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Comparing the Efficacy of Surfactant Administration by Laryngeal Mask Airway and Endotracheal Intubation in Neonatal Respiratory Distress Syndrome

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Abstract

Objectives: This study aimed to compare the efficacy of surfactant administration by laryngeal mask airway (LMA) and endotracheal intubation in the management of respiratory distress syndrome (RDS) in preterm infants.

Materials and Methods: In a prospective interventional study in NICU at Al-Zahra hospital, 50 premature infants with gestational age of 33-37 weeks and birth weight of 1800 g or more who needed surfactant replacement therapy for RDS were randomly allocated to 2 groups. Twenty-five neonates in ETT group received surfactant by endotracheal intubation and the LMA were used for the administration of surfactant in 25 neonates (LMA group).

Results: The mean gestational age in LMA group was 32.88±1.32 and it was 33.76±2.12 weeks in ETT group ($P=0.15$). The mean RDS score was not statistically different 2 two groups, 7.68±0.80 vs. 7.24±1.17 ($P=0.79$). Mechanical ventilation was needed for 1 neonate in the LMA group and 3 infants in the ETT group ($P=0.16$). After surfactant administration, the mean FiO_2 requirements to maintain oxygen saturation between% 88 to 92% showed a statistically significant decrease in both groups. The needed FiO_2s were 0.60±0.12 and 0.57±0.12 before surfactant therapy and decreased to 0.42±0.15 and 0.36±0.10 after surfactant administration in LMA and ETT groups, respectively ($P<0.001$). No choking or vomiting occurred during surfactant therapy in either group.

Conclusions: Based on our findings, the LMA may be a safe and effective alternative way for surfactant administration in late preterm infants. Future multicenter studies are recommended for determining safety and efficacy of LMA in preterm infants.

Keywords: Surfactant administration, Endotracheal intubation, Laryngeal mask, Respiratory distress syndrome

Introduction

Respiratory distress syndrome (RDS) is a common problem in preterm infants. RDS is caused by surfactant deficiency which is necessary for normal lung function (1). Surfactant replacement therapy has reduced the mortality and morbidity of the preterm infants who are at risk of developing RDS (2-4). The immediate effect of surfactant therapy is oxygenation improvement followed by the increase in functional residual capacity and lung compliance. Surfactant therapy has been widely studied in recent years. Its early administration is more beneficial than late therapy (5-7). Where possible, avoidance of mechanical ventilation or reducing its duration is recommended. Surfactant administration via endotracheal intubation with short-term ventilation followed by immediate extubation to CPAP, known as INSURE: Intubate-Surfactant-Extubate, eliminates the need for mechanical ventilation (8,9). Laryngoscopy and endotracheal intubation, which are required for the administering the surfactant, may be hazardous. The successful and easy intubation needs skill and experience. On the other hand, elective intubation for surfactant administration usually needs premedication that may cause respiratory depression and necessitate delay in extubation after surfactant administration. Potential risks of intubation include tracheal tube mal-position or dislocation, hypoxia, bradycardia, infection, stress response reflex and local trauma (10,11). Therefore, 2 less invasive administrative techniques of surfactant administration including a firm flexible catheter were introduced to the trachea using laryngoscopy and Magill's forceps while the infant is supported by continuous positive airway pressure (CPAP) and rigid thin vascular catheter positioned in the trachea by direct laryngoscopy

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introduced in recent years (12-16).

These methods have been compared with routine endotracheal intubation for surfactant administration. The results are encouraging with reduced use of mechanical ventilation and bronchopulmonary dysplasia (BPD) (14); however, this is still uncertain (15).

Despite the benefits of surfactant administration by endotracheal tube, there are some negative aspects related to the laryngoscopy and endotracheal tube insertion. They are invasive and traumatic. The laryngeal mask airway (LMA) is a practical airway device that is less invasive than the endotracheal tube (ETT) (17). It can be used without laryngoscopy which is inserted orally and directed by the index finger of the operator along the hard palate. The cuff is inflated and esophagus occlusion occurs (18,19). LMA is a supra-glottic device that can be used in adults and children to deliver positive pressure ventilation (PPV) easily and noninvasively (18-21).

