Respiratory monitoring during neonatal resuscitation using a laryngeal mask airway vs. a face mask

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ABSTRACT

Objective: To evaluate the respiratory function of asphyxiated infants resuscitated with i-gel laryngeal mask airway (LMA) vs. face mask (FM) in a low-resource setting.

Methods: In this sub-study from the NeoSupra trial, respiratory function during the first 60 inflations was evaluated in 46 neonates (23 with LMA and 23 with FM) at the Mulago National Referral Hospital, Uganda. The primary outcome was the mask leak (%). The secondary outcomes included inspired (VTi) and expired (VTe) tidal volumes, and heart rate response to ventilation.

Results: Mean leak was 39% (SD 20) in LMA and 46% (SD 24) in FM arms (p=0.32). Mean VTe was 8.2 ml/kg (SD 3.4) in LMA and 8.8 ml/kg (SD 5.8) in FM arms (p=0.66), while mean VTi was 15.6 ml/kg (SD 5.6) in LMA and 16.2 ml/kg (SD 8.0) in FM arms (p=0.77). A shorter time was needed to achieve heart rate >100 bpm in LMA (median 13 s IQR 9-15) with respect to FM arm (median 61, IQR 33-140) (p=0.0002).

Conclusion: Respiratory function was not statistically different between neonates resuscitated with LMA vs. FM. LMA was associated with faster heart rate recovery compared to FM in

neonates with bradycardia. Further research is needed to investigate possible advantages of LMA on respiratory function at birth.

INTRODUCTION

The current neonatal mortality rates in Sub-Saharan Africa remain 22 times higher than the average ratio of 1 in 600 found in high-resource settings. [1] Intrapartum-related death or birth asphyxia is the third leading cause of under-5 mortality [2] and contributes significantly to global long-term developmental disability. [3] According to expert estimation, effective resuscitation has the potential to reduce 30% of these deaths. [4]

After the onset of respiration, a rapid transition from placental to pulmonary gas exchange begins with the clearance of fetal lung fluid, lung aeration and increase in pulmonary blood flow. [5,6] Proper drying and stimulation can result in the onset of spontaneous breathing, [7] but effective positive pressure ventilation (PPV) remains essential for a good outcome in the most depressed neonates. [8] PPV is routinely initiated with a face mask (FM). Still, it is challenging to perform, and the implementation of neonatal resuscitation educational programs show discordant results. [9,10] The major obstacles to effective FM ventilation are mask leakage, [11-14] airway obstruction, [5] and unnecessary pauses during PPV. [15] The current evidence suggests that the neonatal laryngeal mask airway (LMA) is a safe alternative to face mask ventilation (FMV). [16-18] The i-gel® size 1 is a cuffless LMA (Intersurgical, Wokingham, Berkshire, UK), which is user-friendly and provides a good seal for PPV delivery, with the potential to enhance performance in neonatal resuscitation. [19-22] Recent studies demonstrated that the use of LMA by midwives could reduce resuscitation time in settings with high rate of asphyxia at birth. [23,24] The main objective of this study was to compare the respiratory function in asphyxiated neonates resuscitated with LMA vs. FM in a low-resource setting.

METHODS

Study design

This sub-study from the NeoSupra trial [18] investigated respiratory monitoring during neonatal resuscitation. The study was carried out at the Department of Obstetrics and Gynecology, Mulago National Referral Hospital, Kawempe Division in Kampala, Uganda, where about 25,000 deliveries occur every year. Participants were recruited at the labour ward, and the operating theatre where 15-20 caesarean sections take place every day, most of them on an emergency basis.

Patients

Neonates with gestational age $\geq$34 weeks (by the best obstetric estimate based on the last menstrual period or ultrasound scan), expected birth weight $\geq$2000 g, need for PPV at birth and written parental consent were eligible for inclusion. Exclusion criteria included the presence of major malformations incompatible with sustained life or affecting the airways.

