REGULAR ARTICLE

Continuous positive airway pressure in children with severe pneumonia and hypoxaemia in Papua New Guinea: an evaluation of implementation

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ABSTRACT

Aim: To prospectively evaluate the use of bubble continuous positive airway pressure (CPAP) in children with very severe pneumonia and other acute lower respiratory infections, during its trial introduction in a low resource hospital in Papua New Guinea.

Methods: Prospective observational study of children treated with CPAP who had severe pneumonia and severe respiratory distress with hypoxaemia (SpO_2 <90%). CPAP was driven by oxygen concentrators in which the fraction of inspired oxygen could be adjusted, and using low-resistance tubing and nasal oxygen prongs.

Results: A total of 64 children were commenced on CPAP: 29 (45.3%) survived and were discharged well, 35 (54.7%) died. Prior to commencing CPAP, the median SpO2 was 78% (IQR 53.3–86.8%), at one hour SpO_2 was 92% (IQR 80–97.75%, n = 64), and at 84 hours (3½ days) 98% (IQR 93–98%, n = 29), in survivors at each of these time points. A higher SpO_2 at one hour after commencement of CPAP predicted survival (p = 0.013), and human immunodeficiency virus infection was an independent predictors of death (p = 0.017). Technical and clinical problems encountered are described.

Conclusion: Bubble CPAP improved oxygenation and reduced the severity of respiratory distress in some children with severe pneumonia; however, mortality was high reflecting high severity of illness and comorbidities. CPAP requires a quality system to be safe and effective.

INTRODUCTION

In Papua New Guinea (PNG) as in many other low- and middle-income countries pneumonia and other acute lower respiratory infections (ALRI) are the most common causes of serious illness and death. In PNG, these illnesses account for 25–30% of all hospitalisation in children, and 15% of all deaths, with case fatality rates for ALRI of all severity being 5% (1,2). Hypoxaemia is the strongest risk factor for deaths from pneumonia, and detection of hypoxaemia with pulse oximetry and provision of oxygen therapy can substantially reduce deaths from pneumonia (3,4). However despite this,

mortality rates for *severe* pneumonia in PNG hospitals average 10% (1,2) and this is similar in many low-income countries (5–10). In addition, nearly 30% of all admissions of children to hospitals in PNG are in the neonatal period and neonatal deaths account for just over one-third of all childhood deaths (1).

Beyond oxygen therapy, continuous positive airway pressure (CPAP) may have a role in the management of severe acute lower respiratory tract infection and in

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Abbreviations

ALRI, Acute lower respiratory tract infection; CPAP, Continuous positive airway pressure; FiO_2, Fraction of inspired oxygen; HFNC, High-flow nasal cannula oxygen; HIV, Human immunodeficiency virus; ICU, Intensive care unit; IQR, Interquartile range; LFNC, Low-flow nasal cannula oxygen; LMIC, Low- and middle-income countries; PjP, Pneumocystis jiroveki pneumoniae; PNG, Papua New Guinea; RCT, Randomised controlled trial; RDS, Respiratory distress score; ROC, Receiver operating characteristics; SpO_2, Arterial oxygen saturation by pulse oximetry; WHO, World Health Organization.

Key notes

- The conditions under which continuous positive airway pressure (CPAP) may be effective in the management of pneumonia in low-income countries are uncertain.
- In a hospital in Papua New Guinea with limited resources, CPAP improved oxygenation and reduced the severity of respiratory distress in some children with very severe pneumonia; however, mortality was high, because of illness severity and comorbidities.
- Continuous positive airway pressure is a complex therapy requiring an overall quality of care approach.

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newborn respiratory disease. There are several methods for delivering CPAP, one is bubble CPAP (11). In bubble CPAP, an underwater seal on the expiratory limb of a breathing circuit creates positive expiratory pressure. CPAP improves lung mechanics in neonatal respiratory distress syndrome: it helps to maintain functional residual capacity, promotes gas exchange in the alveoli, improves lung volume recruitment and prevents atelectasis (12). CPAP may also maintain energy reserves by reducing work of breathing and energy expenditure, but some studies in severe acute lung injury in older patients suggest this is only achieved to a major extent if inspiratory pressure support is also given (13).

