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Reducing preterm mortality in eastern Uganda: The impact of introducing low-cost bubble CPAP on neonates <1500g

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Abstract

Background Complications of prematurity are the leading cause of deaths in children under the age of five. The predominant reason for these preterm deaths is respiratory distress syndrome (RDS). In low-income countries (LICs) there are limited treatment options for RDS. Due to their simplicity and affordability, low-cost bubble continuous positive airway pressure (bCPAP) devices have been introduced in neonatal units in LICs to treat RDS. This study is the first observational study from a LIC to compare outcomes of preterm neonates in pre- and post-CPAP periods. Methods This was a retrospective study in Mbale Regional Referral Hospital Neonatal Unit (MRRH-NNU), a government hospital in eastern Uganda. Two study periods were identified. A 14-month study period beginning at the opening of MRRH-NNU and covering the period until bCPAP was introduced (pre-bCPAP) and an 18-month period after bCPAP was introduced (post-bCPAP). After the introduction of bCPAP, it was applied to preterm neonates with RDS when clinically indicated and if a device was available. Clinical features and outcomes of all neonates <1500g were compared before and after the introduction of bCPAP. Results The admission records of 377 preterm neonates <1500g were obtained. 158 were admitted in pre-bCPAP period and 219 after. The mortality rate in pre- bCPAP period was 39.2% (62/158) compared with 26.5% (58/219, P=0.012) in post-bCPAP period. There were no differences in birthweight, sex, presence of signs of respiratory distress or apnoea between the two groups. Conclusion Specialized and resource-appropriate neonatal care that appropriately addresses the challenges of healthcare provision in LICs has the potential to reduce neonatal deaths. The use of a low-cost bCPAP to treat RDS in preterm neonates <1500g resulted in a significant improvement in their survival in a neonatal unit in eastern Uganda. Implementing bCPAP with adequate training and supervision could significantly reduce preterm mortality in LICs.

Background

Complications of prematurity are the leading cause of deaths in children under the age of five.(1) In fact in 2015, complications from preterm birth led to the death of 1.055 million neonates worldwide, with the majority occurring in low- and middle-income countries (LMICs) like Uganda.(1) The predominant reason for these preterm deaths was respiratory distress syndrome (RDS), with more than 50% of neonates born before 30 weeks of gestation developing RDS.(2, 3) In high-income countries (HICs), continuous positive airway pressure (CPAP) has been shown to reduce preterm mortality by 48%, and reduce the need for mechanical ventilation by 50%.(4) CPAP is now the standard of care in HICs and with the option of mechanical ventilation and artificial surfactant if required. However, in low-income countries (LICs), ventilation, surfactant and CPAP are rarely accessible or affordable leaving limited treatment options for preterm neonates with RDS.

Due to their simplicity and affordability, low-cost bubble CPAP (bCPAP) devices have been introduced in many neonatal units (NNUs) in LMICs.(5) However, there have been no randomized trials conducted in LMICs investigating the efficacy of bCPAP. Four observational studies from middle-income countries have compared outcomes of preterms in a pre- and post-CPAP periods.(6-9) Implementation of home-made bCPAP in India reduced mortality from 10.7% to 2.4%.(6) In another study in India, introduction of CPAP

reduced up-transfers from 74% to 37%.(8) Findings were similar in South Africa, with up-transfers reduced from 16.7% to 5.1%.(7) Finally, in Kenya, the survival-to-discharge rate was increased from 61% to 85% after bubble CPAP was implemented.(9)

In LICs, three observational studies in hospitals without access to mechanical ventilation or artificial surfactant, have documented the use of bCPAP.(10-12) In a dedicated physician-led neonatal ward in Malawi, implementation of a commercial low-cost bubble CPAP device for treatment of severe respiratory distress in neonates >1000g showed a 27% improvement in neonatal survival.(12) The study from Uganda, in a dedicated physician-led neonatal unit, and the study from Rwanda, in three rural district hospitals providing basic neonatal care, had no comparison groups and thus could only conclude that bCPAP was feasible for low-resource settings.(10, 11) The Rwandan study did observe a trend towards improved outcome of VLBW infants using bCPAP however they still reported low survival rates of VLBW infants treated with CPAP of 42%.