There are limited studies reporting that the LMA might be an effective and less invasive device for surfactant administration to the lungs in preterm infants with RDS (22-24). This route of surfactant administration has some advantages such as easier insertion, avoidance of sedation (25), an attenuated hemodynamic stress response, less subsequent intraventricular hemorrhage (IVH) (26), and minimal increase in intraocular pressure, less interference with pulmonary physiology, avoidance of bronchial or esophageal intubation, and avoidance of laryngeal edema; in the newborn, 1 mm of edema reduces the cross-sectional area of the larynx by 65% (18). Another potential advantage of using LMA over ETT for surfactant administration is the avoidance of muscle relaxants and LMA insertion does not need the use of neuromuscular blocking agents. There is not any experience of surfactant administration through LMA in the NICUS in our country.

We decided to determine the efficacy of surfactant therapy via LMA and compare short-term outcome in neonates treated with surfactant via LMA with those neonates managed by routine surfactant administration through the ETT.

Materials and Methods

This study was a randomized clinical trial performed in NICU at Al-Zahra hospital, Tabriz. Iran. The study population consisted of inborn preterm infants with gestational age of 33 to 37 weeks and birth weight of 1800 g or more who had RDS based on clinical signs and radiologic findings.

Exclusion criteria were Apgar score of less than 4 at 5 minutes of birth, major congenital anomalies, esophageal artesia, the presence of pneumonia or pneumothorax before surfactant therapy, and birth weight less than 1800 g, since the appropriate LMA size for them is not studied.

Infants were allocated to LMA or ETT groups by computer-generated random numbers in sealed opaque envelopes.

In LMA group, laryngeal mask (Hangzhou Shanyou Co. LTD, China) size 1 was inserted orally and directed by index finger without laryngoscopy using the recommended insertion technique (18,19). There are different modified and improved versions of LMA, however, only the classic model is available in size 1 for use in neonates.

Then air cuff filled with 4 cc of air until its situation was stabilized. Sedation with analgesic drugs was not used for LMA insertion. Infants in ETT group were initially received 1-2 mcg/kg/dose intravenous fentanyl and then intubation was done with the appropriate size ETT using direct laryngoscopy by a skilled neonatology fellow or attendant (Figure 1). Following LMA insertion or endotracheal intubation, all infants underwent PPV delivered by T-piece resuscitator. Effective PPV establishment was confirmed by symmetric chest movement, good breath sounds, pink color change, the presence of vapor in the tube and yellow color change of co_2 detector.

In both groups, surfactant 100 mg/kg (Survanta, Abbot Lab, USA) were administered in 4 divided doses by a thin catheter inserted in the endotracheal tube lumen or LMA tube. During surfactant administration, oxygen saturation and heart rate were monitored. Following surfactant administration, when the spontaneous respirations resumed, LMA and ETT were removed and the infants were weaned from PPV and then NCPAP was applied. Mechanical ventilation was replaced in case of clinical deterioration, respiratory acidosis and recurrent apnea, which is known as INSURE failure.

The primary outcome was a reduction in patient's FiO_2 requirement following surfactant administration and the need to repeat the surfactant dose. The secondary outcome included mortality, pneumothorax, BPD, IVH, patent ductus arteriosus (PDA) and retinopathy of prematurity (ROP). Pneumothorax was defined as radiologic evidence of air leak in pleural space. BPD was defined as the continued need for supplemental oxygen beyond 28 days after birth. Cranial ultrasound examination was performed on days 5 to 7 of birth for the diagnosis of IVH by an experienced pediatric radiologist. PDA was diagnosed based on clinical signs and confirmed by echocardiography performed by an expert pediatric cardiologist.

Chest x-ray was obtained from all infants before and 6 hours after surfactant therapy and RDS severity was determined by an expert pediatric radiologist.

Arterial blood gas parameters were recorded at admission and 3 hours after surfactant administration. Clinical severity of RDS was assessed using Downs RDS scoring system in all patients (Table 1).

