Impact of improved oxygen systems on child deaths from pneumonia: a multi-hospital effectiveness study in Papua New Guinea

Trevor Duke, MD
Centre for International Child Health, Department of Paediatrics, University of Melbourne, Royal Children's Hospital, Melbourne
Discipline of Child Health, School of Medicine & Health Sciences, University of PNG

Francis Wandi, MMed
Kundiawa Hospital, Simbu Province, PNG

Merilyn Jonathan
Family Health Services, PNG National Department of Health

Sens Matai
PNG National Department of Health

Magdalene Kaupa
Mt Hagen Hospital, Western Highlands Province, PNG

Martin Saavu
Mendi Hospital, Southern Highlands Province, PNG

Rami Subhi
Centre for International Child Health, Department of Paediatrics, University of Melbourne, Royal Children's Hospital, Melbourne

David Peel, DPhil
Ashdown Consultants, Hartfield, TN7 4ET, East Sussex, England

ABSTRACT

Background

Oxygen is an essential part of the management of severe pneumonia, but in most rural hospitals in developing countries oxygen supplies are poor, and detection of hypoxaemia is difficult. Oxygen concentrators and pulse oximeters may address these needs however introduction of even basic technology in developing countries is challenging, and requires critical evaluation. We sought to understand the impact of an improved oxygen system on deaths from pneumonia in children, and to estimate the costs of such a system.

Method

We introduced an improved oxygen system in five hospitals in Papua New Guinea (PNG), conducted a before- and after- study of over 11,000 admissions for pneumonia and compared case fatality rates. We recorded all costs associated with establishing and sustaining this system.

Results

There was a highly significant reduction in mortality rates for pneumonia. In the years before the system was introduced in the five hospitals, there were 356 deaths out of a total of 7161 admissions for pneumonia: case fatality rate (CFR) 4.97% (95% confidence interval 4.5% – 5.5%), as compared to 133 deaths out of a total of 4130 admissions in the 27 months following the introduction of the system: CFR 3.22% (95% confidence intervals 2.7% – 3.8%). The risk of a child with pneumonia dying in hospital after the system was introduced was 35% lower than in the era before the project began: risk ratio 0.65 (95% confidence interval 0.52-0.78), Chi^2 $p<0.001$. The effect on pneumonia mortality was different between hospitals.

The estimated costs of the system were US$51 per patient treated, US$1673 per additional life saved and $50 per DALY averted.

Conclusions

The reduction in pneumonia mortality observed was most likely a result of the appropriate application of pulse oximeters and oxygen concentrators in managing hypoxaemia. The cost effectiveness of this system compared favorably to other public health interventions to reduce global pneumonia mortality. There is potential for such technology to alleviate oxygen shortages and improve quality of care for ill children.

INTRODUCTION

Worldwide acute respiratory infection causes 2 million child deaths per year, 98% of which are in developing countries.[1;2] In Papua New Guinea (PNG) the major cause of death among children under the age of 5 years old is pneumonia. Hypoxaemia is the major fatal complication of pneumonia,[3] and is also a complication of other common diseases, particularly among newborns.[4] The World Health Organization (WHO) recommended treatment of children with very severe pneumonia includes both antibiotics and oxygen,[5] but in PNG, like in many developing countries, oxygen shortages are common, particularly in rural and remote facilities, due to the high cost and complex logistics of transporting oxygen cylinders. Oxygen concentrators - machines that generate concentrated oxygen from ambient air - have been proposed to address this problem.

Detection of hypoxaemia using clinical signs is difficult, especially among heavily pigmented children and in poorly illuminated health facilities, wherein clinical signs, including cyanosis, are difficult to detect.[3;4;6] Pulse oximetry is the most reliable, non-invasive way of detecting hypoxaemia,[7] and its relevance to pneumonia management in developing countries has been highlighted in part by the poor sensitivity and specificity of clinical predictors of hypxoaemia, and by the increasing affordability of pulse oximeters.