There is some evidence that bubble CPAP is an effective method of respiratory support in some settings (14–16). However, it should not be accepted that this will be successful in all contexts and there is a need for implementation and effectiveness research on bubble CPAP in low-income countries.

In this study, we aimed to investigate the use of bubble CPAP in the management of severe respiratory distress in children in PNG. We aimed to evaluate the clinical and other characteristics of children who responded well to CPAP support compared to those who did not, and to document the technical, clinical and training requirements for implementing bubble CPAP.

METHODS

This was a detailed prospective observational study, conducted in the children's ward intensive care area and the special care nursery in Port Moresby General Hospital, a teaching hospital in Port Moresby, Papua New Guinea. The study was conducted between March 2014 and August 2016.

Children were eligible if they had signs of severe acute lower respiratory infection, with hypoxaemia (SpO_2 <90%) or severe respiratory distress despite standard oxygen therapy. In such patients, the best treatment available in PNG has been standard oxygen therapy via nasal prongs or nasal catheter with the aim of maintaining oxygen saturation SpO_2 above 90%. Oxygen saturation was measured using pulse oximeter (Life box: www.lifebox.org). If the SpO_2 was <90% despite optimising the flow rate of nasal prong oxygen, and the child still had severe respiratory distress, parental consent was sought, and if provided bubble CPAP was commenced.

Bubble CPAP was administered using oxygen concentrators (Airsep Intensity, modified by Diamedica: www.diamedica.co.uk) with an air-oxygen mix function and low-resistance nasal oxygen prongs at the flow rate of approximately 2 L/kg/minute for neonates and children <8 kg. For children over 8 kg, CPAP was started at 5 L/minute oxygen and 5 L/minute air. The CPAP level was 5–8 cm H_2O. We developed and followed a clinical guideline (17).

We recorded vital signs: pulse rate, body temperature, respiratory rate and oxygen saturation. Signs of respiratory distress were assessed using a respiratory distress score (RDS) (17). The respiratory score ranges from 1 to 3 and the

cumulative score was out of 12. The variables included were SpO_2, respiratory sounds (grunting, wheezing, and crepitation), signs of respiratory distress (nasal flaring, tracheal tugging and chest in-drawing) and feeding. A score >7/12 indicated the patient was in severe respiratory distress. The same variables were reassessed after one hour, and every 12 hours thereafter.

Continuous positive end-expiratory pressure was started at 5 cm of water and adjusted to obtain adequate bubbling, the child's oxygen saturation >90%, and a settling of the clinical signs of severe respiratory distress. The fraction of inspired oxygen (FiO_2) was adjusted to maintain SpO_2 >90% and the flow titrated to produce continuous bubbling.

When oxygen saturation and respiratory distress improved, bubble CPAP was continued for at least the first 24 hours. If the child was still hypoxic after commencing CPAP, but the SpO_2 had improved from baseline at one hour, CPAP was continued and supplementary oxygen via face mask or optimisation of CPAP from the concentrator. If the child was still hypoxic or the SpO_2 was lower than the initial reading, CPAP was changed back to standard oxygen and additional oxygen via face mask at 6–8 L/minute was added, or CPAP was given by off-wall 100% oxygen (rather than the air-oxygen mix of the concentrator).

General care included antibiotic treatment following WHO guidelines (18), fluids to avoid over-hydration, and enteral nutrition via a nasogastric tube when safe to do so, and suctioning. The children were nursed in the intensive care area of the children's ward, where the nurse: patient ratio is usually 1:4, but sometimes less. A paediatric registrar is rostered on for the ICU area during the day, and a registrar is on-call 24 hours a day but between 5 pm and 8 am works across three wards so is not in the ICU area all the time. A paediatrician does a ward round each morning, and reviews patients at 4–5 pm, and is on-call the remainder of the time. Intravenous infusion pumps are used to regulate the volume of fluids given. The children in the ICU area are monitored with pulse oximetry and heart rate regularly or continuously, but no invasive monitoring such as arterial lines or central venous pressure. There is no mechanical ventilation or other non-invasive bi-level respiratory support, and inotropic agents are not available.