Procedures

Detailed description of the procedures during the main trial is provided elsewhere. [18] Prior to the main trial, approximately 200 midwives and doctors involved in neonatal resuscitation participated in a one-day modified Helping Babies Breathe (HBB second edition) refresher course, including a training module for the use of the LMA evaluated in two previous studies. [18,23-25] In this sub-study, the recruitment of eligible participants took place each time a study doctor was available to manage the monitoring equipment. The health staff and research assistants were not blinded to the allocation arm. Neonates were cared for, following an updated Mulago Hospital neonatal resuscitation flowchart based on HBB (second edition) and the American Heart Association & American Academy of Pediatrics 2015 guidelines. [8] HBB-trained health staff on duty performed the resuscitations. All

resuscitations were recorded on video using an HD 1080P Black Box AI-IP018 camera (Shenzen Aishine Electronics Co. Ltd, China). The video footage provided an accurate assessment of ventilation time, heart rate (HR), assistance by supervising physician, and conversion to the alternative device. A research assistant recorded the time from birth to the onset of drying/stimulation with a stopwatch. HR was registered using an electrocardiogram-based signal. A dry-electrode monitor (NeoBeat Newborn Heart Meter, Laerdal Global Health, Stavanger Norway) and/or a 3-lead ECG monitor (Philips Intellivue X2; Koninklijke Philips NV, Amsterdam, the Netherlands) was placed on the neonates who did not respond to stimulation. PPV was started in case of apnea and/or gasping, and administered with a 240-mL silicon self-inflating bag that had a pop-off valve limit at 40 cm H_2O (Laerdal Medical, Stavanger, Norway) connected to i-gel® LMA or a silicone, round-shaped FM (Laerdal Medical, Stavanger, Norway).

A variable orifice pneumotachometer (Avea VarFlex Flow Transducer, Vyaire Medical, Yorba Linda, USA) was placed between the self-inflating bag and LMA or the FM, and used to measure flow and airway pressure. The probe added 2.8 cm to the height of the self-inflating bag-mask unit and a dead-space of 0.7 mL. An unobtrusive tubing system connected the probe to a New Life Box (Advanced Life Diagnostics, Weener, Germany) neonatal respiratory function monitor (RFM). The monitor integrates the signals to display the flow data and calculate inspired tidal volume (VTi) and expired tidal volume (VTe). The formula (leak % = ((VTi - VTe)/VTi) x100) was used to calculate the leak from the LMA or FM, and a threshold of 10% was applied by the system to exclude minor leaks. Peak inspiratory pressure (PIP) was recorded with a deviation of <1.5% of the expected pressure, the highest accuracy of any currently available system. [26]

Health workers initiated PPV in room air at a frequency of 40-60 inflations per minute. Neonates

who failed on the assigned device (poor HR response and/or lack of chest rise) received corrective measures, including mask reposition, opening the mouth, suctioning, and increasing ventilation pressure. In case of obstruction of the trachea, the mask was removed, and deep rescue oropharyngeal suctioning was performed using a re-expandable bulb suction device. Direct meconium suctioning through the LMA was not possible. Conversion to the alternative device (LMA or FM) was recommended in the case of continued inadequate response after 3 min resuscitation. All neonates with respiratory distress, hypothermia (axillary temperature <36.0°C, 5 min Apgar score $\leq$6) or signs of encephalopathy, were transferred to the neonatal unit.

Three research assistants on duty recorded perinatal data. The research assistant supervisor and 2 co-investigators (S.M.H and N.J.P) reviewed videos. The data were double-entered on a server using Open Data Kit 2.0 tool suite. [27]

Outcome measures

The primary outcome measure was mask leak, calculated as (VTi - VTe)/VTi) x100 and expressed as a percentage for each participant. The secondary outcome measures included VTe (ml/kg); PIP (cm H_2O); VTi (ml/kg); time-to-start ventilation; ventilation time; HR response to ventilation (HR was measured at start and after 30 and 60 inflations); time to obtain HR$\geq$100 bpm; switch to other device; need for intubation; and need for rescue suctioning. Respiratory data for the first 60 breath counts were analysed to avoid contamination between arms.

