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Clinical paper

A randomized trial of oropharyngeal airways to assist stabilization of preterm infants in the delivery room

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Abstract

Objective: Positive pressure ventilation (PPV) using a ventilation device and a face mask is recommended for compromised newborn infants in the delivery room (DR). Airway obstruction and face mask leak during PPV may contribute to failure of resuscitation. Using an oropharyngeal airway (OPA) may improve efficacy of mask PPV. To determine whether the use of an OPA with mask PPV in the DR during stabilization of infants <34 weeks' gestational age, reduces the incidence of airway obstruction.

Intervention and measurements: An international two center unblinded randomized trial. Infants assessed by the clinical team to require PPV, were randomly assigned to receive PPV using a T Piece device with either a soft round face mask alone or in combination with an appropriately sized OPA. Resuscitation protocols were standardized. A hot-wire anemometer flow sensor measured respiratory function during the first five minutes of stabilization. The primary outcome was the incidence of airway obstruction, either complete (no gas flow) or partial (minimal gas flows resulting in expired tidal volumes <2 mL/kg).

Main results: A total of 137 infants were enrolled. Obstructed inflations were more frequently observed in infants stabilized with an OPA (81% vs. 64%; p = 0.03). Partial obstruction was more common in infants stabilized with an OPA (70% vs 54%; p = 0.04). There were no differences in mortality or respiratory outcomes for the whole cohort or in gestational age subgroups.

Conclusions: Airway obstruction is common in preterm infants receiving mask ventilation in the DR. Using an oropharyngeal airway significantly increases the incidence of airway obstruction.

Registered clinical trial: Australian and New Zealand Clinical Trials Register; **ACTRN** 12612000392864.

Keywords: Infant, Newborn, Neonatal resuscitation, Prematurity, Positive pressure ventilation, Airway obstruction, Oropharyngeal airway

Abbreviations: DR, delivery room; HR, heart rate; LMA, laryngeal mask airway; NICU, neonatal intensive care unit; NLS, neonatal life support (UK) program; NRP, neonatal resuscitation program; OPA, oropharyngeal airway; PIP, peak inflating pressure; PEEP, peak end expiratory pressure; RWH, Royal Women's Hospital, Melbourne.

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Background

Whilst most infants are vigorous immediately after birth, stabilization of newborn infants is one of the most commonly applied medical interventions globally.[1–3] Approximately 10% of newborn infants do not initiate spontaneous respirations after receiving stimulation and require positive pressure ventilation (PPV) in the delivery room (DR).[4] International and national neonatal resuscitation guidelines recommend a face mask in combination with a manual ventilation device to provide respiratory support after birth.[1–3] A tight seal between mask and face and appropriate positioning of the infant's upper airway are important for effective mask ventilation.[5,6] However, during the application of manual inflations, leak around the face mask is common and obstruction may occur, both leading to inadequate ventilation.[5,7–11] Mask leak and obstruction during mask PPV often remain unrecognized,[9,10,12] which may compromise resuscitation with insufficient positive inflating and end expiratory pressure (PIP/PEEP),[13] and delay lung aeration and establishment of effective gas exchange.[14,15]

When infants do not respond to initial inflations, the neonatal resuscitation program (NRP, USA)[2] and neonatal life support group (NLS, UK)[16] suggest a structured approach for escalation of care. Mask repositioning, upper airway suctioning, increasing the peak inflation pressure and considering an alternative airway; a laryngeal mask airway (LMA) or endotracheal tube are recommended by NRP and taught using the acronym MR. SOPA.[1–3] In contrast, the NLS suggests using a two-person technique or inserting an oropharyngeal airway (OPA) before intubation.[16] The Guedel™ (OPA) airway has been used for more than 80 years, mainly in anesthetized or unconscious/semi-unconscious patients.[17,18] Both LMAs and OPAs are supraglottic devices designed to maintain a patent airway between the oral cavity and the laryngeal inlet and thus may reduce the incidence of airway obstruction during mask PPV. However, currently available LMAs are too large for very preterm infants.[18,19] Neither device has been studied in a clinical trial to stabilize very and extremely preterm infants in the DR. The aim of this study was to determine the safety and efficacy of an oropharyngeal airway during mask PPV of infants <34 weeks' postmenstrual age (PMA) in the DR.