Variables such as RDS score, oxygen demand before and after the administration of surfactant, need for re-intubation or frequent use of the surfactant, radiological evidence of recovery of RDS and other complications during hospitalization were measured. For all patients,

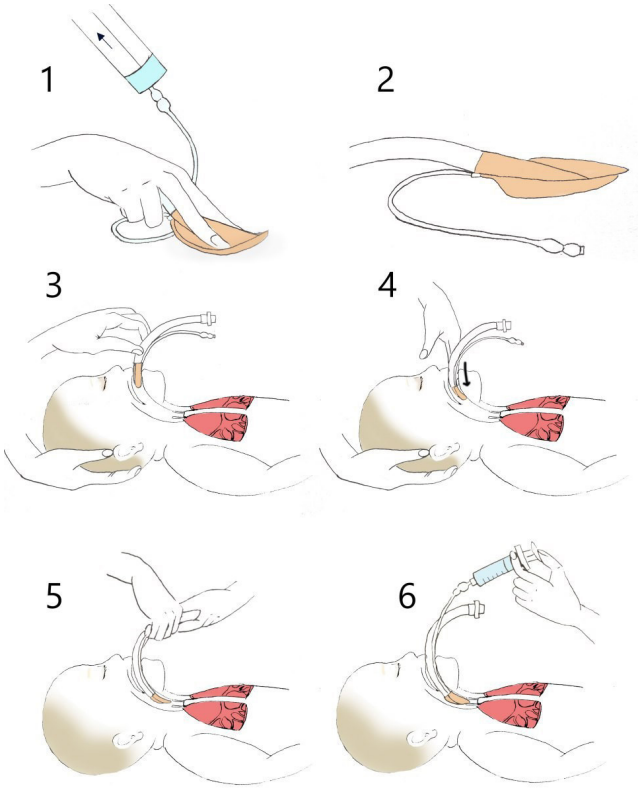

Figure 1. LMA Insertion Technique.

checklists were completed by an NICU nurse who was unaware of the aim of the study and patients groups.

Data Analyses

Data were analyzed using statistical software SPSS version 20.0 by a person who did not intervene in the diagnosis and treatment of infants. All data were analyzed by descriptive statistics (mean ± SD and percentage) and independent samples *t* test and chi-square test were used. Normality of data distribution was measured by the Kolmogorov-Smirnov test. A *P* value less than 0.05 was considered statistically significant.

Results

A total of 50 neonates were included in this study, with 13 (52%) girls and 12 (48%) boys in each group ($P > 0.05$).

The mean gestational age in the LMA group was 32.88 ± 1.32 and 33.76 ± 2.12 weeks in the ETT group ($P = 0.15$). The mean birth weight was 2078 ± 669 g in the LMA group and 2198 ± 669 g in the ETT group ($P = 0.18$). The mean RDS score was not significantly different between 2 groups (7.68 ± 0.80 in the LMA group vs. 7.24 ± 1.17 the ETT group, $P = 0.79$). All patients received surfactant during the first 10 hours of life (8.12 ± 1.77 in the LMA group and 5.16 ± 2.94 hours in the ETT group, $P = 0.49$). Maternal risk factors including the history of previous infant death, diabetes mellitus, hypothyroidism, prenatal infections or bleeding and preterm rupture of membranes (PROM) were not significantly different between two groups. The mean FiO_2 required to maintain oxygen saturation between 88% and 92% was significantly reduced after surfactant therapy in both groups (0.60 ± 0.12 and 0.57 ± 0.12 vs.0.42 ± 0.15 and 0.36 ± 0.10 before and after surfactant therapy in the LMA and the ETT groups, respectively, $P < 0.001$) (Table 2).

The second dose of surfactant was needed in 1 patient

Table 1. RDS Score

RDS Score	0	1	2
Cyanosis	None	Cyanotic in air	Cyanotic in 40% O_2
Retractions	None	Mild	Severe
Grunting	None	Audible with stethoscope	Audible without stethoscope
Air entry-make baby cry and listen to breath sounds while baby cries	Clear	Delayed or decreased	Barely audible
Respiratory rate	60	60 to 80	80 or apnea episodes

Table 2. Oxygen Saturation Variations Before, During and After Surfactant Administration

	Before Treatment	After Surfactant Therapy	*P* Value
LMA group	90.44±1.85	93.56±1.73	<0.001
ETT group	90.12±0.8	94.20±1.60	<0.001
	Before Treatment	**During Surfactant Therapy**	
LMA group	90.44±1.8	84.50±3.88	<0.001
ETT group	90.12±0.8	90.52±1.52	0.17
	During Surfactant Therapy	**After Surfactant Therapy**	
LMA group	84.50±3.88	93.56±1.73	<0.001
ETT group	90.52±1.52	94.20±1.60	<0.001