Previous studies in PNG show that the prevalence of hypoxaemia is much greater in highlands hospitals (40% of all admissions) than on the coast (10% of all admissions). This difference was largely due to the relative incidence of acute respiratory tract infection. On the day of admission oxygen was not available for 22% of children requiring it.[8]

There has been very limited research on the clinical impact and cost effectiveness of oxygen in the treatment of pneumonia among children in hospitals in developing countries.[3;9-12] Most cost-comparison analyses of oxygen systems have focused on equipment costs only and estimations have been made by theoretical modeling.[13] However the true cost of improving technology in developing countries is more than the funding that is required for equipment, and countries need to know the complete costs of implementation, and the feasibility of sustaining such a system.

We conducted a trial of oxygen concentrators and pulse oximeters in five hospitals in PNG and evaluated whether installation of a reliable, sufficient and affordable source of oxygen, coupled with the use of pulse oximetry, would reduce the case fatality rate for pneumonia.

METHODOLOGY

Given that oxygen is the standard of care for hypoxaemia, we decided that a randomized study comparing the performance of facilities that have difficulty accessing oxygen with others in which an improved oxygen system was introduced would be unethical. Therefore we conducted a before and after comparison in the five hospitals to which the system was introduced. We measured case fatality rates for pneumonia and for all admissions, and compared these for the pre-intervention and post-intervention eras.

Study sites and implementation

The five study sites were: three highlands provincial hospitals (Mt Hagen, Mendi and Kundiawa) at 1600-1800m above sea-level; one coastal provincial hospital (Wewak); and one in-land district hospital at 400m above sea-level (Maprik). The combined population served by these hospitals is over 1.2 million. Two hospitals had a paediatrician, two hospitals had a general medical officer designated to the paediatric ward, and one hospital had one general medical officer in charge of all hospital wards at the one time. The hospitals had between 2-6 nurses working during the day and 2-3 nurses overnight. Over the 6 years of study, the 4 provincial hospitals had between 38-62 paediatric beds and admitted an average ranging between 1029-2442 children annually, while Maprik district hospital had 28 beds and admitted an average of 566 children annually.

In the pre-intervention period compressed gaseous oxygen was transported in cylinders from commercial supply plants in major centres. The distances traveled were large, often using several modes of transport (road and ship).

Standardized features of pneumonia case management in the pre-intervention and post-intervention eras are compared in Table 1. For decades PNG has had a Standard Treatment approach, which is closely adhered to in all hospitals.[14] Pneumonia is diagnosed according to WHO's criteria, although the severity categories are given different names. Antibiotics are also consistent with WHO's treatment guidelines: amoxicillin for mild (WHO non-severe) pneumonia; benzylpenicillin for moderate (WHO severe) pneumonia; and chloramphenicol for severe (WHO very severe) pneumonia. Other antibiotics, such as third-generation cephalosporins and beta-lactamase stable penicillins are not used as first line therapy and rarely used to treat pneumonia, because of limited availability and because these are not part of standard treatment. Breast feeding of children with pneumonia is encouraged unless the infant has severe respiratory distress, in which case nasogastric feeding with expressed breast milk is given, or in very severe cases, intravenous fluids are given in the acute stage. Hospital access is free for children, and there are no charges for antibiotics, oxygen or other treatments.

In June and July 2005 oxygen concentrators and pulse oximeters were introduced in the five hospitals. We developed a model for introducing this technology, which outlined the type of equipment needed for such settings, the installation, commissioning and testing processes, and the training required for nurses, doctors and hospital engineers. This is described in detail elsewhere.[15]

A protocol for the clinical use of oxygen was introduced.[3] Staff were taught to use pulse oximetry to screen all children for hypoxaemia on admission. Hypoxaemia necessitating oxygen delivery was defined as an arterial oxygen saturation (SpO_2) <90%. It was advised that oxygen should be delivered via nasal prongs at a starting flow rate of 0.5 or 1 L/min, titrated to achieve an SpO_2 of 90% or greater. The monitoring protocol outlined included daily examination for changes in clinical status, and SpO_2 measurements with the child breathing room air for up to 15 minutes, to assess whether supplemental oxygen was still required. It was emphasized that this trial without oxygen should not be done if children were clinically unstable, or had low SpO_2 while still on oxygen. Children received supplemental oxygen until their SpO2 was >90%.