Methods

Patients and study design

This two center, unblinded randomized controlled study was conducted between December 2011 and December 2014 at the Royal Women's Hospital (RWH), Melbourne, Australia and between June 2014 and December 2014 at the Royal Alexandra Hospital (RAH), Edmonton, Canada (similarly sized tertiary perinatal centers with an average of 7000 births and 1500 admissions to the neonatal intensive and special care nurseries per year). Infants <34 weeks PMA born at the participating centers were eligible for inclusion. Medical and nursing staff at both centers received training in neonatal resuscitation in accordance with international and national (neonatal resuscitation program; NRP and Australian Resuscitation Council; ARC) resuscitation guidelines.[2,16] At the time of the study all infants received immediate cord clamping. Doctors performed all airway maneuvers and interventions. The study was approved by the Human Research and Ethics Committees at both sites and registered with the Australian and New Zealand Clinical Trials Register (ACTRN 12612000392864).

Consent

Where possible, parental consent was obtained before birth. If this was not possible, eligible infants were randomized and deferred consent was sought from the parents as soon as possible after birth.[20,21] Deferred consent was obtained to analyze data already collected from the DR and to continue collecting secondary outcome data until primary hospital discharge.

Randomization

A computer-generated block randomization sequence with variable block sizes was used, stratified by PMA (24–27 and 28–33 weeks) and by site. Sequentially numbered sealed opaque envelopes containing computer generated treatment groups were stored on a mobile trolley housing the computer and respiratory function monitor. Envelopes were opened after birth when the clinical team determined that an eligible infant required PPV. It was not possible to blind care providers due to the nature of the intervention.

Study intervention

Positive pressure was provided by a Neopuff™ Infant Resuscitator (Fisher & Paykel, Auckland, New Zealand) T-Piece. The flow rate was set at 8–10 L/min and the initial gas was 30% oxygen for infants <32 weeks' gestation and 21% oxygen if ≥32 weeks' PMA. If the infant had poor respiratory effort and/or a heart rate (HR) <100 beats per minute (bpm), the team commenced PPV using a soft round silicone mask (Laerdal or Fisher & Paykel). The initial settings were 25 cmH_2O PIP and 5 cmH_2O PEEP. PPV was provided at 40–60 inflations per minute. For all infants, standard mask ventilation techniques were applied; namely applying jaw thrust and chin lift to maintain the airway opening[6] and holding the mask using the two point top hold technique as previously described.[7]

After birth, the infants breathing efforts were assessed and if deemed inadequate or apneic, a randomization envelope was opened for group allocation. For infants randomized to receive the intervention, an appropriately sized oropharyngeal airway (OPA) was selected by measuring from where the incisors would appear in the infant gum to the angle of the jaw. The following Guedel™ OPAs (Mallinckrodt Dar, Mirandola, Italy) were available; size (length) 000 (3 cm), size 00 (4 cm) and size 0 (5 cm). The OPA was inserted into the mouth using the curvature of the device over the infant tongue between the operator's finger resting on the lips and guided by the contour of the hard palate (Supplemental online figure S1). The face mask was then applied to cover the mouth and nose before commencing PPV.

To determine the primary outcome, a pressure line was connected to the breathing circuit and a hot-wire anemometer flow sensor (Florian Respiratory Function Monitor [RFM]; Accutronic Medical Systems, Zug, Switzerland) was placed between the T-piece and the face mask to measure pressure and gas flow respectively. Inspired and expired tidal volumes were automatically calculated by integrating the flow signal. The flow sensor has an accuracy of ±8%.[13] The output from the RFM was sampled at 200 Hz using the Spectra program (Grove Medical Limited, Hampton, UK) installed on a dedicated computer. The data and the waveforms from the RFM were masked from the clinical team. Following stabilization in the DR, enrolled infants were cared for in accordance with clinical practice guidelines at each institution.