Table 3. Heart Rate Variations Before, During and After Surfactant Administration

	Before Treatment	After Surfactant Therapy	*P* Value
LMA group	141.88±6.69	145.96±7.92	0.02
ETT group	148.92±7.56	139.96±8.10	0.6
	Before Treatment	**During Surfactant Therapy**	
LMA group	141.88±6.69	121.60±20.52	<0.001
ETT group	148.92±7.56	136.84±11.56	0.46
	During Surfactant Therapy	**After Surfactant Therapy**	
LMA group	121.60±20.52	145.96±7.92	<0.001
ETT group	136.84±11.56	139.96±8.10	0.24

in the LMA group. INSURE failure occurred in 4 neonates in the ETT group and 1 neonate in the LMA group (P= 0.16). Blood gas parameters are shown in Table 2.

In the LMA group, the initial chest x-ray (CXR) was compatible with mild RDS in 7 neonates (28%) and moderate RDS in 18 neonates (72%). In the ETT group, 9 neonates (36%) had mild and 16 neonates (64%) had moderate RDS. No significant difference was observed in the primary x-ray between the 2 groups (P=0.54).

In the CXR obtained after surfactant therapy, an improvement was reported in 20 neonates (80%), unchanged in 3 neonates (12%) and unilateral improvement in 8% in the LMA group.

CXR improvement was seen in 23 neonates (92%) and unchanged in 2 patients (8%) in the ETT group (P=0.33).

No pneumothorax was reported in either group. There was no case of soft tissue trauma (epiglottis, uvula, tongue) in either group. There was no mortality in studied neonates. We found no cases of intraventricular hemorrhage, BPD and ROP in studied neonates. PDA was diagnosed in 1 case in LMA group.

The oxygen saturation and heart rate fluctuations are showed in Tables 3 and 4. There was no significant difference between the average heart rates of neonates in 2 groups (P=0.4), although the mean heart rate was lower in the LMA group.

No choking or vomiting occurred during surfactant administration in either group. Apnea occurred in one neonate after surfactant administration in the LMA group.

Discussion

We evaluated a less invasive surfactant administration technique in preterm infants with RDS. We found no adverse effect during surfactant administration via LMA. Based on our findings, RDS was successfully managed by this route of surfactant delivery.

Exogenous surfactant therapy results in reduced mortality and morbidity in preterm infants with RDS. The routine technique of surfactant administration is by endotracheal intubation. Oxygen desaturation may occur during its administration. Airway and subsequent pulmonary injury may be associated with intubation and mechanical ventilation. Although the heart rate and oxygen saturation in LMA group were lower than ETT group, severe bradycardia (heart rate less than 100/min) and oxygen saturation less than 80% were not recorded in any infant.

Administration of a liquid above the glottis is a potential complication of surfactant therapy by LMA. However, none of our patients showed signs of laryngospasm. Complications following LMA use include coughing, laryngospasm, retching, breath holding, vomiting, stridor, desaturation and excessive salivation with an incidence of 10 to 13% (27). The potential disadvantages of LMA are the risk of aspiration and gastric inflation during PPV, inadequate alveolar ventilation and impossibility of airway suctioning.

A larger dose of surfactant may be needed to attain an identical pulmonary dose (24). We have used the same doses of surfactant in all patients without significant difference in clinical response.

Only a few studies reported the use of LMA for surfactant therapy in preterm neonates (23,24). Lopez-Gil et al reported the successful use of LMA for the administration of surfactant in 2 preterm neonates with birth weight of 1.36 and 3.2 kg. They found an improvement in respiratory function within 3 to 6 hours (24).

Trevisanuto et al showed an improvement in oxygenation in all 8 neonates who were treated by surfactant via LMA. The studied neonates had a median gestational age of 31 weeks and birth weight of 1700 g, 2 of whom were subsequently intubated. They had one case of pneumothorax (23).

In our study, the neonates were in the supine position after surfactant administration, but in the animal model study, they were suspended in the upright position that may affect surfactant distribution (28). Roberts et al showed in their animal model study that the improvement in oxygenation after surfactant administration via LMA did not differ from its administration via ETT with less physiological perturbations. They suggested that surfactant administered above the glottis via LMA reaches

Table 4. The Needed FiO2 Before and After Surfactant Replacement Therapy in Both Groups

Needed Fio_2	LMA Group	ETT Group	*P* Value
Before treatment	60.8±12.8	57.2±12.7	<0.001
After surfactant therapy	42.8±15.6	36.0±10.6	<0.001

the lungs and its distribution is similar to that occurs when the surfactant is administered below the glottis via an ETT (28).

