Skin-to-skin stabilisation and uninterrupted respiratory support for preterm infants after birth: feasibility of a new and simplified rPAP system

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ABSTRACT

Background  The rPAP respiratory support system, used for delivery room stabilisation with nasal prongs, has been shown to reduce the need for intubation in extremely preterm infants. A simplified version of the system has been developed. The purpose of this study was to determine the feasibility of providing uninterrupted respiratory support with the simplified rPAP from birth up to 4 hours of life and to assess ease of use for skin-to-skin stabilisation.

Methods  This was a non-randomised feasibility study conducted at Karolinska University Hospital, Sweden. Respiratory support with continuous positive airway pressure (CPAP) and positive pressure ventilation if needed was given with the simplified rPAP using heated humidified gases. Respiratory support was provided in the delivery room, during transportation and in the neonatal unit, for a maximum of 4 hours.

Results  32 preterm infants with a mean (SD) gestational age of 33.4 weeks (±1.2) were included. Of 17 infants born vaginally, 13 were stabilised skin-to-skin. The remaining infants were stabilised on a resuscitation table. All infants received CPAP and nine received positive pressure ventilation. 31 infants received continued support during transport and after arrival in the neonatal unit. Minor interruptions in CPAP support occurred in all infants. The study did not reveal problems with usability of the system.

Conclusion  It is feasible to stabilise preterm infants with the simplified respiratory support system both skin-to-skin and on a resuscitation table, and to provide continued respiratory support with the same system during transportation and in the neonatal unit.

Trial registration number  NCT04244890.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The WHO recommends early continuous positive airway pressure (CPAP) and kangaroo mother care for preterm and low birthweight infants. Devices that can be used for stabilisation with both positive pressure ventilation and continued nasal CPAP have previously not been available.

WHAT THIS STUDY ADDS

⇒ This is the first study evaluating a simplified version of the rPAP respiratory support system in clinical settings.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The simplified system can be of value in clinical studies and practice, by providing an option for stabilisation with prongs, humidification and uninterrupted support the first hours of life.

INTRODUCTION

Requiring non-invasive respiratory support after birth is common in preterm infants.  1,2 This is often due to inadequate breathing or saturation. Even though most infants have breathing efforts, many receive positive pressure ventilation (PPV).  3

Traditionally, the need for respiratory support results in early cord clamping and stabilisation on a resuscitation table away from the mother with a T-piece system and face mask. When regular spontaneous breathing is established, the respiratory support can be continued with a nasal continuous positive airway pressure (nCPAP) system that is fixated with a cap. This allows the infant to be put in a more comfortable position in the incubator or skin-to-skin with the parent.

Using nasal interfaces for stabilisation has become more common in clinical practice and is proposed as an alternative to face mask by international guidelines. 4 Furthermore, meta-analyses have suggested that nasal interfaces for PPV could have some advantages over face mask. 5,6

The rPAP respiratory support system used with nasal prongs has been shown to reduce the need for delivery room intubation and mechanical ventilation during the first week of life in extremely preterm infants. 7-9 The original system is pressure stable but requires a driver unit and two tubes for the fresh gas flow. A simplified system with a single tube for the fresh gas flow has been developed. The rPAP generator geometry is intact and the system has the same performance as the original system. 7 The fresh gas flow is supplied by an air-oxygen blender and a separate wide-bore tube is connected to an adjustable pressure limiting (APL) valve and a manometer (figure 1). In the simplified rPAP, the fresh gas flow is split inside the generator by a small leak canal proximal to the nasal interface. This eliminates the need for a dedicated driver unit and simplifies humidification. The CPAP pressure is determined by the fresh gas flow and the peak inspiratory pressure is set by adjusting the APL valve. When providing PPV, the outlet is occluded with...
a finger and the pressure in the system rises until the APL valve opens. The system can be used with either nasal mask, prongs, or face mask and fixed with a cap and straps when nasal interfaces are used. Instead of early separation from parents for respiratory support, infants may benefit from receiving pressure-stable nCPAP with heated humidified gases close to their parents. This is in accordance with the recently issued WHO recommendations on the care of preterm and low birthweight infants that endorse providing CPAP and kangaroo mother care as soon as possible after birth.10 While pressure-stable nCPAP can be provided with conventional CPAP systems, need for PPV requires changing to a T-piece system.