Study outcomes

The primary outcome was incidence of airway obstruction, both complete and partial, during PPV in the DR expressed as a proportion of infants experiencing any obstruction. Each manual inflation was analyzed for the first five minutes of PPV. Spontaneous breaths, unless superimposed on a manual inflation, were excluded from the analysis. Inspired (V_{Ti}) and expired (V_{Te}) tidal volumes of inflations were determined for these inflations. Leak was considered to be present when the inspiratory flow wave did not return to the zero-baseline, and the expiratory flow wave was smaller than the inspiratory flow wave or absent. The percentage of leak was calculated using the formula [$100 \times (V_{Ti}$ minus $V_{Te})/V_{Ti}$].[22] Leak values between -10% and 0% were assigned the value of 0%. The presence of obstruction was determined in all inflations where leak was less than 30%. Complete obstruction was defined as zero gas flow with no delivered V_T visible during a manual inflation. Partial obstruction was defined as reduced gas flows resulting in expired V_T less than 2 mL/kg. In the absence of a universally agreed definition of partial obstruction, we defined partial obstruction where the expired V_{Te} was less than the estimated anatomical dead space of the lung (2 mL/kg). This was deemed to be of clinical importance. Examples of complete, partial obstruction and leak from a single infant are shown in Fig. 2. Physiological data were analyzed post hoc by one investigator at each site (COFK at RWH and GMS at RAH).

Secondary outcomes were Apgar scores, oxygen saturation (SpO_2) and HR, intubation (in the DR) and rates of pulmonary air leak syndromes, severe (grade 3 or 4) intraventricular hemorrhage,[23] duration of endotracheal ventilation, incidence of bronchopulmonary dysplasia (BPD), and mortality. BPD was defined as infants receiving supplemental oxygen and/or respiratory support at 36 weeks corrected for gestational age. Pre-specified subgroup analyses investigated the effects of gestation.

Sample size and statistical analysis

We hypothesized that using an OPA would reduce the incidence of airway obstruction during mask PPV in the DR. The incidence of severe obstruction (defined as reduction of more than 75% of V_T delivery) in our previous study was 25%.[10] Further analysis showed the incidence of partial obstruction (expired tidal volume <2 mL/kg) was 46%. A sample size of 132 (66 in each group) was sufficient to detect a 50% reduction in partial (moderate) airway obstruction from 46% to 23%, with 80% power and a 2-tailed alpha error of 0.05.