In Uganda, the Neonatal Mortality Rate has not changed over 2 decades, remaining high at 28/1000 live births and the leading cause of these deaths is complications of prematurity.(13) The UN Sustainable Development Goals seek to reduce global neonatal mortality to 12 deaths per 1000 live births by 2030.(14) For this to be achieved, mortality from preterm complications must be drastically reduced. Specialized and resource-appropriate neonatal care that appropriately addresses the challenges of healthcare provision in LICs is needed to help meet this goal. Our study sought to determine the impact of bCPAP on the outcome of preterm neonates <1500g in a neonatal unit in eastern Uganda.

Study location

The study was conducted in Mbale Regional Referral Hospital (MRRH), a government hospital in eastern Uganda that serves a population of 4.5 million people. Since 11 May 2015, MRRH has had a dedicated neonatal unit (NNU) that admits over 2000 neonates a year including around 140 very low birth weight (VLBW <1500g) infants.(15) Neonates are admitted directly from the labour ward, referred from surrounding health facilities and, due to a high rate of home deliveries, some neonates are brought directly from home.(13) The MRRH-NNU is staffed by a full-time neonatal doctor, two neonatal clinicians, 6 specially trained neonatal nurses and a rotating intern. The ward has an average of 35 neonates admitted at any one time and 24-hour nursing care is provided by a single neonatal specialist nurse in 8-hourly shifts.

Standard of care

In MRRH-NNU, treatment with intravenous fluids, intravenous antibiotics, anticonvulsants, aminophylline, multivitamins and iron supplements is possible.(15) All VLBW infants are started on broad-spectrum antibiotics, aminophylline and dextrose 10% infusion on day 1. Almost all preterms are fed exclusively with expressed human breastmilk. Feeding is commenced at 25ml/kg/day and advanced by 25ml/kg/day as tolerated either by nasogastric tube or spoon feeding until 150ml/kg/day is achieved. Thermoregulation is achieved using kangaroo care.

Oxygen saturations are checked on admission and once daily on the ward round, aiming for 90-93% in the preterm neonates.(16) Controlled free-flow nasal oxygen can be given from 0.1 – 1.5l/min. On 12th July 2016, bCPAP was introduced in MRRH-NNU. The bCPAP devices (Diamedica UK Ltd, Bratton Fleming, UK) are designed for low-resource settings and can provide a distending pressure of up to 10 cmH_2O and a fraction of inspired oxygen between 21-95%. The devices have an integrated oxygen concentrator, so cylinders are not required. Treatment was delivered using nasal prongs (RAM Cannula, Neotech). bCPAP was applied to preterm neonates with RDS when clinically indicated and if a device was available, treating up to five neonates at one time. If a bCPAP device was not available the neonate continued on oxygen therapy alone as needed. The bCPAP could be initiated by any member of staff including the nurses.

Neonates on bCPAP settings were assessed 1-2 times a day by the neonatal doctor or neonatal clinician. The fraction of inspired oxygen was adjusted to maintain the oxygen saturations 90-93%. The distending pressure was adjusted between 2-8 cmH_2O based on the level of respiratory distress evident on clinical examination.

MRRH-NNU does not routinely have access to echocardiography, blood gas analysis, blood pressure monitoring or portable chest x-ray. Mechanical ventilation and surfactant are not available.

Methods

Two study periods were identified. The first, (11 May 2015 – 11 July 2016) was a 14-month period from the opening of MRRH-NNU when there were no bCPAP machines available until the introduction of bCPAP (pre-bCPAP). The second period (12th July 2016 – 31st Dec 2017) was the subsequent 18 months after bCPAP was introduced to MRRH-NNU (post-bCPAP). The second period was limited by the introduction of back-up power and continuous pulse-oximetry monitoring for all neonates on bCPAP in January 2018. The sample size reflects these time periods.

The inpatient records for all VLBW neonates (birthweight <1500g) admitted to the NNU during the two study periods were identified. The following data elements were extracted: date of birth, date of admission, admission weight, gender, place of delivery, type of delivery, need for resuscitation at birth. Vital signs at admission, signs of respiratory distress, presence of apnoea, method of respiratory support, length of hospital stay and in-patient outcome (discharge, died, referred) were also extracted.

Data from the pre-bCPAP period were compared with those admitted after the introduction of bCPAP. Data were analyzed using SPSS Version 25. Comparison of discrete variables between neonates before and after bCPAP was done using chisquared or fisher's exact tests; student's t-test was used to compare normal continuous variables. Comparison of medians was done using the Mann-Whitney U test.

