ventilation in lungs without surfactant for a short period at 5 minutes induces necrosis and bronchial destruction (2). Surfactant classically is installed through endotracheal tube. It should be noted that this procedure is typically performed on infants under CPAP, so respiratory support has to be canceled and the neonate should be intubated. After instillation surfactant CPAP is established, which its direct complication can also be Dosing-related hypoxia (3).

NCPAP and surfactant therapy is now established as the cornerstone and the first level of intervention in treating neonatal RDS (4), especially in ELBW infants, it is suggested that this approach requires InSurE in order to administer Surfactant (5).

Positive pressure ventilation is the principle of INSURE method (6). As positive pressure ventilation was established for a short time, activation of inflammatory cascades in lung tissue in clinical studies and systematic studies of animals, were shown (7-8). In fact, concerning the effects of mechanical ventilation, during surfactant administration process in InSurE technique, other different surfactant administration techniques has been developed (9-14), such as administration of Surfactant via a thin catheter inserted into the trachea of neonate that is spontaneously breathing (15).Our aim in this study is to compare complications between two different procedures.

METHODS

Study sites

This multi center study was conducted, concomitant within NICU of three university hospitals of Tabriz, Isfahan and Mashhad during 20 months All of the neonates born in delivery room or operation room received uniform protocol in order to stabilize respiratory condition and if required, PEEP was started immediately after birth via neo puff at 5-6 cmH2O level and during transfer to NICU. All of the infants received CPAP before surfactant administration. If for establishing spo2 >85% we needed fio2>30%, surfactant was administered and CPAP was continued unless pco2>50-60mmhg and ph<7.2 then ventilation was continued with ventilator. Surfactant was administered based on two separate protocols, InSurE or TEC accordance to 2010 European Consensus. Written parenteral permission was obtained, before including neonates in this study.

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Study groups

This study was conducted from February 2010 and October 2012.We enrolled 136 neonates with gestational ages between 27-32 weeks whom were eligible for inclusion as mentioned above. They were randomized to two different groups of surfactant administration, (TEC and InSurE). Neonates with Apgar score min 5 less than 6, congenital malformations and congenital heart disease were excluded from this study.

TEC Procedure

NCPAP pressure was increased as much as 8 to 10 cm H20 before the procedure was started.

In order to decrease secretions of the neonate, we administered Atropin 5ug/kg before intubation. A 5f feeding tube was guided through 1 to 2 cm below the vocal cords. After placement the Feeding tube, laryngoscope was removed from the mouth and surfactant was administrated slowly over 1 to 3 minutes (16). Implemented surfactant was Curosurf manufactured by Chiesi Italian factory. Initial dose was 200mg/kg (2.5cc/kg). During administration, if the baby was suffering obstructive apnea then we slowly stimulated the infant and increased the percentage of oxygen. If desaturation continued and the baby was still in apnea then positive pressure ventilation was implemented.

Surfactant reflux into the infant's mouth was normal. It was recommended that if there was no acute respiratory failure, suctioning secretions from baby's mouth should be avoided. If severe respiratory failure occurs and there was no response to stimulation and increased spo2, then we ventilated the neonate with nasal prong or nasal mask or bag and mask, and after recovery administered surfactant. After Surfactant administration CPAP was returned to 6cmH20.

Data collection

All neonates admitted in NICU with gestational ages between 27-32 weeks who required CPAP and surfactant administration were enrolled in this study. Demographic data, mothers data, details related to the procedure and neonatal complications were recorded in questionnaire by the nurse of NICU. Recorded neonatal out comes were pneumothorax,

NEC, stage 2 or 3 of bell, ROP(Retinopathy of prematurity) with grade>2, Proven and suspected sepsis, IVH (Intraventricular hemorrhage) grade 2, BPD defined as oxygen requirement after 36 weeks postconceptional age, PDA, ROP that requires treatment, Mortality, CPAP duration, Mechanical Ventilation duration, Oxygen days and Hospitalization.

ABG was obtained from all the neonates initially and 2 hour after surfactant administration Then parameters as PEEP, Heart Rate, FIO2, SPO2 during minutes 0, 5, 10, 15, 60, 120, 24hr, 48hr, 72hr, all were included in the questionnaire by the nurse (17).

Ethics

This study was approved by the ethics committee of Tabriz University of Medical Sciences.

Statistical Analysis

Data obtained from the study were analyzed via descriptive statistics.

Mean difference test was implemented for independent groups (Independent sample t test), Chi-square test or Fisher's exact test was implemented to examine the relationship between qualitative variables. Repeated Measure of ANOVA was implemented to examine changes of respiratory indexes. Data obtained from two groups of TEC and InSurE were compared and analyzed by software SPSS 19. In this study p 0.05 was statistically significant and all p –values are two-sided.