Measurement of clinical outcomes

To measure the effect on case fatality rate for pneumonia we collected data on children admitted to the five participating hospitals between 2001 and 2007. Admissions falling between January 2001 and December 2004 formed the pre-intervention population and those between July 2005 and October 2007 were the post-intervention population. The first 6 months of 2005 was considered a period of transition leading up to the intervention and was excluded from the observation period. In PNG, it is routine practice for the nurse in charge or ward doctor to record the name, age, initial and final diagnoses and outcome of each child admission. This is compiled in the children's ward admission book of each hospital. This allowed summary data of overall and pneumonia admissions and deaths to be compiled and case fatality rates to be calculated for the pre-intervention and post-intervention eras. We calculated the risk and risk ratio for mortality (95% confidence intervals) in the pre- and post-intervention eras for the five hospitals overall, and for each hospital individually. We estimated the number of lives saved in the post-intervention period by the difference between the observed and expected mortality; the expected mortality being based on the mortality in the pre-intervention period.

Measurement of cost and cost-effectiveness

We prospectively recorded all costs associated with implementing and sustaining this system. These included the costs of equipment, consumables, training, supervision and support visits, repairs and spare parts, maintenance and evaluation.

To estimate the cost per child treated we calculated the number of children with hypoxaemic pneumonia in the post-intervention period, using hospital-specific values obtained by studying a sample of 578 children with pneumonia consecutively admitted to the five hospitals from July 2004-March 2005.[8] It was assumed that only children with hypoxaemic pneumonia received oxygen, and based on the sample of 578 children, these were 59.7% of the total pneumonia admissions to the three highlands hospital (Hagen, Kundiawa and Mendi) and 40.4% of the pneumonia admissions to the two coastal/lowland hospitals (Maprik and Wewak),.

The cost per additional life saved was calculated as the overall cost divided by the estimated number of additional lives saved.

We calculated the cost per disability adjusted life years (DALY) averted, based on an assumption that an infant life saved is worth 33 DALY.[16] This was chosen to produce a conservative estimate; the population of children with pneumonia ranges up to 5 years of age, and a child's death outside infancy is assumed to be worth more DALY.[16]

Ethical approval

The study was approved by the Medical Research Advisory Committee of PNG (MRAC No: 04.02).

RESULTS

Impact on deaths from pneumonia

The 5 hospitals combined provided data on 181 and 121 months of observation in the pre- and intervention phases respectively (median months of observation per hospital: 42 and 27). The observation period varied between hospitals because of the availability of records. There was

a highly significant reduction in hospital mortality rates for pneumonia. In the years before the system was introduced, there were 356 deaths out of a total of 7161 admissions for pneumonia (case fatality percentage 4.97%, 95% confidence interval 4.5 - 5.5%); in the 27 months after the system was introduced, there were 133 deaths out of a total of 4130 admissions for pneumonia (case fatality percentage 3.2%, 95% CI 2.7 - 3.8). The risk of a child with pneumonia dying in the hospitals after the system was introduced was 35% lower than before: risk ratio 0.65 (95% confidence interval 0.52-0.78), p<0.001 (Table 2).

We estimate that this system saved the lives of 72 children (95% confidence intervals 52-94) who would otherwise have died from pneumonia over the 27 month period in the 5 hospitals [(0.0497 x 4130)-133=72.3; 95% CI (0.045 x 4130)-133=52.8 to (0.055 x 4130)-133=94.2].

In the pre-intervention era, there were 1134 deaths in 20,515 overall admissions of children over 1 month of age (CFR 5.53%), as compared to 481 deaths from 11,820 admissions (CFR 4.1%) in the 27 months after the introduction of the system. This represents a significant reduction in overall mortality - risk ratio 0.74 (95% confidence interval 0.65-0.81); p<0.001.