Bubble CPAP was considered clinically effective if the RDS ≤7 and SpO_2 ≥90%. The criteria for weaning off CPAP were if after 24 hours the RDS was ≤7 and SpO_2 ≥90% in 40% oxygen or less. After weaning from CPAP we continued standard oxygen until the child's respiratory distress settled and the SpO_2 was maintained at >90% in room air. CPAP was recommended if after reversion to standard oxygen therapy the patient desaturated, or if they developed worsening signs of respiratory distress (17). Complications associated with CPAP and problems with functioning of the CPAP equipment were also recorded while implementing the study.

Children and neonates were not included if they were known to have congenital heart disease, chronic lung disease (except for acute infective exacerbations), severe anaemia in heart failure (unless anaemia was a comorbidity

of pneumonia or bronchiolitis), and newborns with severe birth asphyxia.

Quality assurance checking

Quality assurance checks for oxygen concentrators and circuits were performed regularly to make sure the performance of equipment was maintained. Circuits were checked for splits and an oxygen analyser was used to check the flow rate and FiO_2. We systematically recorded technical, clinical, human and system problems in the use of CPAP.

Training

Nurses and doctors were trained in how to use the bubble CPAP machine, indications for using CPAP, administering CPAP with required flow rate and oxygen, monitoring of children on CPAP and care of CPAP machines including disinfecting the machine and circuits. Training included the identifying the type of illness and hypoxaemia, the concentrators and how they worked, CPAP equipment and connecting the parts and rectifying equipment malfunctions.

Data extraction and analysis

Data were collected and entered into Microsoft Excel and analysed using STATA version 14 (StataCorp, College Station, TX, USA). For descriptive epidemiology, means and standard deviations, medians and interquartile ranges were calculated to describe the data. Logistic regression was done on univariate and multivariate variables to identify predictors of success or failure of CPAP. A receiver operating characteristics (ROC) curve was also drawn to show the strength of significant variables as predictors of outcome. A $p < 0.05$ was considered significant.

Ethical approval

The study was approved by research committee of School Of Medicine and Health Sciences, Port Moresby General Hospital Management and National Health of Department Medical Research Advisory Committee. Informed consent was gained from parents or guardians of all children involved in the study.

RESULTS

Patient demographics and clinical features

A total of 64 children were enrolled; 41 males and 23 females. The median age was three months (IQR 0.5–6.3); six neonates, 57 infants and seven children over the age of one year. The median weight was 4.7 kg (IQR 3.3 to 6.1 kg). Other clinical characteristics are described in Table 1. The majority of children had community-acquired pneumonia.

Clinical response to CPAP

The response to CPAP is described in Table 2. Pre-CPAP the median SpO_2 on standard flow oxygen was 78% (IQR 53.3–86.8%). After one hour, the SpO_2 increased to a median of 92% (IQR 80–97.8%). The respiratory distress

score (RDS) improved after CPAP was commenced. Pre-CPAP median RDS score was 11 (IQR 10–12), in one hour it was 9 (8–11) and improved to 6.5 (IQR 6–8) at 84 hours for those who survived. Most children had severe hypoxaemia (SpO_2 <85%) pre-CPAP (n = 39, 61.0%), however, at one hour only 29.7% (n = 19) had SpO_2 <85%. The number of survivors reduced from 64 to 29 over the first 84 hours; all those who survived maintained SpO_2 more than 85%. The median duration of CPAP was 3.5 days (interquartile range one to five days), and the median duration of oxygen requirement following CPAP was 3.5 days (IQR two to 6.8 days).

Comorbidities and outcomes

Severe pneumonia accounted for 75% (n = 48) of children put on CPAP (Table 3). Comorbidities associated with pneumonia or as an underlying chronic condition were common. These included anaemia (n = 13, 20.3%), sepsis (n = 8, 12.5%), human immunodeficiency virus (HIV; n = 11, 17.2%), pulmonary tuberculosis (n = 5), meningitis (n = 2), heart failure (n = 18), severe malnutrition (n = 5), Down syndrome (n = 2), brain injury (n = 1), pleural effusion/empyema (n = 1) and low birthweight (n = 3) (Table 4).