The purpose of this study was to determine the feasibility of providing uninterrupted respiratory support with the simplified rPAP system using humidified gases, to preterm infants directly after birth and up to 4 hours of life. Further, we wanted to test if the system could be used for skin-to-skin stabilisation and during transportation from the delivery room to the neonatal intensive care unit (NICU).

METHODS

Study design and intervention

This was a non-randomised feasibility study evaluating the use of the simplified rPAP respiratory support system with humidification for giving uninterrupted respiratory support to preterm infants after birth. The study was conducted at the Karolinska University Hospital in Stockholm, Sweden from February 2020 to February 2023. Prior to starting, the study was registered at ClinicalTrials.gov (NCT04244890).

Newborn infants in need of respiratory support after vaginal delivery at gestational age between 28+0 and 34+6 weeks and days or caesarean section at gestational age between 28+0 and 37+6 weeks and days were included when investigators were available. Higher gestational age in infants born via caesarean section was accepted due to increased risk of needing respiratory support in that group. Need for respiratory support was determined clinically by responsible NICU physician based on respiratory effort and oxygen saturation (SpO2). Initial settings were positive end-expiratory pressure (PEEP) of 5 cmH2O, delivered at a fresh gas flow of 10L/min. The PEEP could be adjusted upwards/downwards by increasing/decreasing the gas flow. Inclusion required antenatal parental consent. Exclusion criteria were known cardiac or airway malformations, syndromes or neuromuscular disorders or anticipated transfer to another hospital within 4 hours after birth.

CPAP and PPV if needed were given with the simplified system using heated humidified gases. The respiratory support system was handled by a member of the neonatal team under the supervision of the investigators. Infants born with a caesarean section were stabilised on a resuscitation table. Initial place of stabilisation after vaginal birth was either skin-to-skin with the mother or on a resuscitation table as decided by the neonatal and obstetric team based on the mother’s condition or if signs of fetal distress were present. The study system was set up and checked in advance. A standard T-piece system was available as a fallback option. Timing of cord clamping was decided by the obstetric team.

Respiratory support with the simplified system was continued as long as needed, both during transportation and after arrival in the NICU, for a maximum of 4 hours (figure 2). If the infant was still in need of respiratory support after the study period, the system was changed to standard CPAP used in the unit. All other treatments followed local protocols and international guidelines.4

The trial was not designed to estimate treatment effects and no power calculations were performed. Recruitment of patients...
was slow in part due to the COVID-19 pandemic. The trial was completed after enrolling 32 infants born both vaginally and by caesarean section. When the aim of including infants requiring both PPV and infants requiring support for the maximum 4 hours was achieved, the ethical review board was contacted and the trial closed.

Collected variables
Baseline characteristics of mother and infant were collected. During the study period, information was gathered on the level of respiratory support, the number, causes and duration of interruptions in CPAP treatment, need for change to backup respiratory support system, ease of use regarding system setup, airway and respiratory support management, fixation and transport. SpO2 and heart rate measurements were obtained using a pulse oximeter and ECG. Data on respiratory support at 48 hours, rare or adverse events such as pneumothorax, need for intubation or chest compressions during stabilisation and problems related to equipment or the research protocol were also collected.

Statistical analysis
Statistical analyses were performed with SPSS Statistics V.27 (IBM Corp). Normal distribution was tested with Shapiro-Wilk test. Normally distributed variables were presented as mean±SD, non-normally distributed variables as median (IQR).

RESULTS
A total of 109 parent couples were approached for study participation of which 75 couples consented and 32 infants with a mean (SD) gestational age of 33.4 weeks (±1.2) and a median (IQR) birth weight of 2118 g (476) were included. Baseline characteristics are shown in table 1.

Uninterrupted respiratory support with the simplified system
All 32 infants received nCPAP and 9 received PPV with the simplified rPAP system using nasal prongs. The median (IQR) duration of PPV was 120 (125) s. Median (IQR) SpO2 was 85% (19) and 95% (5) at 5 and 10 min, while median (IQR) fractional inspired oxygen administered was 0.25 (0.09) and 0.21 (0.09), respectively.

Continued support during transport and after arrival in the neonatal unit was given with the simplified system to 31 infants (97%). One infant did not need continued respiratory support after stabilisation in the delivery room. Minor interruptions of CPAP support occurred in all cases. The most common reasons were placement of nasogastric feeding tube, change in gas supply, suction of secretions or accidental displacement of the interface. At 48 hours of age, seven infants were receiving respiratory support with CPAP and one with high-flow nasal cannula. The remaining infants were breathing room air without support. Two infants had received surfactant with INSURE, at 6 and 14 hours after birth, respectively. None had received mechanical ventilation. Neonatal outcomes are shown in table 2.