Hospitals differed in the effect of this system (Table 2). Mendi and Mt Hagen, the two hospitals with the largest pneumonia case loads, had the only significant decreases in mortality rates for pneumonia. The pneumonia mortality rate in Kundiawa did not change, but was low at baseline. There was also no change in Maprik, and the increasing trend in Wewak hospital was not statistically significant (p=0.11); both of these hospitals had small numbers of pneumonia admissions compared to the highlands hospitals.

Cost and cost effectiveness

The costs are outlined in Table 3. The total cost was US$120,462. The estimated cost per life saved was US$1673 (95% confidence intervals $1282 to $2317). If one assumes that an infant death averted = 33 DALYs,[16] then the cost per DALY averted is $50 (95% confidence interval $39-70).

We estimate that in the 27 months following its introduction, 2351 children required treatment with oxygen, at a cost of US$51.2 per patient.

DISCUSSION

Previous studies of oxygen concentrators suggested them to be much more cost effective than oxygen cylinders, but followed-up to just one year after installation and reported no data describing the clinical impact .[13;17;18] Similarly, while there have been calls for pulse oximetry to be used more widely in the management of pneumonia in developing countries,[9] there has been no evaluation of their potential impact or cost effectiveness. We have shown that it is possible, in remote and resource limited hospitals, to introduce this technology into everyday clinical care and to see an impact on pneumonia and overall mortality rates.

In introducing and evaluating this system, we intended for the entire process to be integrated in the participating hospitals and the PNG health system; so this can be considered to be an effectiveness study. This had the advantage of promoting a local ownership and ensured compatibility of the intervention with existing health systems, but it did mean that enforcement of the intervention protocol was at times not feasible. We could not always

control the availability of data; in the post-intervention period records were only available for 13 months from Mt Hagen Hospital, as the admission record book had been lost. The months of observation in the pre-intervention period were not uniform between hospitals. During the prolonged period of waiting for funding for the intervention to commence, one hospital which was originally participating was closed to in-patients and unable to participate, so two more (Maprik and Wewak) were included at a later date.

This study was a before and after comparison, and has the potential limitations of such a design. These include the possibility of secular trends in mortality rates over time, ascertainment bias, altered thresholds for hospital admission, and other confounding. A period of more than 2 years of observation post-intervention was chosen to reduce the effect of seasonal variation or disease outbreaks.

The patient admission and outcome data were routinely recorded as part of everyday clinical practice, and we believe it is highly unlikely that recording bias existed where fewer pneumonia deaths were reported in the post-intervention era. Nursing staff in PNG take pride in ensuring admission record books are accurate and up to date. While clinical staff knew that we were planning an evaluation of the oxygen system, they did not know that the outcome data were coming from the children's ward admission record books. We have no reason to believe that the method of data collection or the accuracy with which it was recorded changed in any way over the 6 years of the study. The staffing levels, funding resources, availability of antibiotics and standard treatment practices in the hospitals did not change substantially over the 6 years of the study. HIV became more of a problem over the 6 years, but this would not be expected to result in a reduction in pneumonia case fatality rates.

The estimate of 72 (95% confidence interval 52-94) additional lives saved is based on the difference between observed and predicted deaths in the post-intervention period; the predicted number being based on the mortality rate in the pre-intervention period. We think it is reliable given the narrow confidence intervals and the long time of pre-intervention observation. Even the most conservative estimate of 52 deaths avoided would represent a very substantial gain.

There was a three-fold variability in the case fatality rates between hospitals in the pre-intervention era. Case fatality rates from pneumonia will depend on several things, including severity of illness at the time of presentation, the patient load relative to staffing resources, staff training and quality systems to ensure timely treatment and monitoring, availability of antibiotics, oxygen and other treatments, and the proportion of children with comorbidities. The hospitals with lower case fatality rates in the pre-intervention era tended to have generally more trained staff for the patient load, and greater access to cylinder oxygen. Therefore scope for improvement was limited, for example in Kundiawa hospital, where the baseline case fatality rate was 2%, and only 4% of children could not access oxygen on the day of admission.[8] The two hospitals with the most substantial falls in case fatality rates (Mt Hagen and Mendi) had in the pre-intervention era the combinations of very high burdens of disease, limited staffing for the high patient load, and a lower proportion of children able to access oxygen on the day of presentation.[8] The increase in case fatality rates in Wewak hospital is difficult to explain, but likely reflects the small case loads. The predominant illness in Wewak is malaria and this may introduce confounding in the diagnosis of ARI and thus wider outcome variability.

