Indian Academy of Pediatrics (IAP)

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

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UNDER THE AUSPICES OF THE IAP ACTION PLAN 2023

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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!

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Effect of Early High-Flow Nasal Oxygen vs Standard Oxygen Therapy on Length of Hospital Stay in Hospitalized Children With Acute Hypoxemic Respiratory Failure

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BASED ON ARTICLE

Effect of Early High-Flow Nasal Oxygen vs Standard Oxygen Therapy on Length of Hospital Stay in Hospitalized Children With Acute Hypoxemic Respiratory Failure: The PARIS-2 Randomized Clinical Trial. Franklin D, Babl FE, George S, et al. JAMA. 2023;329(3):224–234. doi:10.1001/jama.2022.21805

ABSTRACT

OBJECTIVE To determine the effect of early high-flow oxygen therapy vs standard oxygen therapy in children with acute hypoxemic respiratory failure.

DESIGN, SETTING, AND PARTICIPANTS A multicenter, randomized clinical trial was conducted at 14 metropolitan and tertiary hospitals in Australia and New Zealand, including 1567 children aged 1 to 4 years (randomized between December 18, 2017, and March 18, 2020) requiring hospital admission for acute hypoxemic respiratory failure. The last participant follow-up was completed on March 22, 2020.

INTERVENTIONS Enrolled children were randomly allocated 1:1 to high-flow oxygen therapy (n = 753) or standard oxygen therapy (n = 764). The type of oxygen therapy could not be masked, but the investigators remained blinded until the outcome data were locked.

MAIN OUTCOMES AND MEASURES The primary outcome was length of hospital stay with the hypothesis that high-flow oxygen therapy reduces length of stay. There were 9 secondary outcomes, including length of oxygen therapy and admission to the intensive care unit. Children were analyzed according to their randomization group.

RESULTS Of the 1567 children who were randomized, 1517 (97%) were included in the primary analysis (median age, 1.9 years [IQR, 1.4-3.0 years]; 732 [46.7%] were female) and all children completed the trial. The length of hospital stay was significantly longer in the high-flow oxygen group with a median of 1.77 days (IQR, 1.03-2.80 days) vs 1.50 days (IQR, 0.85-2.44 days) in the standard oxygen group (adjusted hazard ratio, 0.83 [95%CI, 0.75-0.92]; P < .001). Of the 9 prespecified secondary outcomes, 4 showed no significant difference. The median length of oxygen therapy was 1.07 days (IQR, 0.50-2.06 days) in the high-flow oxygen group vs 0.75 days (IQR, 0.35-1.61 days) in the standard oxygen therapy group (adjusted hazard ratio, 0.78 [95%CI, 0.70-0.86]). In the high-flow oxygen group, there were 94 admissions (12.5%) to the intensive care unit compared with 53 admissions (6.9%) in the standard oxygen group (adjusted odds ratio, 1.93 [95%CI, 1.35-2.75]). There was only 1 death and it occurred in the high-flow oxygen group.

CONCLUSIONS AND RELEVANCE Nasal high-flow oxygen used as the initial primary therapy in children aged 1 to 4 years with acute hypoxemic respiratory failure did not significantly reduce the length of hospital stay compared with standard oxygen therapy.

SUMMARY

Background: Respiratory infections continue to be one of the leading causes of hospitalisation for children under age 5. Certain of these conditions can result in acute hypoxemic respiratory failure. Historically, the only treatments available for these children were hospitalisation for observation or intubation and mechanical ventilation. In the early 2000s, the high-flow nasal cannula (HFNC) became a popular alternative to invasive ventilation. The indiscriminate use of HFNC can be detrimental to patients because it prolongs their hospital stay. Prior research has demonstrated that HFNC can reduce the rate of care escalation, but had no effect on admission to the intensive care unit (ICU) or length of stay. Therefore, the purpose of this study was to compare the effects of early high-flow oxygen therapy versus standard oxygen therapy in children with acute hypoxemic respiratory failure.