The majority of children with severe pneumonia who survived had no significant comorbidities. Some cases of congenital heart disease were diagnosed after a severely ill child was commenced on CPAP.

Mortality and predictors of outcome

Among the 64 children and newborns, 29 survived and 35 died. Using univariable logistic regression predictors of death were HIV infection, sepsis, the pre-CPAP SpO_2, and the SpO_2 and RDS one hour after commencing CPAP (Table 5).

Table 1 Clinical characteristics at enrolment

Characteristic	Total, n = 64
Duration of cough in days: median (IQR)	5 (3–11)
Temperature ≥38°C, n (%)	17 (26.5)
Apnoea, n (%)	7 (10.9)
Poor feeding, n (%)	54 (84.4)
Severe chest in-drawing, n (%)	63 (98.4)
Tracheal tugging, n (%)	58 (90.6)
Heart rate, median (IQR)	152 (132–166.5)
Oxygen saturation %, median (IQR)	78 (53.3–86.8)
SpO_2 <80%, n (%)	36 (56.3)
Chest x-ray done, n (%)	46 (71.9)
Radiographic signs, present, n (%)	43 (93.5)
Bilateral consolidation (%)	6 (13.3)
Unilateral consolidation (%)	14 (31.1)
Bilateral interstitial infiltrates (%)	8 (17.8)
Bilateral patchy opacity (%)	10 (22.2)
Bilateral hilar opacity (%)	3 (6.7)
Homogenous opacity (effusion) (%)	1 (2.2)
Pneumothorax/pneumomediastinum/subcutaneous emphysema (%)	1 (2.2)

IQR = Interquartile range.

Table 2 Clinical observations over the first 84 hours (3.5 days) of treatment on CPAP

	Pre-CPAP	One hour	12 hours	24 hours	36 hours	48 hours	60 hours	72 hours	84 hours
Survived, n (%)	64	64 (100)	51 (79.6)	48 (75)	44 (68.8)	39 (60.12)	37 (57.8)	31 (48.4)	29 (45.3)
SpO_2, median (IQR)	78 (53.3–86.8)	92 (8–97.8)	95.5 (87.5–99)	96.5 (91.5–99)	97.5 (89.8–98.3)	98 (89.8–99)	98 (94.8–99)	98 (93–99)	98 (93–98)
SpO_2 <85%, n (%)	39 (60.9)	19 (29.7)	9 (18)	4 (8.7)	8 (19.1)	6 (15.8)	2 (5.9)	3 (10.3)	3 (11.5)
RDS, median (IQR)	11 (10–12)	9 (8–11)	8 (7–9)	8 (7–9)	8 (6.75–9)	7 (6.75–9)	7 (5.75–9)	7 (6–9)	6.5 (6–8)

CPAP = Continuous positive airway pressure; IQR = Interquartile range; RDS = Respiratory distress score.

Table 3 The main diagnosis of children put on CPAP

Diagnosis	All children (%)	Survived to hospital discharge, n (%)	Died, n (%)
Severe pneumonia	48 (75)	21 (43.75)	27 (56.25)
Pulmonary tuberculosis	5 (7.81)	2 (40)	3 (60)
Bronchiolitis	1 (1.56)	1 (100)	
Congenital lung malformation	1 (1.56)	1 (100)	
Brain injury	1 (1.56)		1 (100)
Empyema and breast abscess	1 (1.56)		1 (100)
Neonatal respiratory distress syndrome/low birthweight	2 (3.13)		2 (100)
Meconium aspiration syndrome	4 (6.25)	3 (75)	1 (25)
Bronchiectasis	1 (1.56)	1 (100)	
Total	64	29	35