Sample size

A sample size of 46 neonates (23 per arm) was required to have a 0.9 chance of detecting, as significant at the $p<0.05$ level, a mean difference of 20 (SD 20) in the mask leak percentage between the two arms.

Statistical analysis

Categorical data were summarized as number and percentage, whereas continuous data were summarized as mean and standard deviation (SD), or median and interquartile range (IQR). Categorical data were compared between the two arms using Fisher's test. Continuous data were compared between the two arms using Student's t-test or the Mann-Whitney test. Multiple measures of HR over time were evaluated with a mixed regression model, including arm, time, and interaction arm*time. All tests were two-sided, and a $p<0.05$ was considered statistically significant. Data were analysed using R 4.0 (R Foundation for Statistical Computing, Vienna, Austria). [28]

Ethical considerations

The Mulago Hospital Research and Ethical Committee (MHREC 1168), the Uganda National Council of Science and Technology, the Director-General from the Ministry of Health, Uganda, and the Regional Committee for Medical and Health Research Ethics (REK South East ref 2017/989) in Norway approved the protocol. The sub-analysis presented in this study was included in the statistical analysis plan of the main study. The study purchased LMAs without corporate sponsorship.

RESULTS

The characteristics of the 46 neonates included in the study are shown in Table 1.

Ventilation started at median 39 s after birth (IQR 25-68) and lasted median 103 s (IQR 63-329), with no statistical differences between the arms ($p=0.99$ and $p=0.22$) (Figure 1).

During the first 60 inflations, mean mask leak was 39% (SD 20) using LMA and 46% (SD 24) using FM ($p=0.32$) (Figure 1). Mean VTe was 8.2 ml/kg (SD 3.4) with LMA and 8.8 ml/kg (SD 5.8) with FM ($p=0.66$), whereas mean VTi was 15.6 ml/kg (SD 5.6) with LMA and 16.2 ml/kg

(SD 8.0) with FM (p=0.77). PIP was 39.4 cm H_2O (SD 7.6) with LMA and 34.5 cm H_2O (SD 8.2) with FM (p=0.04) (Figure 1).

Overall, HR response seemed better with LMA vs. FM (p=0.05), and increased during the first 60 inflations (p<0.0001), but the difference between LMA and FM reduced over time (p=0.04) (Figure 2). In 26 neonates with HR<100 bpm at start of ventilation, shorter time was needed to reach HR>100 bpm with LMA (median 13 s, IQR 9-15) compared to FM (median 61 s, IQR 33-140) (p=0.0002).

Resuscitation outcome measures are shown in Figure 3. Three FM neonates and no LMA neonates were converted to the alternative device due to continued unsatisfactory response after 3 min of resuscitation (p=0.23). One neonate in the LMA group and three neonates in the FM group were intubated (p=0.60), with meconium present in three neonates. Four LMA neonates and six FM neonates received rescue suction due to airway obstruction (p=0.72). There were no severe adverse events in either arm. In the FM arm, there were three cases of abdominal distention; in the LMA arm, there was one case of gastric distention and one case of mouth bleeding with good clinical outcome. Detailed information on primary and secondary outcome measures are given in Table 2.

DISCUSSION

The use of LMA for resuscitation did not provide statistically different mask leaks and VTe compared to FMV. The LMA provided higher PIP and faster HR recovery in neonates with bradycardia.