RESULTS

In this multi center study, 136 neonates with gestational ages between 27-32 weeks were enrolled in three university hospitals of Tabriz, Isfahan and Mashhad. They were randomized into two groups of TEC and InSurE.66 infants received surfactant via Tec procedure and 70 infants were treated via InSurE method. Demographic information in infants receiving TEC are compared with method infants (Table 1). Infants in TEC group received surfactant within median time of 3.9 hrs and infants in InSurE group were treated at a median time of 4.5 hrs. TEC procedure was performed by three consultant neonatologists and four neonatal fellows. Desaturation during InSurE method was more than TEC that was statistically significant p<0.00 (Table 2).There was no difference between second dose surfactant requirement between two procedures. Po2 increased after surfactant administration in both groups. Pco2 decreased in both groups 2 hrs after surfactant administration but the slope of this decrease was more steep in InsurE p<0.08. Hco3 increased 2 hrs after surfactant administration in TEC group that was statistically significant p<0.05.PH increased in both groups 2 hrs after surfactant administration but there was no difference statistically. A rapid decrease in CPAP pressure was noted in InsurE after 2hrs but in TEC was shown after 24 hrs (Figure 1). Fio2 requirement decreased rapidly after 15 minutes in TEC but this decrease was shown after1hr in method (Figure 2). Spo2 raised rapidly in both groups after 15 minutes. Heart rate rose to more than 150 bpm in InSurE group after 2 hrs, but it decreased in TEC group after 1hr to less than 145 bpm. Mortality reduced significantly in TEC group p<0.01, RR=0.56,CI 95%(0.42-0.76).There was no difference in Prevalence of BPD between two groups. There was not any difference in other neonatal out comes between two groups of TEC and InSurE (Table 3).

DISCUSSION

Early CPAP implementation from the delivery room accompanied with surfactant administration after stabilizing the new born is accepted as a standard care in preterm infants with RDS (1). Surfactant administration requires endotracheal intubation. Complications of this procedure include sedative administration, Spo2 desaturation, performing PPV and trauma. As PPV or any stress increases prevalence of BPD so Kribs invented a non invasive route of surfactant administration that named surfactant without intubation (16). Non invasive procedure of surfactant administration is applied by a semi rigid catheter through infants' glottis while receiving CPAP. We implemented this route on 66 preterm neonates with gestational ages less than 32 weeks and compared with control group. Our study showed increasing cough p<0.00 and reflux during installation in Tec group. This may be due to uncontrolled rate of surfactant administration. Spo2 desatu-

Table 1: Demographic characteristics.

27-32 weeks	TEC (n=66)	InSurE (n=70)	P value
Study site	Tabriz 31;Isfahan 21;Mashhad 14	Tabriz 40;Isfahan 20;Mashhad 10	
Gestational age(weeks)	29.6 ± 1.7	29.6 ± 1.7	0.9
Birth weight(grams)	1339.3 ± 406	1304 ± 331	0.5
Male gender	33(50%)	42(60%)	0.5
Antenatal corticosteroids	44(66.7%)	44(62.9%)	0.6
Caesarean delivery	48(72.7%)	49(70%)	0.7
5 minute apgar min	8	7	0.09
pprom	20(30.3%)	19(27.1%)	0.6

Table 2: Detailes of procedures.

	TEC n=66	InSurE n=70	P value
Surfactant reflux	4(6.1%)	1(1.4%)	0.1
Cough	8(12.1%)	0(0%)	0.0
Second dose surfactant requirement	25(37.9%)	22(31.4%)	0.4
Intubation requirement	16(26%)	14(20%)	0.5
Desaturation	3(4.5%)	15(21.4%)	0.00