Table 4 Comorbidities

Comorbidities	Total, n (%)	Survived to discharge, n (%)	Death, n (%)
Anaemia	13 (20.3)	7 (53.1)	6 (46.2)
HIV infection	11 (17.2)	1 (9.1)	10 (90.9)
Heart failure	18 (28.1)	4 (22.2)	14 (77.8)
Congenital heart disease	3 (4.7)	3 (100)	0
Severe malnutrition	5 (7.8)	1	4
Septic shock	8 (12.5)	0	8 (100)
Measles	3 (4.7)	2 (66.7)	1 (33.3)
Down syndrome	2 (3.1)	0	2 (100)
Meningitis	2 (3.1)	0	2 (100)
Others	4 (6.3)	3 (75)	1 (25)

HIV = Human immunodeficiency virus.

The area under the ROC curve using these five significant variables on univariate analysis was 0.78, indicating moderately precise prediction (Figure 1). In a multivariable model using the strongest predictor of survival was the SpO_2 one hour after commencing CPAP, and the presence of HIV was a predictor of death.

Despite CPAP, at some stage in their treatment, nine children (14.1%) required additional oxygen via facemask to raise the SpO_2 above 90%. This was ultimately unsuccessful and all 9 children died.

Problems
Technical, clinical, human and system problems in the use of CPAP that were identified during the course of the implementation study are summarised in the Appendix.

DISCUSSION
Continuous positive airway pressure is widely used in intensive care units in high- and middle-income countries

Table 5 Predictors of death in children on CPAP

Characteristic	Total	Survived	Died	Odds ratio (95% CI)	p-value
Neonatal age	6	3	3	0.81 (0.15–4.36)	0.81
Septic shock	8	0	8		**
Anaemia	13	7	6	0.65 (0.19–2.2)	0.49
HIV infection	12	1	11	12.8 (1.5–106.8)	0.018*
Tuberculosis	5	2	3	1.3 (0.2–8.3)	0.80
Severe malnutrition	5	1	4	3.6 (0.4–34.3)	0.26
Any comorbidity	35	14	21	1.6 (0.59–4.3)	0.35
Pre-CPAP SpO$_2$	64	77.4 (72.8–83.0)%	65.3 (57.9–72.7)%		0.013*
Pre-CPAP RDS	64	10.7 (10.2–11.2)	10.8 (10.3–11.4)		0.72
One hour SpO$_2$	64	92.0 (88.5–95.3)%	83.3 (78.4–88.3)%		0.02*
One hour RDS	64	8.8 (8.1–9.4)	9.9 (9.2–10.5)		0.006*

CPAP = Continuous positive airway pressure; HIV = Human immunodeficiency virus; RDS = Respiratory distress score.
*$p < 0.05$.
**All children with septic shock died, so formal odds ratio not able to be generated.

for the management of respiratory disease in neonates and children. It can be delivered by mechanical ventilators or other CPAP drivers. Mechanical ventilators are the cornerstone for intensive respiratory care, but in Papua New Guinea most hospitals do not have mechanical ventilation or intensive care units for children. Bubble CPAP is a simpler and cheaper alternative.

Studies done in low- and middle-income countries have shown that bubble CPAP is effective in treating preterm newborns with respiratory distress (19). Bubble CPAP reduces the need for mechanical ventilation, providing a safe and effective alternative to ventilator CPAP, and can be effectively applied by nurses and other health workers in low- and middle-income countries (20), and may improve neonatal survival and quality of neonatal care in these settings (19).

However, the effectiveness of bubble CPAP in children outside the neonatal period is not clear, studies are few and heterogeneous in terms of patient populations, baseline mortality rates, equipment for generating CPAP and outcomes measured (Table 6). A randomised controlled trial in a district hospital in Ghana among 70 children aged three months to five years showed that CPAP decreased respiratory rate (15). In an RCT in Dhaka, Bangladesh significantly fewer children in CPAP group had treatment failure compared to low-flow oxygen therapy (14). An observational study in Blantyre, Malawi evaluated outcomes of children with the diagnosis of pneumonia or bronchiolitis and showed that most survivors had improvement within 24 hours, and that outcomes were best for bronchiolitis and poorest for those with pneumocystis jiroveci pneumonia (21). In Pune, India a study assessed the effectiveness of a locally assembled nasal bubble CPAP system in children with acute hypoxemic respiratory failure during a swine influenza outbreak. CPAP improved respiratory rate, heart rate and SpO$_2$ after six hours, compared to admission (22). By far the largest study so far was a pragmatic cross-over trial in Ghana, which showed that CPAP did not decrease all-cause two-week mortality in children one month to five

