Indian Academy of Pediatrics (IAP)

nRICH

Newer **R**esearch and recommendations **I**n **C**hild **H**ealth

Lead Author
Arun Bansal

UNDER THE AUSPICES OF THE IAP ACTION PLAN 2023

Upendra Kinjawadekar
IAP President 2023

GV Basavaraja
IAP President 2024

Remesh Kumar R
IAP President 2022

Vineet Saxena
IAP HSG 2022-23

Dear fellow IAPans,

nRICH

Newer **R**esearch and recommendations **I**n **C**hild **H**ealth-aims to bring you the abstracts of some of the breakthrough developments in pediatrics, carefully selected from reputed journals published worldwide.

Expert commentaries will evaluate the importance and relevance of the article and discuss its application in Indian settings. nRICH will cover all the different subspecialities of pediatrics from neonatology, gastroenterology, hematology, adolescent medicine, allergy and immunology, to urology, neurology,vaccinology etc. Each issue will begin with a concise abstract and will represent the main points and ideas found in the originals. It will then be followed by the thoughtful and erudite commentary of Indian experts from various subspecialties who will give an insight on way to read and analyze these articles.

I'm sure students, practitioners and all those interested in knowing about the latest research and recommendations in child health will be immensely benefitted by this endeavor which will be published online on every Monday.

Happy reading!

Upendra Kinjawadekar
National President 2023
Indian Academy of Pediatrics

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Upendra Kinjawadekar

Convenor

Vijay Yewale

IAP nRICH team

Arun Bansal

Vaman Khadilkar

Indu Khosla

Srinivas Murki

Nitin K Shah

Tanu Singhal

Rhishikesh Thakre

Prakash Vaidya

SK Yachha

Arun Wadhwa

Nitin Shah

Randomised controlled trial of oxygen therapy and high-flow nasal therapy in African children with pneumonia

Arun Bansal

Professor, Pediatric Emergency and Intensive Care, PGIMER, Chandigarh, India.

BASED ON ARTICLE

Maitland K, Kiguli S, Olupot-Olupot P, Hamaluba M, Thomas K, Alaroker F, Opoka RO, Tagoola A, Bandika V, Mpoya A, Mnjella H, Nabawanuka E, Okiror W, Nakuya M, Aromut D, Engoru C, Oguda E, Williams TN, Fraser JF, Harrison DA, Rowan K; COAST trial group. Intensive Care Med. 2021 May;47(5):566-576. doi: 10.1007/s00134-021-06385-3.

ABSTRACT

Purpose: The role of oxygen therapy in saving the lives of African children with severe pneumonia is not yet established.

Methods: The open-label fractional-factorial COAST trial randomised eligible Ugandan and Kenyan children with severe pneumonia and severe hypoxaemia stratum (SpO2 80%) to high-flow nasal therapy (HFNT) or low-flow oxygen (LFO: standard care), and hypoxaemia stratum (SpO2 80–91%) to HFNT or LFO (liberal strategies) or permissive hypoxaemia (ratio 1:1:2). Excluded were children with cyanotic heart disease, chronic lung disease, or > three-hours of oxygen administration. The primary endpoint was mortality at 48-hours; secondary endpoints included mortality at 28-days or neurocognitive sequelae.

The trial was terminated early after enrolling 1852/4200 children, including 388 in the severe hypoxaemia stratum (median age 7-months; median SpO2 75%) randomised to HFNT (n = 194) or LFO (n = 194) and 1454 in the hypoxaemia stratum (median age 9-months; median SpO2 88%) randomised to HFNT (n= 363) vs LFO (n= 364) vs permissive hypoxaemia. Per protocol 15% of patients in the permissive hypoxaemia group received oxygen (when SpO2 < 80%). In the severe hypoxaemia stratum, the 48-h mortality rates for HFNT and LFO were 9.3% and 13.3%, respectively. In the hypoxaemia stratum, the 48-h mortality rate for HFNT was 1.1% compared to 2.5% for LFO and 1.4% for permissive hypoxaemia. In the hypoxaemia stratum, the adjusted OR for 48-hour mortality in the liberal versus permissive comparison was 1.16 (0.49–2.74; p = 0.73); the adjusted OR for HFNT versus LFO was 0.60 (0.33–1.04; p = 0.08). The 28-day mortality rates for each stratum were 18.6%, 23.4%, 3.3%, 4.1%, and 3.9%, respectively. Neurocognitive sequelae were rare.

Conclusions: Respiratory support with HFNT showing potential benefit should prompt further trials.