Adverse events and usability
No infant needed intubation, chest compressions or use of T-piece backup system during stabilisation and there were no cases of pneumothorax. No patient died during the study period.

No problems were identified regarding setup and use in the delivery room. Hands-on support from investigators was requested in two cases during the study period. In five cases, we experienced minor problems related to fixation of the system during transportation. In three cases, problems with auxiliary equipment (in one case related to air-oxygen blender and in two cases to humidifier) resulted in change to standard CPAP system after arrival to the neonatal unit prior to reaching the 4-hour study limit.

The mean (SD) temperature was 37.0 (±0.4) and 36.9 (±0.3) before and after transport to the neonatal unit. No cases of hypothermia, defined as skin temperature below 36.0, were observed.

Skin-to-skin stabilisation
Out of the 17 infants born vaginally, 13 were stabilised skin-to-skin, of these 11 with the cord intact. The remaining infants,
including those born via caesarean section, were stabilised on a resuscitation table. 24 (75%) of the included infants received skin-to-skin contact at some point during the study period while they were receiving respiratory support with the study system. The median (IQR) cord clamping time for all infants was 90 s after birth, 300 (708) s after vaginal birth and 50 (25) s after caesarean section.

**DISCUSSION**

In this feasibility study, we found that the simplified rPAP system could be used to give respiratory support including PPV and CPAP from birth and up to 4 hours of age. To the best of our knowledge, this is the first study to evaluate PPV with continued CPAP support for an extended period of time, using a single system.

Skin-to-skin contact after birth has been standard practice for full-term infants, while preterm birth has commonly resulted in separation of the mother and infant. With more studies emerging on early skin-to-skin contact for more vulnerable newborns, the practice is changing. Recent studies have shown that immediate skin-to-skin contact may have beneficial effects on the cardiorespiratory stabilisation of very preterm infants and reduce mortality among low birthweight infants in low-resource settings. In accordance with this, the WHO recently issued new recommendations on the care of preterm and low birthweight infants, endorsing CPAP and kangaroo mother care as soon as possible after birth. The design of the simplified rPAP system with low imposed work of breathing (iWOB) and the possibility of fixation similar to regular nCPAP systems make it a favourable option for such an early CPAP skin-to-skin bundle compared with regular T-piece systems that have high iWOB and are used with face masks. In comparison with regular nCPAP systems, the simplified rPAP has the additional benefit of providing an option to give PPV if needed.

While the continuous distending pressure during CPAP support improves lung volume and optimises gas exchange, interruptions may result in collapse of terminal airways and increased work of breathing. This risk is probably most pronounced in the smallest preterm infants during fetal to neonatal transition and establishment of functional residual capacity. In this study, the use of nasogastric feeding tubes made interruptions in CPAP support inevitable during placement but these were short in duration and probably not of clinical significance.

During the last decade, the benefits of delayed or preferably physiological cord clamping after lung aeration is established have been increasingly recognised. The advantages include better haemodynamic stability during fetal to neonatal transition as well as lower odds of intraventricular haemorrhage and mortality. The study protocol for this feasibility study did not include special directions for cord clamping and the cord clamping time was decided by the obstetric team following local guidelines. In the study, the majority of infants born vaginally were stabilised skin-to-skin which made it possible to start the respiratory support while the cord was still intact.

Admission hypothermia in preterm infants has been associated with increased morbidity and mortality. While the use of cold air for PPV has been linked to hypothermia, heating and humidification of gases during stabilisation after birth have been shown to improve admission temperature in preterm infants. The modification of the rPAP system simplifies heating and humidification of the fresh gas flow. In this feasibility study, there were no cases of hypothermia. This might be attributed to both the use of heated and humidified gases as well as skin-to-skin care in combination with other heat-preserving measures.

In this small feasibility study, no adverse events related to the study system were observed and change to backup system was never required for stabilisation.

**Clinical importance**

The simplified system could be an alternative to the standard T-piece system when stabilising preterm infants at birth. It can be used to deliver CPAP and PPV with heated and humidified gases through nasal prongs. For children born vaginally, the respiratory support can be started with the infant skin-to-skin with the mother and the umbilical cord intact. We believe the simplified system can be of value in future trials providing an option for resuscitation with prongs, humidification and uninterrupted support the first hours of life.