years of age with undifferentiated respiratory distress, however, after adjustment for confounding factors the authors reported a lower mortality for infants treated with CPAP than those treated with standard oxygen therapy (23).

Our study was a prospective observational effectiveness study, and bubble CPAP was a second-line treatment when standard oxygen therapy via nasal prong or nasal catheter failed to maintain SpO$_2$ >90% or relieve severe respiratory distress. While we showed definite improvement in oxygenation and respiratory distress, the mortality rate (54.7%) was very high compared to the above studies, comparable only to the study from Malawi, and only to the subset of children who did not have bronchiolitis (16). Case-mix and illness severity plays a strong role in understanding the heterogeneity of these studies. The high-mortality rate in our study was likely because these children were very sick, had severe hypoxaemia despite standard flow oxygen, and complex comorbidities. Other studies have shown that underlying chronic conditions markedly increase the risk of death from pneumonia (24). CPAP, like oxygen is only supportive care, not curative, and the underlying illness and comorbidities need to be treatable or self-resolving for CPAP to be effective. Our study also confirms a limit to the role of CPAP, while potentially valuable for many children with moderately severe ALRI, without mechanical ventilation and intensive care some children with severe respiratory failure will not be saved by CPAP alone. This is not to downplay the benefit of using CPAP, but to introduce a sense of realism and avoid vertical thinking that might lead people to believe that CPAP is the answer to pneumonia mortality.

A seriously ill child on CPAP requires a high level of monitoring and supportive care that can only be in place if a quality system supports it. Supportive care includes careful fluid balance to avoid over-hydration, nasogastric tube for feeding, nursing head up 20–30 degrees and management of associated comorbidities. Having a minimal handling approach is important, including gentle

Table 6 Previous studies of bubble CPAP in severe pneumonia

Study author and setting	Study method	Number of patients and population studied	CPAP method	Outcome measures	Number (%) of patients that survived and results of primary outcome
Wilson et al., 2014 Ghana district Hospital	RCT	70 children with tachypnea plus at least one sign of respiratory distress (e.g. chest in-drawing, nasal flaring)	Commercial equipment: DeVilbiss IntelliPAP CPAP machine Hudson RCI CPAP nasal cannula Oxygen added through nonrebreather face mask or through the CPAP circuit	Clinical response at two hours after commencing CPAP	67/70 (96%) survived
Kinikar et al., 2011 Pune, India	Observational	36 moderately unwell children with ALRI during swine flu pandemic, requiring more than 40% oxygen to maintain SpO_2 >94%, excluded children with shock	Modified oxygen prongs and plastic saline bottle 70% oxygen as flow driver (blender not specified)	Clinical response at six hours after commencing CPAP	36/36 (100%) survived
Christi et al., 2013 Dhaka hospital, Bangladesh	Three-arm RCT CPAP, high-flow and low-flow oxygen	225 children with severe pneumonia and hypoxaemia 79 received CPAP	Modified oxygen prongs and plastic shampoo bottle Oxygen concentrator or wall oxygen as flow driver	Rates of clinical failure (composite outcome) with bubble CPAP compared to standard low-flow (LFNC) and high-flow oxygen therapies (HFNC) Death rate secondary outcome	76/79 (96%) treated with CPAP survived Treatment failure: five in b-CPAP; 16 (24%) in LFNC; 10 (13%) in HFNC
Machen et al., 2013 Blantyre paediatric hospital, Malawi	Observational	79 with respiratory distress. 42 bronchiolitis, 21 pneumonia, 15 likely Pneumocystis jiroveci pneumonia.	'Pumani' bubble CPAP flow generator and blender. Oxygen blended from cylinder or concentrator. Commercial nasal CPAP interface	Comparative survival rates for children with pneumonia, bronchiolitis, PJP	56/79 (71%) survived Pneumonia 11/21 (52%) Bronchiolitis 39/42 (93%) PjP 6/15 (40%)
Jayashree et al. Paediatric Emergency Unit, Teaching and Referral Hospital, Chandigarh, North India	Observational	330 children with pneumonia, 163 required CPAP because of hypoxaemia or failure of nasal oxygen. Entry criteria: history of cough and/or difficulty in breathing of less than three weeks duration, increased respiratory rate (rate 60/min if age less than two months, 50/min if age two to 11 months and 40/minute if age 12–59 months) and lower chest in-drawing. 240 (72.7%) had pneumonia and a quarter 90 (27.3%) had bronchiolitis. Escalation to intubation and mechanical ventilation possible	Gas flow source (unspecified, ventilator?), blender, nasal oxygen prongs, glass bottle for underwater seal.	Need for intubation Mortality Change in respiratory distress score	Nine deaths out of 330 (2.7%), all in intubated patients. Primary outcome: three children in b-CPAP group (n = 163) required intubation (failure rate 1.8%); one of these died