While a recent study did not demonstrate better efficiency in term of decreased mortality and short-

term neurological outcome, [18] general reporting suggests that LMA may be more effective than FM in terms of shorter resuscitation and ventilation times, with less need for endotracheal intubation. [16] This can be explained by LMA design that may avoid the leak around the mask and by-passes the airway blockage.[25,26] The i-gel® LMA used on a manikin had a mask leak of only 5.7% and outperformed six other LMAs and two FMs. [22] To our knowledge, this is the first report evaluating respiratory function in neonates during PPV with LMA in the delivery room. As LMA bypasses distensible dead space in the oro/nasopharynx and may/should reduce the amount of gas entering the stomach that occurs with FM, it is reasonable to hypothesize an increased VTe using LMA. However, our data showed comparable VTe using LMA and FM, thus suggesting that relevant leak may occur also using LMA in humans, in disagreement with the manikin study. [22]

The mean oropharyngeal leak pressure reported for the LMA in paediatric anaesthesia ranges between 20-27 cm H_2O and compares favourably to other devices. [29] LMA leak may have been caused by the PIP (39.4 cm H_20) exceeding the maximum oropharyngeal leak pressure. A high rate of upper airway obstructions was suggested by abundant meconium-stained secretions, as observed during video review. Mask leak during FMV was similar to the findings by Thallinger et al. [30] Excessive mask leak (>60%) could be clinically significant and occurred in 17.4% in the LMA group and 30.4% of the FM group.

The optimal tidal volume for PPV with LMA is unknown, but a delivered VTe of 9.3 mL/kg produced the highest increase in HR during FMV in Tanzania. [31] Van Vonderen et al. [31] monitored VTe in preterm neonates and reported lower VTe in the group receiving PPV with ETT compared to FMV. The authors speculated that FMV pressurizes the upper airways above the glottis, and the high compliance of the oropharyngeal area could result in added dead space and inadequate gas exchange. Mask distention may also contribute to VTe in FMV. [32]

We found abdominal movements during video reviews, suggesting that air entering and exiting the stomach contributed to VTe. We speculated that this phenomenon could be clinically relevant in neonates with airway obstruction, low lung compliance, or a closed glottis. [5,6] LMA differs from FM because it bypasses the upper airway structures (and that portion of the airway dead space), thus ventilation with LMA could establish functional residual capacity earlier despite a lower VTe. VTe <2.5 mL/kg could also have clinical significance and occurred in 0% of the LMA arm and 17% in the FM arm.

An increase in HR is a critical indicator of effective ventilation during neonatal resuscitation. [33,34] LMA ventilation gave faster HR recovery compared to FMV. However, Apgar score at one minute and initial HR was lower in the FM arm. We cannot exclude that subjects in the FM group were more depressed at birth (since their Apgar score at 1 min was also lower) and FM could be exerting pressure upon trigeminal nerve resulting in a prolonged period of bradycardia. [35] Time-to-start ventilation was not different between LMA and FM, and was adherent to neonatal resuscitation guidelines. [8,34] Clinical studies, including training of local healthcare staff, have a positive impact on the management of patients. [7,36-42] Furthermore, the switch rate to the other device was lower than the rate reported in a previous feasibility study, [23] suggesting an improved FMV performance.

Ventilation time with LMA was shorter compared to FMV, in agreement with earlier studies. [23,43-46] Presence of meconium-stained fluid may cause upper airway obstruction, limiting the effectiveness of ventilation. While FM and intubation have already been evaluated in the presence of meconium-stained fluid, information on LMA is lacking. [16] We found that a large proportion of neonates in both arms was born through meconium-stained amniotic fluid, of which four neonates needed rescue suction in the LMA arm and six neonates in the FM arm. PPV failed because of airway obstruction in one neonate in the LMA arm and in three neonates in the FM arm. Future research is required to

investigate this aspect. [16]

Our study has some limitations. First, the recruitment of eligible participants for this sub-study could only take place when a researcher was available to manage the monitoring equipment, thus potentially influencing the generalisability of the findings. Second, the actual effect size proved to be smaller than expected thus we could not report a statistically significant difference in leak between the arms. The same considerations could be made for some secondary outcomes.

Our findings could be interesting for both high and low-resource settings since this is the first report on respiratory function and HR response during resuscitation with LMA. Further studies are required to test the hypothesis of better ventilation with LMA compared to FM and the impact on neonatal resuscitation and long-term outcomes.