Overall there was decrease in the number of pneumonia admissions per month of observation (median 33 per month compared with 27 per month) from pre to post-intervention era. Among the hospitals where there was a substantial reduction in pneumonia case fatality rates, Mendi had an increase in pneumonia admission numbers (28 compared with 39), and in Mt Hagen the number of admissions were largely unchanged (65 and 66 in the pre- and post-intervention eras respectively). While the higher number of admissions in Mendi in the post-intervention era might conceivably point to a lower threshold for admission, partly accounting for the lower mortality rates, the criteria for admission did not change. There was also a reduction in overall mortality, which was less than the reduction in pneumonia mortality. This may have been due to the effect of oxygen on conditions other than pneumonia. Health workers were taught to do oximetry on every child being admitted, not just those with clinical signs of pneumonia. We know that hypoxaemia is common in conditions other than ALRI in PNG, and improvements in oxygen systems are very likely to benefit other common childhood conditions also. The reduction in overall mortality may also have been due to improved general quality of care; establishing effective systems for monitoring and oxygen delivery may result in general improvements in care and better outcomes. However given that this was not a randomised trial we cannot discount the idea that secular trends influenced the results.

The estimate of cost per child treated ($51) is moderately high, but compares favourably to other interventions, such as hospitalization for oral rehydration solution (about $75) and hospitalisation for antibiotics for pneumonia (about $150), based on studies from other regions (South East Asian and sub-Saharan African regions of WHO).[19] Based on these studies $51 would add about a third to the overall cost of in-hospital management of a child with very severe pneumonia.[19] The estimated cost of $50 per DALY averted adds to the estimated cost of standard case management for pneumonia ($70 per DALY averted),[19] and compares favourably to other newer interventions to reduce deaths from pneumonia, including pneumococcal conjugate vaccine (estimated $100 per DALY averted).[20]

We did not include patient costs (nursing wages, antibiotics etc) as these are costs already incurred by the health system; rather the evaluation included the costs and effectiveness of adding this oxygen system to the services already provided by the hospitals. On the other hand, this cost per child treated is a conservative estimate, not factoring in children with conditions other than pneumonia who were treated with oxygen.[4;8;21] Furthermore because the life-span of this equipment is longer than 2.5 years, the costs per patient treated, the cost per life saved and the cost per DALY averted will be less over time. If the system is well maintained the lifetime of the equipment should be between 5 and 10 years for a low additional cost.

It is noteworthy that the equipment costs were only 65% of the total costs to sustain such a system; so budgeting is needed for a comprehensive approach to training and maintenance if such a system is to be introduced. We included evaluation visits in the cost analysis because training, maintenance and repair were done during these visits. The model of implementation that has been used in PNG involves an annual visit to all hospitals by a team which includes an engineer with expertise in oxygen technology and a clinician who can do clinical training.[15]

We chose not to evaluate the impact of concentrators or oximeters separately, and therefore we cannot specify the individual contribution of each component of the system to the observed reduction in mortality rates. We believe this would have been an artificial separation of such a system. An appropriate method for giving oxygen must be coupled with an accurate method for detecting hypoxaemia, along with training in all aspects of the system if substantial benefit is to be gained. This study highlights the need for informed implementation and ongoing training and support to ensure that such technology is feasible and relevant to the setting to which it is introduced.[15]

Conclusions

A methodical approach to improving oxygen systems has been evaluated for its impact on pneumonia mortality in children. The approach involves technical, clinical and training and management expertise, and has a focus on improving quality of care. We observed a significant reduction in mortality; the most likely explanation for which is the improved system, and the better quality of care that can accompany such improvements.