Table 6 (Continued)

Study author and setting	Study method	Number of patients and population studied	CPAP method	Outcome measures	Number (%) of patients that survived and results of primary outcome
Wilson et al. 2017 two non-tertiary hospitals in Ghana	Randomised cross-over trial (intervention with contemporaneous control hospital)	2200 (1025 treated with CPAP, 1075 in control hospital). Children one month to five years with undifferentiated respiratory distress; criteria were fast breathing for age and respiratory distress	Commercial equipment: DeVilbiss IntelliPAP CPAP machine Hudson RCI CPAP nasal cannula	All-cause mortality at two weeks after enrolment	995 (97%) survived among 1021 analysed that received CPAP

ALRI = Acute lower respiratory infection; CPAP = Continuous positive airway pressure; HFNC = High-flow nasal cannula oxygen; LFNC = Low-flow nasal cannula oxygen; PjP = Pneumocystis jiroveki pneumoniae; RCT = Randomised controlled trial.
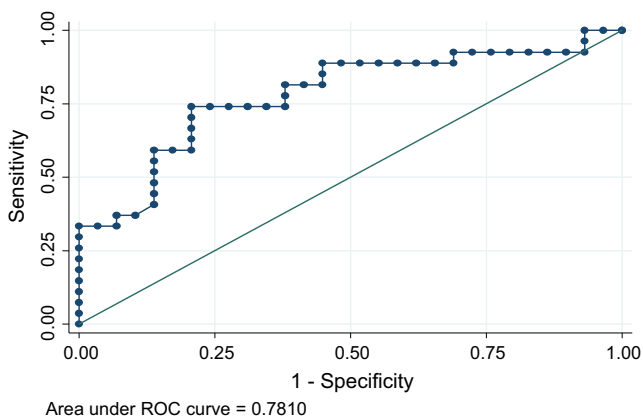

Area under ROC curve = 0.7810

Figure 1 Area under the ROC curve for HIV, sepsis, the pre-CPAP SpO_2, and the SpO_2 and respiratory distress score one hour after commencing CPAP. CPAP = Continuous positive airway pressure; HIV = Human immunodeficiency virus; ROC = Receiver operating characteristics.

suctioning only if needed, judicious use of nebulised saline or bronchodilators based on an objective assessment of benefit, and avoiding very high FiO_2 which can risk masking type II respiratory failure or lead to oxygen toxicity to the lungs.