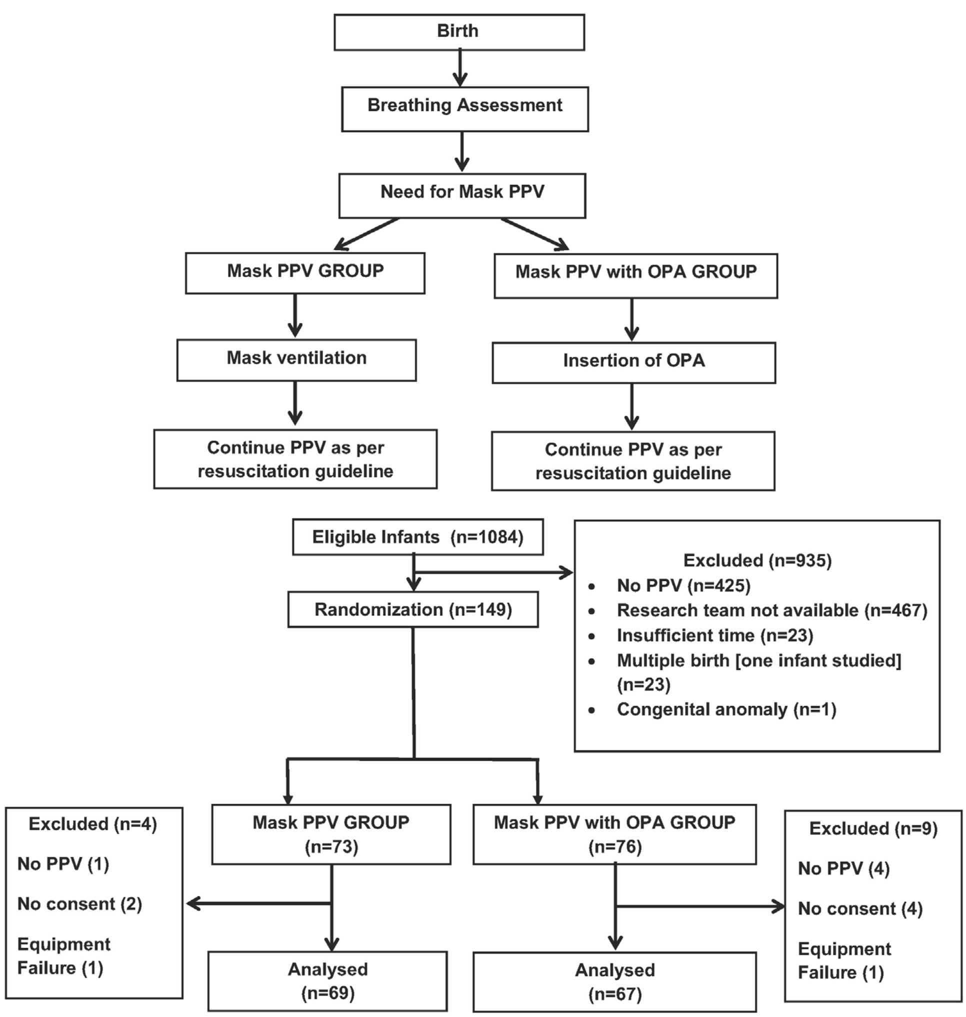

Fig. 1 – Study flow chart and participant CONSORT flow diagram for the SOAP study.

Data were analyzed using Stata software (Intercooled 12, Statacorp, College Station, Texas). Analysis of the primary and secondary outcomes was on an intention-to-treat basis. The primary outcome and dichotomous secondary outcomes are expressed as proportions and compared using Pearson X^2 test. Continuous outcome variables are presented as mean (standard deviations, ±SD) if normally distributed, and as median (interquartile range, IQR) if data were skewed. Student's *t*-test was used for parametric and Mann–Whitney-*U* test for non-parametric comparisons. *P* values were two sided and considered statistically significant if <0.05.