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**Table 2  Neonatal outcomes**

<table>
<thead>
<tr>
<th></th>
<th>Median (IQR)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP/PPV started age (min)</td>
<td>1.4 (1.6)</td>
<td>32 (100)</td>
</tr>
<tr>
<td>Received PPV</td>
<td></td>
<td>9 (28)</td>
</tr>
<tr>
<td>PPV duration (s), median (IQR)</td>
<td>120 (125)</td>
<td></td>
</tr>
<tr>
<td>Cord clamping time (min)</td>
<td>Median (IQR)</td>
<td>15 (4.4)</td>
</tr>
<tr>
<td></td>
<td>(Range)</td>
<td>(0.25–21)</td>
</tr>
<tr>
<td>Place of stabilisation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin-to-skin (%)</td>
<td>13 (41)</td>
<td></td>
</tr>
<tr>
<td>Resuscitation table (%)</td>
<td>19 (59)</td>
<td></td>
</tr>
<tr>
<td>Apgar score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 min, median (IQR)</td>
<td>9 (2)</td>
<td></td>
</tr>
<tr>
<td>10 min, median (IQR)</td>
<td>10 (1)</td>
<td></td>
</tr>
<tr>
<td>FiO2, at 5 min</td>
<td>Median (IQR)</td>
<td>0.25 (0.09)</td>
</tr>
<tr>
<td>FiO2, start of transport</td>
<td>Median (IQR)</td>
<td>0.21 (0.04)</td>
</tr>
<tr>
<td>FiO2, arrival NICU</td>
<td>Median (IQR)</td>
<td>0.21 (0.02)</td>
</tr>
<tr>
<td>Saturation at 5 min, %</td>
<td>Median (IQR)</td>
<td>85 (19)</td>
</tr>
<tr>
<td>Saturation start of transport, %</td>
<td>Median (IQR)</td>
<td>98 (2)</td>
</tr>
<tr>
<td>Saturation on arrival in NICU, %</td>
<td>Median (IQR)</td>
<td>97 (4)</td>
</tr>
<tr>
<td>PCO2 level on arrival in NICU, kPa</td>
<td>Median (IQR)</td>
<td>7.45 (1.2)</td>
</tr>
<tr>
<td>Temperature leaving DR, °C</td>
<td>Mean (SD)</td>
<td>37.0 (0.4)</td>
</tr>
<tr>
<td>Temperature arrival in NICU, °C</td>
<td>Mean (SD)</td>
<td>36.9 (0.3)</td>
</tr>
<tr>
<td>Interruptions in CPAP</td>
<td>n, median (IQR)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Duration (s), median (IQR)</td>
<td>15 (20)</td>
<td></td>
</tr>
<tr>
<td>Patients alive at 48 hours</td>
<td>n (%)</td>
<td>32 (100)</td>
</tr>
</tbody>
</table>

FIo2, inspired oxygen; NICU, neonatal intensive care unit; PCO2, partial pressure of carbon dioxide; PPV, positive pressure ventilation.
Limitations
This was a small feasibility study including mostly moderately and late preterm infants. The presence of study investigators is a potential source of bias regarding the assessment of feasibility. However, prespecified variables were collected.

Adequately powered randomised controlled trials are needed to determine the efficacy of this approach compared with routine care. More infants of very low birth weight and gestational age would need to be studied to evaluate the potential clinical benefit of avoiding interruptions in respiratory support during the first hours after birth.

CONCLUSION
It is feasible to stabilise preterm infants with the simplified rPAP respiratory support system both skin-to-skin and on a resuscitation table. It was possible to provide continued respiratory support with the same system during transportation and in the neonatal unit with few interruptions. Skin-to-skin stabilisation after vaginal births promoted late cord clamping in the majority of infants. The study did not reveal any problems with the system.

Correction notice This paper has been corrected since it was first published.

Kolbrún Gunnarsdóttir and Sonja Baldursdóttir share first authorship.

Contributors SB and KG—study design, recruitment of patients, data collection, data and statistical analysis, manuscript writing and review. TD—study design, equipment development, manuscript writing, review and study guarantor. SD and BJ—study design, manuscript writing and review.

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Competing interests TD is one of the designers of the original and simplified rPAP respiratory support system.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the Swedish Ethical Review Authority (number 2019-05581). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

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