Letters

RESEARCH LETTER

Solar-Powered Oxygen Delivery in Low-Resource Settings: A Randomized Clinical Noninferiority Trial

Oxygen is an essential medicine for life-threatening hypoxemic illnesses, including pneumonia, which is currently the leading cause of childhood mortality worldwide.[1,2] However, oxygen is not available in many pediatric wards in low-income countries. In a survey of 12 African countries, only 44% of 231 health centers, district hospitals, and provincial or general hospitals had access to oxygen on a continuous basis.[3] Pragmatic solutions are needed to improve access to oxygen in low-resource settings.

Author Audio Interview

Supplemental content

In resource-constrained settings, compressed oxygen cylinders and oxygen concentrators are commonly used. Oxygen cylinders are ready to use and do not require any electricity; however, their availability may be compromised by weak stock management, the need for transportation from supplier to hospital, and leakage from ill-fitting regulators. Oxygen concentrators generate oxygen on site from ambient air through selective adsorption of nitrogen using aluminum silicate sieve beds. Concentrators overcome the logistical supply barriers of cylinder oxygen, require minimal service and maintenance, and are more user-friendly than cylinders. However, oxygen concentrators require a continuous and reliable source of electricity. A systematic review found that only 34% of hospitals in sub-Saharan Africa have reliable access to electricity.[4] Interruptions in oxygen therapy owing to power outages are therefore frequent and potentially fatal in the settings in which most deaths from pneumonia occur.[4]

Methods | We tested a novel strategy, solar-powered oxygen delivery, which concentrates oxygen from ambient air using solar energy.[5] We conducted a randomized, placebo-controlled clinical trial of solar-powered oxygen delivery vs standard oxygen delivery using compressed oxygen cylinders among children younger than 13 years with hypoxemic illness at 2 resource-constrained hospitals in Uganda. The trial protocol and methods have previously been published[6] (trial protocol in the Supplement) and the trial was registered (clinicaltrials.gov NCT02100865). The trial was designed to demonstrate noninferiority of solar-powered oxygen delivery relative to oxygen cylinders, using a clinically meaningful end point, length of hospital stay, expressed as a continuous variable using the date and hour of admission and discharge, using a noninferiority margin of 1 day. The study was reviewed and approved by the Makerere University School of Biomedical Sciences Research Ethics Committee (REC Protocol SBS 139), the Uganda National Council on Science and Technology (Ref SS 3331), and the University Health Network Research Ethics Committee, Toronto, Canada (UHN REB No. 13-6168-AE). Parents of all patients provided written informed consent for participation in the study.

Table. Baseline Characteristics of the 2 Treatment Groups

Characteristic	Children, No. (%)	
	Solar-Powered Oxygen (n = 65)	Cylinder Oxygen (N = 65)
Female sex	27 (42)	32 (49)
Age, median (IQR), mo	10 (3-19)	10 (1-22)
Clinical features at enrollment		
Cough	53 (82)	51 (78)
Difficulty breathing	58 (89)	56 (86)
Unable to drink or feed	25 (38)	28 (43)
Results of clinical examination at enrollment		
Weight, median (IQR), kg	8.0 (5.0-10)	7.0 (4.3-10)
Underweight[a]	9 (14)	9 (14)
Oxygen saturation, median (IQR), %	83 (72-87)	84 (76-87)
Respiratory rate, median (IQR), min^{-1}	68 (54-78)	66 (48-80)
Tachypnea[b]	48 (74)	47 (72)
Pulse rate, median (IQR), min^{-1}	160 (145-176)	158 (146-178)
Tachycardia[c]	33 (51)	34 (52)
Temperature, median (IQR), °C	37.6 (36.6-38.5)	37.3 (36.9-38.3)
Fever[d]	26 (40)	34 (52)
Intercostal retractions	44 (68)	47 (72)
Subcostal retractions	52 (80)	41 (63)
Diagnoses at admission		
Severe pneumonia or very severe disease	65 (100)	65 (100)
HIV	1/59 (2)	2/55 (4)
Malaria[e]	5 (8)	4 (6)
Radiographic findings		
Alveolar consolidation	12/54 (22)	12/55 (22)
Other infiltrate	25/54 (46)	26/55 (47)
No consolidation, infiltrate or effusion	16/54 (30)	18/55 (33)

Abbreviation: IQR, interquartile range.

[a] Weight for age less than first percentile on World Health Organization growth charts.

[b] Respiratory rate greater than 99th percentile for age.