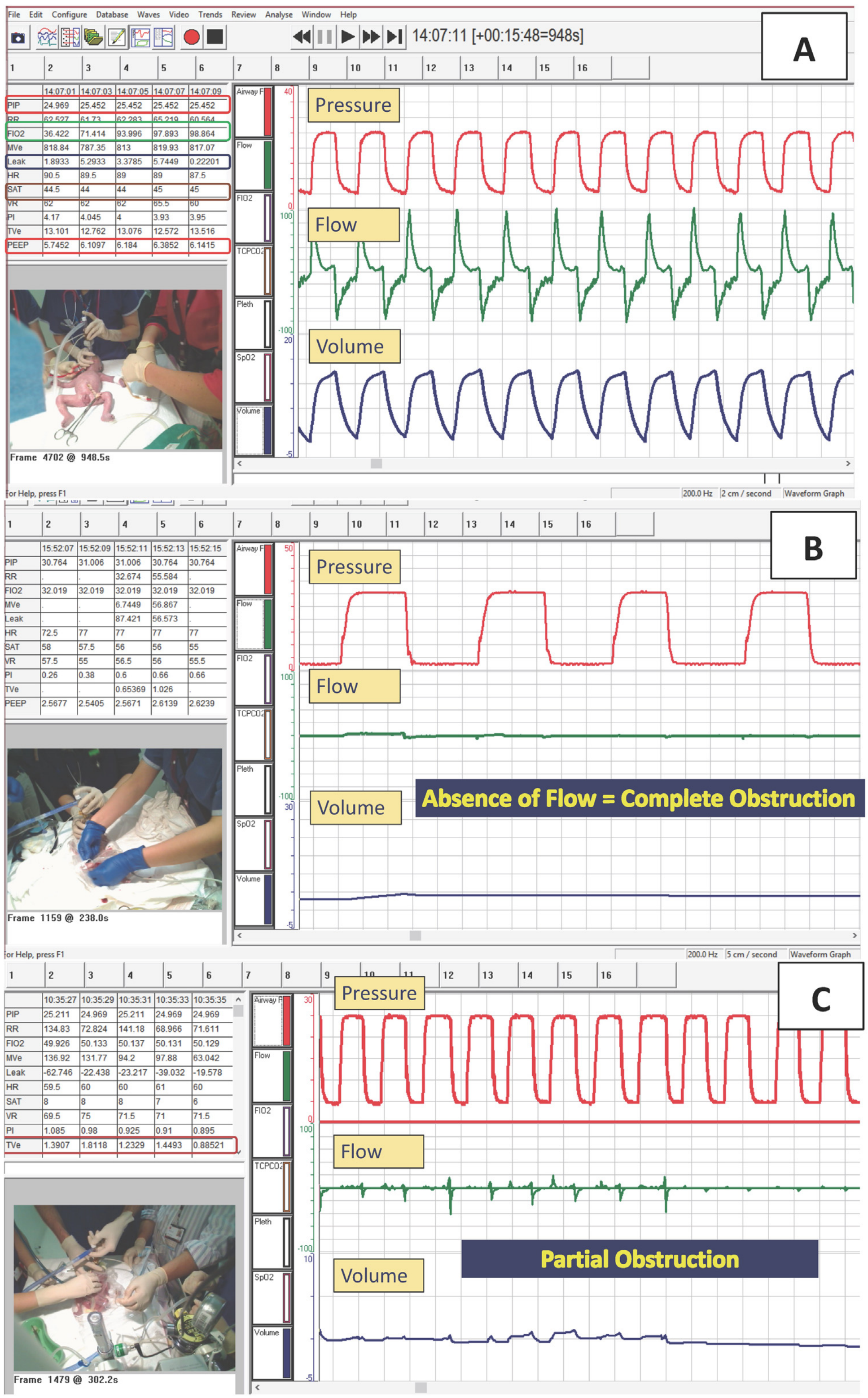

Fig. 2 – Respiratory function monitor recording demonstrating complete and partial obstruction during mask ventilation in the delivery room.

Results

During the study period 149 infants were randomized. Thirteen infants were excluded because they did not receive respiratory support in the DR, no data was obtained due to equipment failure or because their parents did not provide consent (Fig. 1). The remaining 136 infants were followed to hospital discharge or death (67 in the intervention group and 69 in the control group), and included in the analysis. All the infants received the allocated treatment but in 19 (28%) infants allocated to an OPA, the clinical team considered the device to be impeding PPV and so removed the device and continued PPV. Infants were well matched for baseline demographic characteristics (Table 1), although more males were randomised to the OPA. The median Apgar of 5 at 1 min in both groups suggest that infants randomised had some but minimal tone and respiratory effort.

The median (IQR) time from birth for the first inflation was similar; 69 (53,108) and 62 (50,101) seconds in intervention and control groups, respectively (p = 0.33). The total duration of PPV was similar; 193 (133,245) and 162 (88,272) seconds (p = 0.54), as was the number of inflations per participant; 107 (70,163) and 104 (46,147) in the intervention and control groups respectively (p = 0.21).

Primary outcome

The number of infants with at least one obstructed inflation (either partial obstruction or both), was greater if they were stabilized with the OPA (54; [81%]) compared to standard care in the control group (44 [64%]; p = 0.03). Similarly, the incidence of partial obstruction (V_{Te} <2 mL/kg) was significantly higher in infants stabilized with an OPA compared with the control group (47 (70%) vs 37 (54%); p < 0.04). The incidence of complete obstruction was similar in both groups (p = 0.29). Sub-group analysis by PMA showed no difference in the incidence of partial or complete obstructed inflations provided to infants <28 weeks compared to infants of 28–33 weeks PMA (Table 2).