About the study: Children between one and four years old who presented to 14 emergency departments in Australia and New Zealand with acute hypoxemic respiratory failure and required hospitalisation. Exclusion criteria included craniofacial anomalies, upper airway obstruction, cyanotic heart disease, tracheostomies, apneas, immediate high-level care in the ICU, and the need for non-invasive or invasive mechanical ventilation. High flow oxygen was administered using the AIRVO-2 high-flow system at varying weight-based flow rates as compared to nasal cannula at 2L/min or face mask up to 8L/min. In order to maintain the desired oxygen saturations, the oxygen flow rate was reduced to its minimum level. The treating team decided to escalate treatment for children in the standard group who were unable to achieve the desired oxygen saturations. Reactive airway disease, pneumonia, pneumonitis, viral-induced wheeze, and bronchiolitis were the most common diagnoses. The primary outcome was hospital stay duration, defined as the time between randomization and hospital discharge or death. Secondary outcomes included the duration of oxygen therapy from the time of randomization, the length of hospital stay beginning with the patient's arrival in the ED, the proportion of children requiring a change in therapy on the general ward, the proportion of children requiring ICU admission or transfer to a hospital with a paediatric ICU, the proportion of children requiring escalation of care to non-invasive or invasive ventilation, adverse events, tolerance of intervention, and clinical triggers that warranted a change in that child's care. Randomization of 1,567 patients determined that 782 would receive high-flow oxygen and 785 would receive standard oxygen. After randomization, the primary outcome, length of hospital stay, was found to be significantly longer in children receiving HFNC than in those receiving standard oxygen (adjusted hazard ratio, 0.83 [95%CI, 0.75 to 0.92]; P .001). This difference was apparent when HFNC was compared to standard oxygen; however, it did not exist when comparing children with obstructive versus non-obstructive disease, wheezy versus non-wheezing children, or children stratified by age. Four of the nine secondary outcomes specified beforehand exhibited no significant difference. After randomization, the median duration of oxygen therapy was longer in the HFNC group (1.07 versus 0.75 days). Additionally, the HFNC group had a longer median length of stay in the ED and a longer median duration of oxygen therapy. Children in the HFNC group required a higher rate of transfer to the ICU. 18.5% of children receiving standardised oxygen were converted to high-flow oxygen, compared to

42.9% of children receiving high-flow oxygen. There were four adverse events noted. One death in the group receiving high-flow oxygen was unrelated to treatment. None of these occurrences could be linked to the interventions.

Strengths: This study is a pragmatic approach to test the efficacy of nasal high-flow therapy in children with acute hypoxemic respiratory failure. Because the study was conducted in a wide range of hospital settings, including regional, metropolitan, and tertiary hospitals, the findings will be highly generalizable. Due to the visual disparities between the two trial interventions, blinding of the intervention was not possible.

Limitations: The allotted oxygen therapy could not be blinded, which may have led to a bias in clinical decision-making to move from the allocated oxygen therapy to the alternate oxygen therapy. The proportion of children in the high flow oxygen group who were switched to standard oxygen was higher than the proportion of children in the standard oxygen group who were switched to high flow oxygen due to intolerance to high flow therapy. The study did not collect any clinical data during the weaning process.

What is the way forward? Data from this randomised controlled trial comparing standard oxygen therapy to HFNC oxygen therapy for acute hypoxemic respiratory failure revealed that children on HFNC spent more time in the hospital (1.77 days vs 1.5 days) and were admitted to the intensive care unit (ICU) more frequently than children on standard oxygen therapy. We are unsure how much of a clinical difference 0.25 days will make in a real-world situation. It is unknown why HFNC children are frequently admitted to ICU, but the authors speculate that it may be due to an unconscious assumption that HFNC children are sicker than those on regular oxygen, resulting in a more cautious weaning plan. This makes sense given that one of the trial's flaws was the inability of clinical teams to remain blind to treatment allocation. When compared to standard oxygen therapy, nasal high-flow oxygen therapy used as the initial primary therapy in children aged 1 to 4 years with acute hypoxemic respiratory failure did not significantly reduce the length of hospital stay.