CONCLUSIONS

Mask leak and expiratory tidal volume were not statistically different with a cuffless LMA compared to the standard FM. LMA provided higher PIP and faster HR recovery in neonates with bradycardia. Further research is needed to investigate possible advantages of LMA on respiratory function at birth.

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Abbreviations

ECG: Electrocardiogram; FM: Face Mask; FMV: Face Mask Ventilation; HBB: Helping Babies Breathe; HR: Heart Rate; IQR: Inter Quartile Range; LMA: Laryngeal Mask Airway; MHREC: Mulago Hospital Research and Ethics Committee; PIP: Peak Inspiratory Pressure; PPV: Positive Pressure Ventilation ; RCN: Research Council of Norway; RFM: Respiratory Function Monitoring; SD: Standard Deviation; VTe: Expired Tidal Volume; VTi: Inspired Tidal Volume

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FIGURE LEGENDS

Figure 1. Ventilatory outcome measures: comparison between LMA and FM of leak (%), expiratory tidal volume (ml/kg), inspiratory tidal volume (ml/kg), peak inspiratory pressure (cm H_2O, time-to-start of ventilation (s) and ventilation time (s) with respiratory function monitor.

Figure 2. HR response to ventilation: comparison between LMA and FM of HR at start of ventilation (bpm), after 30 and after 60 given inflations.

Figure 3. Resuscitation outcome measures: comparison between LMA and FM in the proportion of neonates switched to the other device, intubated and in need of suction because of failed ventilation.

Table 1. Infant characteristics: Comparison of demographic characteristics between the study arms

	LMA (n=23)	**FM (n=23)**
Male: Female	11:12	14:9
Birth weight, g	3,000 (2,490-3,425)	3,240 (2,800-3,430)
Caesarean section	17 (74%)	15 (65%)
Meconium stained amniotic fluid	13 (57%)	13 (57%)
Chorioamnionitis [a]	7 (32%)	3 (13%)
Apgar score		
1 min	4 (2-4)	3 (2-4)
5 min	6 (5-6)	4 (4-6)
10 min	7 (7-8)	7 (5-8)

Data expressed as n (%) or median (IQR). [a]The information was unclear in one neonate.

Table 2. Primary and secondary outcome measures

		LMA (n=23)	FM (n=23)	p-value
Primary outcome	Mask leak during first 60 inflations, % [a]	39 (20)	46 (24)	0.32
Secondary outcomes, ventilatory	Expiratory tidal volume during first 60 inflations, ml/kg [a]	8.2 (3.4)	8.8 (5.8)	0.66
	Peak inspiratory pressure during first 60 inflations, cm H_2O	39.4 (7.6)	34.5 (8.2)	0.04
	Inspiratory tidal volume during first 60 inflations, ml/kg [a]	15.6 (5.6)	16.2 (8.0)	0.77
	Time to start ventilation, seconds [b]	36 (27-73)	45 (25-62)	0.99
	Ventilation time, seconds [b]	95 (63-180)	197 (58-662)	0.22
Secondary outcome, circulatory	HR, bpm: [b] at start after 30 inflations after 60 inflations	 97 (70-114) 162 (146-168) 167 (150-182)	 73 (63-115) 134 (74-168) 150 (74-166)	0.05 [d]
	Time for HR >100 bpm, seconds [bc]	13 (9-15)	61 (33-140)	0.0002
Secondary outcome, resuscitation	Switch to the other device	0 (0)	3 (13)	0.23
	Need for intubation	1 (4)	3 (13)	0.60

Data is expressed as n (%), [a]mean (SD) or [b]median (IQR). [c]In 26 infants (13 LMA and 13 FM) with HR<100 bpm at start of ventilation. [d]HR increased during the first 60 inflations ($p<0.0001$), but the difference between i-gel and FM arms reduced with time ($p=0.04$).