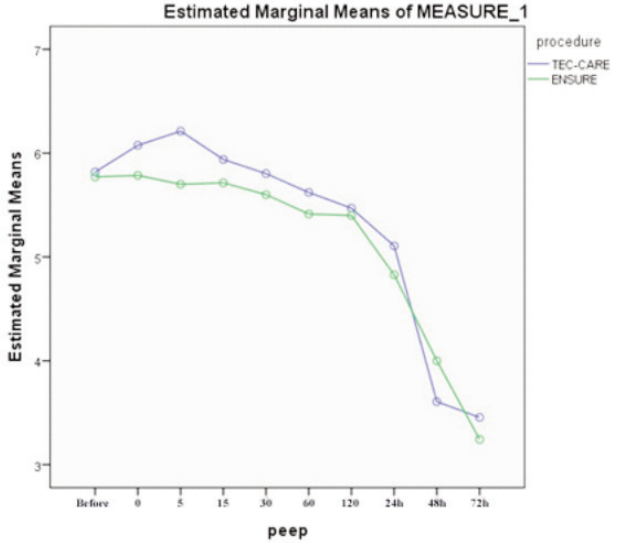

Figure 1

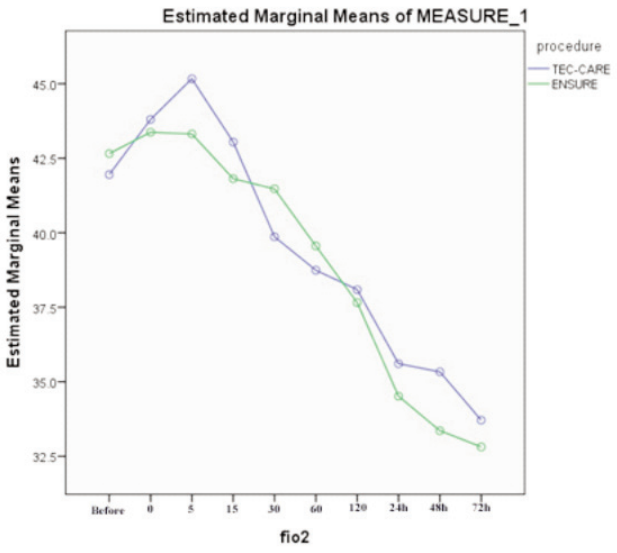

Figure 2

Table 3: Neonatal complications.

	TEC n=66	InSurE n=70	P value
IVH	13(19.7%)	14(20%)	0.96
NEC	1(%1.5)	6(%8.6)	0.06
Sepsis	29(%43.9)	26(%37.1)	0.4
PDA	19(%28.8)	16(%22.9)	0.4
PDA treatment requirement	18(%27.3)	11(%15.7)	0.1
ROP	6(%9.1)	7(%7.4)	0.26
ROP treatment requirement	5(%7.6)	1(%1.4)	0.08
Mechanical ventilation requirement (72hr)	13(%19)	16(%22)	0.6
Mortality	2(%3)	11(%15.7)	0.01
BPD	5(%7.5)	5(%7.1)	0.9
Pneumothorax	3(%4.5)	4(%5.7)	0.75
Mechanical ventilation duration (hr)	25.18 ± 8.7	13.44 ± 3.7	0.2
Total CPAP duration (hr)	SEM 135 ± 106.85	SEM 9.35 ± 82.8	0.13
O2 Supplement (hr)	SEM 29.7 ± 216.30	SEM 26.1 ± 204	0.75
Total hospital duration (days)	SEM 32.7 ± 209	SEM 2 ± 27.04	0.11

ration increased in InSurE which may lead to back ground complications due to ischemia as NEC that increased in control. In our study and Dargavilles study there were no difference in surfactant re administration (18). BPD decreased significantly in Kribs and Kanmazstudy (17, 19) in TEC but there were no difference in our and Dargavilles study between two groups (18). This may be due to high prevalence of sepsis in our wards due to over admission of infants in our NICUs and increase in ratio of patient to nurse (10 to 1). Requirement for PDA treatment increased in our study and Dargavilles and as he argues may be due to lung improvement and increased left to right shunt(18). CPAP duration decreased significantly in two NICU ward in TEC group, $p<0.03$,but its duration increased in the other in TEC, so finally there were no difference between two groups. This shows more controls are required to make standard protocols in multi center studies. Mortality reduced markedly in TEC that was statistically significant, $p<0.01$ RR=0.19, CI95 (0.04-0.83).This may be due to reduction in CPAP duration in our two centers because after CPAP is discontinued, KMC is started as our protocols. Significant Decrease in Fio2 requirement and marked increase in Hco3 may show an improvement of lung disease in TEC in comparison to control may also help mortality reduction. PDA treatment requirement is another reason for lung improvement in TEC. Our patients were randomized before the procedure and analyses blood gases at admission between two groups shows no difference between pao2, paco2, ph, hco3. Other complications as PDA, ROP, IVH, Pneumothorax, Sepsis had no difference between two groups. There was no difference in o2 supplementation, hospitalization and mechanical ventilation requirement between two groups. Guiding a thin catheter through the glottis needs a high skill in intubation, so its performance by pediatric residents is limited. It seems that this procedure is as effective as InsurE in treating RDS. Because of the lack of enough studies on the issue about this procedure wide spread implementing is not recommended.

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