In a recent study, 26 preterm infants with birth weight ≥1200 g with RDS were treated by surfactant through LMA. They showed a reduction in FiO_2 requirement after surfactant therapy without significant difference in subsequent mechanical ventilation and pneumothorax (29).

There are a number of case reports that showed LMA is useful for neonatal inter-hospital transport in situations which other forms of airway management fail (30).

Endotracheal intubation is the widely accepted route of surfactant replacement therapy. Our study demonstrates that surfactant can be administered in a non-invasive manner. Future studies with a large number of patients are needed to show that this manner is as effective as endotracheal surfactant administration. The advantage of our study is that it is one of the first randomized clinical trials compared the efficacy of surfactant therapy via LMA and ETT in late preterm neonates.

Conflict of Interests

None.

Ethical Issues

This research project was approved by Ethics Committee of Tabriz University of Medical Sciences (n = 93116) and registered in the Iranian Clinical Trial Registry (identifier: IRCT201411183915N12). All patient information was kept confidential and parental consent to conduct a study on their children was obtained.

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References

1. Sweet DG, Carnielli V, Greisen G, et al. European Consensus Guidelines on the Management of Respiratory Distress Syndrome - 2016 Update. Neonatology. 2017;111(2):107-125. doi:10.1159/000448985
2. Engle WA, Stark AR. Surfactant-Replacement Therapy for Respiratory Distress Syndrome in the Preterm and Term Neonate: Congratulations and Corrections: In Reply. Pediatrics. 2008;121(6):1291-1292. doi:10.1542/peds.2008-0910
3. Soll RF. Prophylactic natural surfactant extract for preventing morbidity and mortality in preterm infants. Cochrane Database Syst Rev. 2000(2):Cd000511. doi:10.1002/14651858.cd000511
4. Corbet A, Bucciarelli R, Goldman S, Mammel M, Wold D, Long W. Decreased mortality rate among small premature infants treated at birth with a single dose of synthetic surfactant: a multicenter controlled trial. American Exosurf Pediatric Study Group 1. J Pediatr. 1991;118(2):277-284.
5. Stevens TP, Blennow M, Soll RF. Early surfactant administration with brief ventilation vs selective surfactant and continued mechanical ventilation for preterm infants with or at risk for RDS. Cochrane Database Syst Rev. 2002(2):Cd003063. doi:10.1002/14651858.cd003063
6. Papile L-A, Baley JE, Benitz W, et al. Respiratory support in preterm infants at birth. Pediatrics 2014; 133: 171-4.
7. Verder H, Albertsen P, Ebbesen F, et al. Nasal continuous positive airway pressure and early surfactant therapy for respiratory distress syndrome in newborns of less than 30 weeks' gestation. Pediatrics. 1999;103(2):E24.
8. Pfister RH, Soll RF. Initial respiratory support of preterm infants: the role of CPAP, the INSURE method, and noninvasive ventilation. Clin Perinatol. 2012;39(3):459-481. doi:10.1016/j.clp.2012.06.015
9. Verder H, Robertson B, Greisen G, et al. Surfactant therapy and nasal continuous positive airway pressure for newborns with respiratory distress syndrome. Danish-Swedish Multicenter Study Group. N Engl J Med. 1994;331(16):1051-1055. doi:10.1056/nejm199410203311603
10. O'Donnell CP, Kamlin CO, Davis PG, Morley CJ. Endotracheal intubation attempts during neonatal resuscitation: success rates, duration, and adverse effects. Pediatrics. 2006;117(1):e16-21. doi:10.1542/peds.2005-0901
11. Asai T, Koga K, Vaughan RS. Respiratory complications associated with tracheal intubation and extubation. Br J Anaesth. 1998;80(6):767-775.
12. Kribs A, Hartel C, Kattner E, et al. Surfactant without intubation in preterm infants with respiratory distress: first multi-center data. Klin Padiatr. 2010;222(1):13-17. doi:10.1055/s-0029-1241867
13. Dargaville PA, Aiyappan A, Cornelius A, Williams C, De Paoli AG. Preliminary evaluation of a new technique of minimally invasive surfactant therapy. Arch Dis Child Fetal Neonatal Ed. 2011;96(4):F243-248. doi:10.1136/adc.2010.192518
14. Göpel W, Kribs A, Härtel C, et al. Less invasive surfactant administration is associated with improved pulmonary outcomes in spontaneously breathing preterm infants. Acta Paediatr. 2015 Mar;104(3):241-246. doi:10.1111/apa.12883
15. More K, Sakhuja P, Shah PS. Minimally invasive surfactant administration in preterm infants: a meta-narrative review. JAMA Pediatr. 2014;168(10):901-908. doi:10.1001/jamapediatrics.2014.1148
16. Kanmaz HG, Erdeve O, Canpolat FE, Mutlu B, Dilmen U. Surfactant administration via thin catheter during spontaneous breathing: randomized controlled trial. Pediatrics. 2013;131(2):e502-e509. doi:10.1542/peds.2012-0603
17. Brain AI. The development of the Laryngeal Mask--a brief history of the invention, early clinical studies and experimental work from which the Laryngeal Mask evolved. Eur J Anaesthesiol Suppl. 1991;4:5-17.
18. Trevisanuto D, Micaglio M, Ferrarese P, Zanardo V. The laryngeal mask airway: potential applications in neonates.