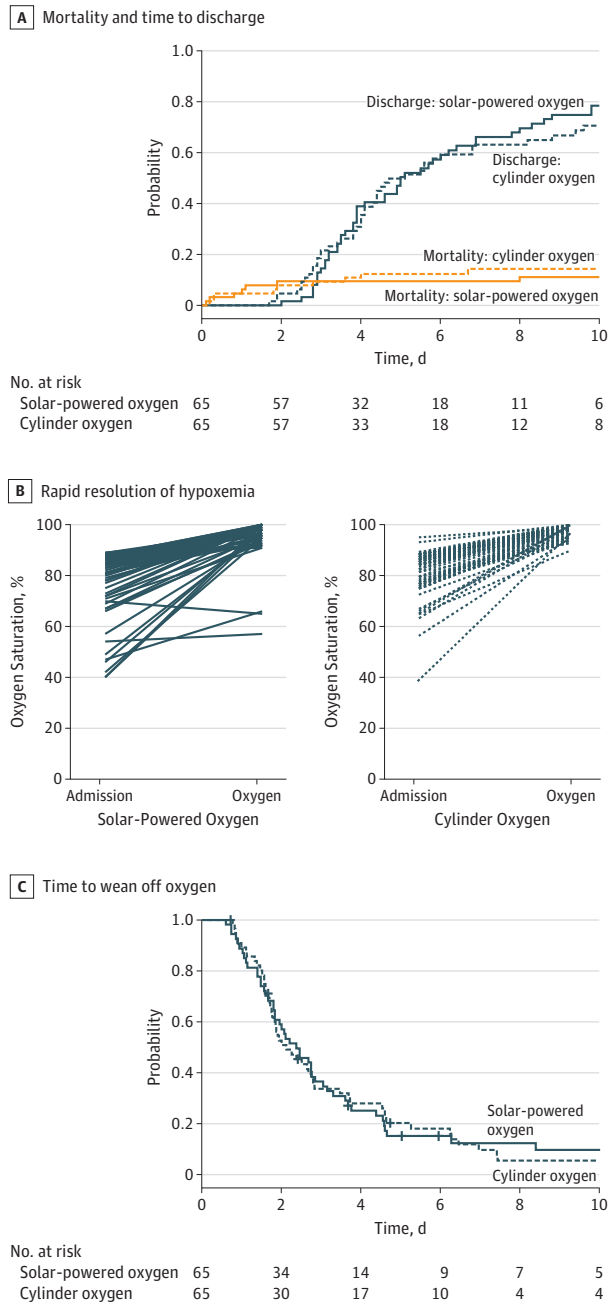
[c] Pulse rate greater than 99th percentile for age.

[d] Axillary temperature greater than 37.5°C.

[e] All children were tested for malaria using rapid diagnostic test (histidine-rich protein–2 antigen) and/or light microscopy of Field-stained peripheral blood film.

Results | A total of 130 children (59 girls [45.4%] and 71 boys [54.6%]; mean [SD] age, 16 [22] months) were enrolled between March 29, 2014, and May 13, 2015; of these, 65 (50.0%) were assigned to solar-powered oxygen delivery and 65 to cylinder oxygen. Baseline characteristics were similar between groups (**Table**). The median length of hospital stay was

Figure. Mortality, Time to Hospital Discharge, Rapid Resolution of Hypoxemia, and Time to Wean Off Oxygen Among Trial Participants



A, Mortality and time to hospital discharge among trial participants. Mortality (orange lines) and hospital discharge (blue lines) in the solar-powered oxygen delivery group (solid lines) and cylinder oxygen comparator group (dashed lines) are modeled as competing risks. Differences between treatment arms were not statistically significantly different for mortality or time to hospital discharge. B, Rapid resolution of hypoxemia among trial participants. Immediate improvements in oxygen saturation were observed in both trial arms after administration of oxygen therapy, with no difference between patients receiving solar-powered oxygen (median change, 15% [interquartile range, 12%-21%]) and cylinder oxygen (median change, 15% [interquartile range, 11%-23%]). C, Time to wean off oxygen among trial participants. The median duration of oxygen therapy was similar in patients receiving solar-powered oxygen (2.6 days [interquartile range, 1.6-4.0 days]) and cylinder oxygen (2.1 days [interquartile range, 1.7-4.9 days]). A standardized protocol for stopping oxygen therapy was observed.

4.1 days (interquartile range, 2.9-5.6 days) in the solar-powered oxygen delivery group and 4.5 days (interquartile range, 3.3-6.9 days) in the cylinder oxygen group; the difference of medians was -0.41 days (95% CI, -1.2 to 0.43), meeting the prespecified criterion for noninferiority. In-hospital mortality was similar between groups: 11 patients (17%) in the solar-powered oxygen delivery group vs 8 patients (12%) in the cylinder oxygen group (risk difference, 4.6%; 95% CI, -7.8% to 17%). In a competing risk analysis with in-hospital mortality and hospital discharge as competing events, the time to discharge and mortality were not statistically different between groups (**Figure**, A). The increase in peripheral blood oxygen saturation (Figure, B), and the time to wean off oxygen were similar (Figure, C). Adverse events were similar in both groups.