Secondary outcomes

DR management was similar in both groups with no differences in the rates of endotracheal intubation (Table 3). Only one infant randomized to OPA received cardiac compressions. No differences in neonatal morbidities or length of hospital stay were seen between the two groups. Group comparisons of physiological parameters recorded using the RFM and pulse oximeters in the DR showed no differences (Table 4). The median (IQR) mask leak was similar; 38 (24–55)% and 34 (21–61)% and in intervention and control groups, respectively.

Table 1 – Infant demographics.

	Mask PPV with OPA (n = 67)	Mask PPV (n = 69)
Gestation (weeks)	28.0 (±2.3)	28.1 (±2.5)
Birth weight (g)	1088 (±405)	1071 (±427)
Caesarean section	57 (85%)	55 (79%)
Male infants*	42 (63%)	30 (43%)
Any antenatal steroids	57 (97%)	69 (100%)
Apgar 1 min	5 (3–5)	5 (2–6)
Apgar 5 min	8 (6–8)	8 (6–8)

Data are presented as mean (±SD), n (%) proportions or median (IQR).
* p < 0.03.

Table 2 – Primary Outcome[a].

All Infants	Mask PPV with OPA (n = 67)	Mask PPV (n = 69)	*P* Value
No obstruction	13 (19)	25 (36)	0.03
Partial obstruction	47 (70)	37 (54)	0.04
Complete obstruction	15 (22)	21 (30)	0.29
Any obstruction	54 (81)	44 (64)	0.03
Primary outcome by PMA sub-group			
<28 Weeks PMA	Mask PPV with OPA (n = 28)	Mask PPV (n = 25)	*P* Value
No obstruction	5 (18)	7 (28)	0.38
Partial obstruction	19 (68)	16 (64)	0.77
Complete obstruction	8 (29)	10 (40)	0.38
Any obstruction	23 (82)	18 (72)	0.38
28-33 Weeks PMA	Mask PPV with OPA (n = 39)	Mask PPV (n=44)	*P* Value
No obstruction	8 (21)	18 (41)	0.046
Partial obstruction	28 (72)	21 (45)	0.03
Complete obstruction	7 (18)	11 (25)	0.44
Any obstruction	31 (79)	26 (59)	0.046

Data presented are counts (percentages) unless otherwise stated.
[a] At least one obstructed inflation during recording.

Adverse events of oropharyngeal airway insertion

An attempt was made to insert the OPA in all 67 infants randomized to the intervention, with difficulty experienced in 15 (22%); these were exclusively related to airway opening and inserting the OPA above and behind the tongue. The OPA had to be either down or upsized in these 15 infants. No trauma (bleeding from oropharynx) was seen. Gagging was observed in 6 (9%). During PPV, the OPA was dislodged (pushed out by the movements of the tongue) in 23 (34%) infants. Operators were either unable to insert the airway and maintain the airway in position to provide PPV or felt more comfortable to remove the airway in order to continue PPV in 19 (28%) infants.

Discussion

This is the first randomized trial to investigate oropharyngeal airways as an airway adjunct during neonatal resuscitation. Contrary to our hypothesis, the use of an OPA resulted in significantly more infants receiving obstructed inflations compared to the use of a soft round silicone face mask alone. In keeping with previous reports,[5,10–12,24,25] our findings confirm that mask leak remains very common when preterm infants receive PPV in the DR.

It is very difficult to create a good seal between the mask and face of patients and leak around the mask is common.[9,11–13] Sometimes, to

Table 3 – Secondary outcomes.

	Mask PPV with OPA (n = 67)	Mask PPV (n = 69)	p-value
Intubation in DR	20 (30%)	22 (32%)	0.7
External cardiac compressions	1	0	0.31
Days mechanical ventilation	1 (0–5)	2 (0–9)	0.04
All Air leak*	4 (6%)	9 (13%)	0.16
Pneumothorax**	3 (4%)	5 (7%)	0.51
BPD	33 (49%)	26 (38%)	0.17
Death	1 (1.5%)	2 (3%)	0.58
Death or BPD	33 (45%)	28 (41%)	0.31
Length of stay in level 3 NICU (days)	57 (28-81)	62 (24-92)	0.83

Data are presented as n (%); DR (delivery room), BPD (Bronchopulmonary dysplasia), NICU (Neonatal Intensive Care Unit).
* All air leak (including pulmonary interstitial emphysema, pneumothorax, pneumomediastinum).