SUMMARY

Background: The availability of oxygen therapy varies, and many hospitals provide little or no oxygen therapy to children with severe pneumonia. The World Health Organization (WHO) currently recommends that children with severe pneumonia or SpO2 < 90% receive oxygen therapy. There is currently little evidence to back up this practise. The objective of the Children's Oxygen Administration Strategies Trial (COAST) was to examine the effect of various oxygen therapy strategies on children with severe pneumonia.

About the study: COAST was a multicenter, open, fractional factorial, two-stratum randomised controlled trial conducted in four Ugandan and two Kenyan hospitals. Children older than 28 days with severe pneumonia and severe hypoxaemia (SpO2 80%) were randomised to HFNT or LFO (standard care), and hypoxaemia stratum (SpO2 80–91%) to HFNT or LFO (liberal strategies) or permissive hypoxaemia (ratio 1:1:2). Children with cyanotic heart disease, chronic lung disease, or those receiving oxygen for more than three hours were excluded. The primary endpoint was mortality at 48 hours; secondary endpoints included neurocognitive sequelae or mortality at 28 days. 1,842 eligible children were enrolled into the COAST trial. In comparison to the hypoxaemia arm of the study, patients in the severe hypoxaemia arm were younger (7 months vs. 9 months), had a lower median weight, and had a higher incidence of cyanosis. A greater proportion of LFO patients (60%) were in the severe hypoxaemia stratum compared to HFNT patients (55%) at baseline. In addition, 14.9% of LFO patients compared to 9.8% of HFNT patients were severely malnourished. Hypothermia, dehydration, and unresponsiveness were more prevalent in the LFO arm than in the HFNT arm. HFNT was delivered via AIRVO2 device. HFNT was initiated at 21% with oxygen and flow rates titrated according to a protocol. LFO was administered via nasal cannulae/prongs, with higher flow rates administered via standard masks. Children with oxygen saturations between 80 and 91% were permitted to have permissive hypoxaemia in the hypoxaemia stratum. If O2 saturation levels in the hypoxemia stratum fell below 80%, low-flow oxygen was administered. Children who could not tolerate HFNT have been switched to LFO. From 2 hours after enrolment, oxygen was weaned/stopped if SpO2 on room air remained 92% and restarted if SpO2 dropped to 92%. At 48 hours after enrolment, HFNT children were switched to LFO. Unfortunately, the trial was unable to recruit the predetermined target of 4200 children with acute illness. The Trial Steering Committee prematurely terminated the study due to ethical concerns in Uganda regarding the permissive hypoxaemia strategy. However, the analysis of the 1,842 enrolled children provides valuable information. In the severe hypoxaemia stratum, mortality at 48 hours was 9.3% for HFNT and 13.4% for LFO, with an aOR of 0.60 (95% CI 0.33-1.00; p=0.076). Mortality at 28 days was 18.6% versus 23.4%. Importantly, the observed deaths in the trial's less severe stratum (SpO2 80-92%; observed mortality, 23/1,454; 1.6%; expected mortality, 9%) were significantly lower than expected. The fact that the mortality rate in the group with permissive hypoxaemia was identical to that of the group receiving low-flow oxygen was perhaps the most surprising finding in this stratum. This finding has significant implications for the utilisation of oxygen, a scarce resource in settings with limited resources. Only 15% of children in the permissive hypoxaemia group required a dose increase.

What does this study highlight: This study recommends the use of high-flow nasal therapy, if available, to reduce mortality in African children with severe pneumonia and a SpO2 of less than 80%. This contradicts the standard practise of targeting 92-96% O2 saturations in the majority of children with pneumonia and suggests that a permissive hypoxaemia strategy of tolerating O2 sats between 80-92% may be safe. The study's strengths include its pragmatic, well-designed approach to answering an important clinical question, its patient-centered outcomes, and its excellent randomization and minimal protocol deviations. After 28 days, subject retention was 99.3 percent. In both the severe hypoxaemia and hypoxaemia strata, the mortality rate at 48 hours was significantly lower than anticipated. The authors hypothesised that this was due to an increase in childhood vaccination rates, which decreased the incidence of bacterial pneumonia. A major limitation of the study is that it was not possible to fully assess the effect of the permissive hypoxemia strategy or the impact of HFNT in severe hypoxaemia due to its premature termination. The open label design, which prevented blinding of treating physicians and nurses, may have introduced bias.

What is the way forward? The findings of this study support the need for similar trials in the future, especially in settings with limited resources. Many children with pneumonia-caused hypoxia may experience clinical improvement with humidified, high-flow air alone; this warrants further study.