Five episodes of battery depletion involving 7 patients required recharging the batteries of the solar-powered oxygen system using the hydroelectric grid or switching patients to the backup oxygen supply. Conversely, 4 patients randomized to receive cylinder oxygen were switched to the backup oxygen supply when cylinders stocks were depleted, despite our best efforts to maintain adequate stocks of cylinders.

Discussion | Solar-powered oxygen delivery is noninferior to standard oxygen delivery using cylinders among African children hospitalized with hypoxemic illness. This technological innovation may be suitable for low-resource hospitals with pediatric inpatient services where the supply chain of cylinders and electrical power are not reliable. Solar-powered oxygen delivery addresses a critical gap in access to oxygen and has the potential for global consequences, given the magnitude of childhood pneumonia deaths, currently estimated at 900 000 per year.[1]

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Incidence of 4 Lysosomal Storage Disorders From 4 Years of Newborn Screening

Newborn screening is recognized as a highly effective public health program to detect certain diseases before detrimental long-term health consequences occur. With advances in screening technologies and therapeutic options becoming available, the US Department of Health and Human Services recently added 2 lysosomal storage disorders (LSDs), Pompe disease and mucopolysaccharidosis I (MPS I), to the Recommended Uniform Screening Panel.[1] In addition, several states have legislative mandates to screen for other LSDs not on the Recommended Uniform Screening Panel. The Missouri State Public Health Laboratory has used a fluorimetric enzyme activity test on a digital microfluidic platform to screen all samples from newborns that were received since January 11, 2013, for Pompe, MPS I, Gaucher, and Fabry disorders.[2] We herein present our findings on incidence rates for these LSDs from 4 years of full-population testing. These results represent, to our knowledge, the longest prospective, unblinded, full-population testing and follow-up for these LSDs in the United States.

Methods | Enzyme activity for acid α-glucosidase deficiency (Pompe disease), acid α-galactosidase deficiency (Fabry disease), acid β-glucocerebrosidase deficiency (Gaucher disease), and acid α-L-iduronidase deficiency (MPS I) was measured from dried blood spots using a fluorescence enzyme assay on the digital microfluidic platform (Baebies, Inc) as previously described.[2,3] Missouri newborn specimens received for screening from January 11, 2013, through January 10, 2017, were tested; approximately 308 000 newborns were screened. All 4 LSDs were screened simultaneously from a single newborn dried blood spot sample. Samples with positive findings (with mean triplicate screening values breaching referral cutoff limits for 1 of the LSDs) were referred to 1 of 4 state-contracted genetic referral centers for confirmatory testing and follow-up. The Department of Health and Senior Services received approval from the Institutional Review Board Committee after a full review to waive informed parental consent for the LSD implementation. Missouri had a legislative mandate to screen for LSDs and full population screening would be conducted on every infant equally with referral of positive screening results to our contracted genetic referral centers for follow-up confirmatory testing and treatment if needed.

Results | We identified 133 newborns who were confirmed through diagnostic testing results to have 1 of the 4 LSDs (**Table**), including 32 with Pompe disease (8 infantile and 24 late-onset), 5 with Gaucher disease, 94 with Fabry disease, and 2 with MPS I. An additional 19 infants were confirmed to have genotypes of unknown significance or onset. These infants need continual follow-up to monitor for potential late-onset disorders. The Table also includes the number of newborns identified with pseudodeficiency, as carriers, or with false-positive findings (confirmatory enzyme activity was in the reference range, and no DNA testing was conducted). False-positive rates ([pseudodeficient + carrier + false-positive findings]/total number screened), incidence rates (confirmed disorder/total number screened), and positive predictive values ([confirmed disorders + genotypes of unknown significance]/number with positive screen results) were also calculated.

Discussion | We report findings from, to our knowledge, the longest unblinded, full-population, prospective study of 4 LSDs in the United States. Although many pilot studies have been performed on blinded samples, Taiwan has the only other collection of newborn screening programs worldwide that has performed population screening for Pompe and Fabry diseases with clinical follow-up for a longer period.[4] Incidence rates for Pompe and Fabry diseases in Missouri are similar to those reported in Taiwan, whereas the false-positive rates in Missouri are lower and positive predictive values are higher.[4] Incidence rates for Pompe and Fabry disease in Missouri are also higher than recently published rates in Illinois.[5] The incidence rates for Gaucher disease and MPS I are similar to those previously reported in other pilot studies.[4,5] Rates of pseudodeficiency and genotypes of unknown significance for Pompe disease and MPS I are similar to published rates in Illinois.[5] False-positive rates compare well with other newborn screening assays currently performed in Missouri. Missouri State Public Health Laboratory