** Pneumothorax requiring drainage.

Table 4 – Physiological measurements.

	Mask PPV with OPA (n = 67)	Mask PPV (n = 69)	Median or mean* difference (95% CI)	p-value
V_{Te} (mL/kg)	4.7 (3.4–6.6)	5.7 (3–9.1)	−0.9 (−2.4,0.62)	0.24
Mask leak (%)	32 (24–55)	34 (21–61)	3.2 (−9.0,15.4)	0.60
PIP (cm H_2O)	25.5 (24.0–27.9)	25.5 (24.0–29.5)	0.64 (0.38,1.06)	1.00
PEEP (cm H_2O)	4.7 (3.2–5.2)	4.8 (3.7–5.7)	0 (-0.66,0.66)	1.00
HR at 3 min (bpm)	113 (35)	119 (35)	6.6 (−6.5,19.8)	0.32
HR at 5 min (bpm)	132 (32)	137 (29)	4.5 (−6.8,15.7)	0.43
SpO_2 at 3 min (%)	44 (21)	48 (22)	4.3 (4.2,12.7)–	0.32
SpO_2 at 5 min (%)	70 (24)	74 (24)	3.9 (−5.0,12.8)–	0.39

Data are presented as median (IQR), mean (SD); V_{Te} (expired tidal volume), PIP (peak inflation pressure), PEEP (positive end expiratory pressure), HR (heart rate), SpO_2 (oxygen saturation).

prevent leak, caregivers press too firmly on the mask which can cause obstruction.[26] More often the presence and magnitude of mask leak goes unnoticed by the stabilizing team and may contribute to failure of resuscitation.[11,27] Inappropriate positioning and central hypotonia of the infant can also contribute to airway obstruction. When mask ventilation is unsuccessful, neonatal resuscitation guidelines recommend care providers to consider an alternative airway.[28] However, there are regional differences: the NRP,[2] widely taught in North America advises the use of a LMA whereas the NLS,[16] UK recommends the use of an OPA. Our observations suggest that newborn infants who show some signs of respiratory effort are different from hypotonic or anaesthetized infants. The clinical team struggled to place and maintain the OPA in a satisfactory position. Whilst, NLS guidelines recommend inserting an OPA with direct vision using a laryngoscope, our protocol recommended using the index finger between the tongue and the upper gum to guide the OPA to avoid any potential orofacial vagal stimulation. This may have contributed to difficulties seen in maintaining the airway in situ. Most commonly the OPA became dislodged anteriorly by the tongue which may have resulted in the increased incidence of obstruction seen in our study.

It is well recognized that the oropharynx is the primary site of airway obstruction in the unconscious or anaesthetized patient. Oropharyngeal airways, as first described by Arthur Guedel were designed with a curvature to conform to the contours of oropharynx to prevent posterior glossal and epiglottic movement causing obstruction, whilst maintaining a patent airway for respiratory gases through a central channel.[17] The European Resuscitation Council Guidelines state that the most appropriately sized airway can be selected by comparing the length of the device with the distance between the patient's incisors and the angle of the jaw. In our study, we found this guideline could not be applied as the identified OPA size by measured length was often too bulky to be inserted into the infant's oral cavity and had to be downsized. We speculate that perhaps the smaller OPA may have been pushed against the posterior tongue, causing obstruction. Alternatively, every OPA has a hollow central channel for inspiratory and expiratory gas flow; with the potential to being either too narrow or obstructed by secretions. Adult studies have used X-rays or fibre-optic examinations to identify the level of obstruction in the upper airway, neither of which are feasible in very preterm infants during resuscitation in the DR. The sites of obstruction reported in adults include the base of the tongue, the epiglottis and when the distal tip of the airway was lodged in the vallecula.[18,29,30]