With an increasing recognition that a holistic approach is required to reduce the global burden of child mortality from pneumonia, we hope that more countries will consider developing similar programs.

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<table>
<tr><th></th><th>Pre- oxygen systems intervention</th><th>Post- oxygen systems intervention</th></tr>
<tr><td>Diagnosis and severity classification</td><td colspan="2">Moderate pneumonia
Cough, fast breathing and chest indrawing
Severe pneumonia
Cough, fast breathing and chest indrawing plus
• Too sick to feed properly, or
• Cyanosed or restless, or
• Heart failure (heart rate >160 and hepatomegaly)</td></tr>
<tr><td>Antibiotics</td><td colspan="2">Moderate pneumonia
IM crystalline penicillin followed by oral amoxicillin

Severe pneumonia
IM chloramphenicol followed by oral chloramphenicol</td></tr>
<tr><td>Oxygen supply</td><td>Oxygen cylinders</td><td>Oxygen concentrators</td></tr>
<tr><td>Indications for giving oxygen</td><td>Clinical signs
• Central cyanosis
• Too sick to feed
• Heart failure (tachycardia and enlarged liver)</td><td>$SpO_2 < 90\%$ by pulse oximetry and clinical signs</td></tr>
<tr><td>Oxygen delivery method</td><td>Nasal or nasopharyngeal catheter</td><td>Nasal prongs or nasal catheter</td></tr>
<tr><td>Indications for stopping oxygen therapy</td><td>Not standardized, based on clinical signs of reduction in respiratory distress</td><td>Able to maintain a stable SpO_2 >90% following a 15 min trial on room air, plus clinical signs of improvement</td></tr>
</table>

Table 1. The standard treatment of pneumonia in hospitals in PNG in the pre-intervention and post-intervention eras

Hospital	**Pre-intervention 2001-2004**				**Intervention 2005-2007**				**Risk ratio (95% CI) for death post-intervention**	**p-value**
	Months of observation	Admissions (% of total admissions to 5 hospitals)	Median monthly admissions (IQR)	Deaths (mortality %)	Months of observation	Admissions (% of total admissions to 5 hospitals)	Median monthly admissions (IQR)	Deaths (mortality %)		
Hagen	45	3477 (48.6)	65 (46-90)	222 (6.4)	13	1254 (30.3)	66 (60-139)	42 (3.3)	0.52 (0.38-0.72)	<0.001
Kundiawa	42	1525 (21.3)	33 (21–52)	31 (2.0)	27	1044 (25.3)	32 (27-49)	25 (2.3)	1.18 (0.70-1.98)	0.54
Maprik	23	288 (4.0)	8 (7-19)	11 (3.8)	27	216 (5.2)	7 (4-12)	8 (3.7)	0.97 (0.40-2.40)	0.95
Mendi	45	1509 (21.1)	28 (18-51)	84 (5.6)	27	1242 (30.1)	39 (29-62)	42 (3.3)	0.61 (0.42-0.87)	0.006
Wewak	26	362 (5.1)	14 (12-21)	8 (2.2)	27	374 (9.1)	11 (8-20)	16 (4.2)	1.94 (0.84-4.47)	0.1143
Total	181	7161 (100)	33 (19-60)	356	121	4130 (100)	27 (11-44)	133 (3.22)	0.65 (0.52-0.78)	<0.001

Table 2. Pneumonia admissions, deaths and risk ratio for mortality in the 5 hospitals

Components of the system	**Description**	**Cost (US$)**
Equipment	Oxygen concentrators 8 L/min (n=9)	26,299
	Oxygen concentrators 5L/min (n=5)	8,929
	Pulse oximeters (n=7)	25,459
	Oximetry sensor probes (n=30)	6,507
	Installation materials / consumables	11,631
	Total equipment costs	78,825
Implementation	Travel, accommodation and expenses for the oxygen team (4 people) for 30 days plus on-site training for clinical and technical staff	13,571
Review visits and evaluation	Review visits in 2006 and 2007 (including cost of spare parts and repairs)	13,218
	Evaluation in October 2007	14,848
Total		120,462

Table 3. Costs of the oxygen system