Ethics

The Mbale Regional Referral Hospital Research & Ethics Committee (MRRH-REC) approved the study and local permission to conduct the study was obtained from Mbale Clinical Research Institute and Mbale Regional Referral Hospital.

Results

During the study period 377 preterm neonates <1500g were admitted. 158 were admitted in the period before bCPAP was introduced and 219 after. There were no major statistical differences between the two groups in terms of place of birth, type of delivery or need for resuscitation at birth (Table 1). The admission weight, gender, admission observations and history of resuscitation were similar between the two groups. There was no difference in the admission vital observations between the groups, the presence of signs of severe respiratory distress or apnoea. There were significantly more neonates with subcostal recession in the post-bCPAP period suggesting this group of patients may have been sicker and therefore one might have anticipated worse outcomes.

Table 1: Demographics and outcomes of VLBW infants treated at the MRRH NNU

The primary outcome, mortality rate (Table 2), was significantly lower in the post-bCPAP period (39.2% vs. 26.5%; *P*=0.012). Overall, there was a 44% reduction in mortality (OR 0.56, 95%CI 0.36-0.86, *P*=0.01). The reduction in mortality was similar in VLBW neonates (1000-1499g) and ELBW neonates (<1000g), from 31.5% to 19.7% (*P*=0.023) and 75% to 61.1% (*P*=0.290) respectively. The impact in ELBW did not reach statistical significance; this was likely due to a relatively small number of ELBW neonates. The introduction of bCPAP in MRRH-NNU also led to a significant reduction in the average length of hospital admission (38.0 v. 26.6 days; *P*=0.053).

Table 2 Comparison of outcomes pre- and post-bCPAP

Discussion

To our knowledge, this is the first retrospective study comparing a pre- and post-bCPAP era in a low-income country. The survival of VLBW neonates at MRRH-NNU was significantly improved by the introduction of bCPAP for the treatment of RDS. This supports data from similar studies in MICs.(6-9)

Due to the retrospective nature of this study, it has certain limitations. Firstly, no accurate gestational data was available since many women had not had a dating scan and the dates of the last normal menstrual period were often not known. The outcomes in this study can only be interpreted compared to birth weight. It was not possible to ensure that all other variables remained constant during the two periods, however to our knowledge there were no changes in practice in MRRH labour ward during this time. In addition, no other equipment was introduced to the NNU apart from the bCPAP during the study. There was no change in neonatal protocols, medications or training. Neonatal nursing staff in the NNU did change over during this period, although no additional staff were added. All neonatal nurses received the same neonatal training on commencing work in the NNU.

It was not uncommon to have more neonates that required bCPAP than the five machines that were available. Unfortunately, data on these numbers was not available, therefore it is likely that the impact on mortality would be have been greater if more bCPAP machines were available.

There are multiple risk factors for poor outcomes in preterm neonates that were not possible to measure during this study. Firstly, documentation on the use of antenatal corticosteroids was not available. In addition, at the time of the study it was not possible to diagnose other co-morbidities such as intraventricular haemorrhage, retinopathy of prematurity and patent ductus arteriosus.

Despite the limitations, this study still clearly proves that low-cost bCPAP can have a dramatic impact on preterm mortality in a low-resource setting. In fact, given the limited number of bCPAP machines, the reported reduction in mortality may actually be an underestimate. This study also demonstrates that it is feasible to introduce bCPAP into a NNU that is mainly staffed by nurses and clinical officers, making it an attractive choice for widespread implementation in LICs. If this relatively simple and affordable intervention could be scaled-up across NNUs in Uganda and other LICs, there is a potential to reduce preterm mortality by over 40%. This would have a huge impact on global neonatal mortality.

Conclusion

The use of a low-cost bCPAP to treat RDS in preterm infants <1500g resulted in a significant improvement in survival. Implementing bCPAP with adequate training and supervision could reduce preterm mortality in LICs.

Declarations

Funding

No funding was received for this study. All authors volunteered their time.

Authors' contributions

KB conceived the study idea and designed the data collection tools. POO helped in setting up the study and study coordination. JI, LA and EE refined the data collection tools, did data collection and management. KB and FO undertook the statistical analysis. KB and KL wrote the manuscript. All authors critically revised, read and approved the final manuscript.

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Conflict of Interest

Kate S.M. Loe is employed by Diamedica UK Ltd at the time of submission. Loe became involved in this study in January 2019, after data collection and analysis was completed by the other authors.

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