Another possible explanation for our findings is that the site of obstruction is distal to the tip of any supraglottic device (either OPA or LMA). Recent work using phase contrast imaging techniques in rabbit pups, suggest the glottis is often closed immediately after birth, particularly if the newborns are apneic.[31] This may be the most important site of obstruction in neonates, which requires further study in humans, and may explain the obstruction seen in both groups. If the site of obstruction is the glottis, then supraglottic airways will not work and may even be counterproductive. Indeed, laryngeal reflexes are very sensitive to the presence of objects within the pharynx, causing the larynx to close and induce swallowing, which may explain the higher incidence of obstruction in the OPA group. Thus, laryngeal closure may impede non-invasive PPV at birth[31] and may reduce the effectiveness of respiratory support provided, regardless if a supraglottic airway (either OPA or LMA) is used.

Our findings suggest that in non-obtunded transitioning newly born preterm infants in the DR with poor respiratory drive, oropharyngeal airways used as an airway adjunct, may be harmful; more obstructed inflations may impede lung aeration and potentially lead to an escalation in resuscitation. We cannot recommend the routine use of an OPA when PPV is initiated but our study was not designed to assess its effectiveness as part of package of dealing with a difficult airway when initial attempts at PPV have been unsuccessful. Clinical trials have compared LMAs as an alternative to mask ventilation indicating a potential utility of the device when endotracheal intubation is either unsuccessful or not feasible.[18,19,32,33] Further evaluation of this device, incorporating respiratory function monitoring is required. If the glottis is the major site of obstruction,[31] then all supraglottic airway devices are likely to have similar effects as those seen in this study. Whilst high quality compelling evidence on LMAs is missing, healthcare providers should be encouraged to improve their resuscitative techniques to optimize airway opening, minimize mask leak and to consider increasing peak inflating pressures and PEEP as initial strategies to deal with a difficult airway. Respiratory function monitoring may assist with these aims and the results of a large randomized study in this population is keenly awaited (MONITOR Trial; www.toetsingonline.nl; NL43055.058.12)

Neonatal resuscitation is not only one of the commonest medical interventions performed annually worldwide but also a complex task requiring trained personnel using specific equipment, effective communication and coordination within the team.[34] There is a paucity of evidence in many emergency or resuscitation settings because of the inherent difficulties in performing studies in this environment. Whilst the evidence base may be growing, the neonatal resuscitation algorithm remains a hybrid of evidence and expert opinion on best practice. We have shown that recommendations in medical management stemming from expert opinion should be evaluated using appropriate trial design. With a physiological outcome, a limitation of our study was that a dedicated research team and time to set up recording equipment were necessary and this accounts for the large number of eligible infants not enrolled. Even with the completion of this study, the site of obstructed inflations, frustratingly, remains elusive. Clinical trials in emergency medicine are difficult to conduct but we have shown in this and prior studies, that DR intervention studies using deferred consent are feasible and accepted by families and care providers.[5,35–39] It is important to continue to perform RCTs in the DR if we are to increase the evidence base for neonatal resuscitation.

Conclusions

The use of an oropharyngeal airway as an adjunct to face mask ventilation during the stabilization of very preterm infants causes significantly more obstructed inflations compared to using a soft silicone round face mask alone, and cannot be recommended.

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Contributor's statement

C. Omar F. Kamlin conceptualized the study. He recruited patients and performed the analyses. He wrote the first draft of the paper, and contributed to the editing process.

Georg M Schmölzer helped with study conceptualization, recruitment, and contributed to the editing process of the final draft.

Jennifer A. Dawson helped with recruitment, analyses, and contributed to the editing process of the final draft.

Lorraine McGrory helped with recruitment, and contributed to the editing process of the final draft

Joyce O'Shea helped with recruitment, and contributed to the editing process of the final draft.

Susan M. Donath was the trial statistician, generated the randomization sequence, assisted with data analyses, and approved the final draft.

Laila Lorenz assisted with data analyses and contributed to the editing process of the final draft.

Stuart Hooper helped with study conceptualization and contributed to the editing process of the final draft.

Peter G Davishelped with study conceptualization, recruitment, and analyses and contributed to the editing process of the final draft.

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Conflict of interest

None of the authors have any conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.08.035.

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