We identified technical, clinical, human and system problems, which we think are likely to be common in sustaining CPAP as a therapy in LMIC (Appendix). Few other studies have evaluated the conditions required to make CPAP effective. In Andhra Pradesh, India, while nurses perceived CPAP for neonatal respiratory support as beneficial and enabled them to provide care more independently, shortages of supplies, infrastructure and staff meant CPAP was not always available or of the highest quality, and that the introduction of CPAP needed strong organisational support (25). As we also identify, these technical, human and system factors are crucial in successfully using a complex therapy like CPAP, however, simple it seems in highly resourced settings. In high-income countries, hospitals that use CPAP often use disposable circuits and oxygen tubing, in low-income countries this is not affordable, and CPAP technology needs to be cleanable, reusable, robust and safe from bacterial contamination. In high-income countries spare parts and engineering capacity are taken for granted, but these are often lacking in settings like PNG. Nurse–patient ratios are enforced in high-income countries, but in PNG and other low- and low–middle-income countries CPAP needs nurse–patient ratios of no less than 1:4 to be safe and effective, as demonstrated in Bangladesh (14). There is a complex interaction between familiarity with equipment and willingness to use it in a timely manner. It is likely that if CPAP is applied to a less unwell cohort of children the case fatality rate will be lower, but in early phases of implementation often the children who are given CPAP are at a more advanced stage of disease, where CPAP will be helpful in improving oxygenation, but may not be sufficient to save lives (13).

CONCLUSIONS

Bubble CPAP improves oxygenation and reduces respiratory distress in some children with severe pneumonia and hypoxaemia despite standard oxygen therapy. However, children will do poorly despite CPAP if they have comorbidities that are not identified or cannot be treated. HIV, septic shock, low SpO_2 pre-CPAP and low SpO_2 and RDS at one hour after starting CPAP were significant predictors of poor outcome.

Continuous positive airway pressure is a complex therapy that requires a quality system to support it. This includes proper clinical and technical training for nurses and doctors, a consistent technical model, biomedical engineering support, a process for maintenance and troubleshooting of equipment, clinical guidelines and other quality and safety measures.

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APPENDIX: PROBLEMS IDENTIFIED: TECHNICAL, CLINICAL, HUMAN AND SYSTEM

Problems and pitfalls identified	Solutions
Technical	
• CPAP circuits split if they are washed multiple times or stepped upon. This leads to air leaks and ineffective CPAP. • Oxygen concentrators run at high-flow rates (e.g. at the limits of their performance), may produce lower concentration of oxygen • Some humidifiers are ineffective, and if using high flows for prolonged time can result in drying of airway secretions and clinical failure	• Need to check integrity and performance of all equipment regularly, at least weekly. • Use of robust circuits that can be autoclaved or cleaned will reduce the risk of splits and leaks • Need an oxygen analyser to check flow rates and oxygen concentration weekly • Need to ensure effective humidification if using high gas flows • Need an environment free from dust to avoid concentrator malfunction
Clinical	
• Important to identify comorbidities, severe malnutrition, anaemia, HIV, alternative diagnoses such as congenital heart disease • Delay in administration of CPAP	• Requires senior clinical input and supervision • Guidelines for indications for CPAP and contraindications • A structured ward round each day to identify these problems • Protocols for escalation if CPAP is ineffective
Human	
• Familiarity only occurs with use, confidence can be eroded by bad outcomes, bad outcomes perpetuate late use, and late use is associated with poor outcomes • Nursing shortages • Paediatric doctor availability to review patients on CPAP	• Needs ongoing training on indications for use of CPAP for nurses and doctors • Simple guidance for health care staff, and supportive supervision • Nurse: patient ratios not less than 1:4 in the high dependency/intensive care area • A paediatric doctor to be available 24 hours a day and review patients on CPAP regularly, no less than every four hours
System	
• CPAP is a new therapy for many health workers and is being introduced into an environment that has little technology • Need for a mechanism for review and escalation	• A detailed set of guideline is needed to guide administration of CPAP • Need a trained technologist to maintain the oxygen concentrators, nasal prongs, circuits, spare parts • Ward nurses need to be fully familiar with equipment, cleaning, routine maintenance and use • Monitoring charts with alerts for review and escalation • A Medical Emergency Team system provides an opportunity for review and escalation as needed • Mechanism and funding stream for procurement of spare parts and commodities, integrated with other drug and equipment procurement

CPAP = Continuous positive airway pressure; HIV = Human immunodeficiency virus.