Arch Dis Child Fetal Neonatal Ed 2004; 89(6): F485-F489. doi: 10.1136/adc.2003.038430
19. Brain AI. The laryngeal mask--a new concept in airway management. Br J Anaesth. 1983;55(8):801-805.
20. Brimacombe J, Berry A. The laryngeal mask airway--anatomical and physiological implications. Acta Anaesthesiol Scand 1996; 40: 201-9.
21. Berry AM, Brimacombe JR, Verghese C. The laryngeal mask airway in emergency medicine, neonatal resuscitation, and intensive care medicine. Int Anesthesiol Clin. 1998;36(2):91-109.
22. Abdel-Latif ME, Osborn DA. Laryngeal mask airway surfactant administration for prevention of morbidity and mortality in preterm infants with or at risk of respiratory distress syndrome. Cochrane Database Syst Rev. 2011(7):Cd008309. doi:10.1002/14651858.CD008309.pub2
23. Trevisanuto D, Grazzina N, Ferrarese P, Micaglio M, Verghese C, Zanardo V. Laryngeal mask airway used as a delivery conduit for the administration of surfactant to preterm infants with respiratory distress syndrome. Biol Neonate. 2005;87(4):217-220. doi:10.1159/000083370
24. Brimacombe J, Gandini D, Keller C. The laryngeal mask airway for administration of surfactant in two neonates with respiratory distress syndrome. Paediatr Anaesth. 2004;14(2):188-190.
25. Lopez-Gil M, Brimacombe J, Alvarez M. Safety and efficacy of the laryngeal mask airway. A prospective survey of 1400 children. Anaesthesia. 1996;51(10):969-972.
26. Fujii Y, Saitoh Y, Tanaka H, Toyooka H. Cardiovascular responses to tracheal extubation or LMA removal in children. Can J Anaesth. 1998;45(2):178-181. doi:10.1007/bf03013260
27. Trevisanuto D, Verghese C, Doglioni N, Ferrarese P, Zanardo V. Laryngeal mask airway for the interhospital transport of neonates. Pediatrics. 2005;115: e109-e111. doi: 10.1542/peds.2004-1468
28. Roberts KD, Lampland AL, Meyers PA, Worwa CT, Plumm BJ, Mammel MC. Laryngeal mask airway for surfactant administration in a newborn animal model. Pediatr Res. 2010;68(5):414-418. doi:10.1203/PDR.0b013e3181ef7619
29. Attridge JT, Stewart C, Stukenborg GJ, Kattwinkel J. Administration of rescue surfactant by laryngeal mask airway: lessons from a pilot trial. Am J Perinatol. 2013;30(3):201-206. doi:10.1055/s-0032-1323592
30. Fraser J, Hill C, McDonald D, Jones C, Petros A. The use of the laryngeal mask airway for inter-hospital transport of infants with type 3 laryngotracheo-oesophageal clefts. Intensive Care Med. 1999;25(7):714-716.