High-flow nasal oxygen therapy outside the intensive care unit

High-flow nasal oxygen (HFNO) therapy is the provision of a heated and humidified air/oxygen mixture at high flow rates via a large-bore nasal cannula.[1] By heating and humidifying the air/oxygen gas mixture, much higher flow rates of up to 60 L/min, as opposed to 15 L/min with conventional oxygen face masks, can be provided. The physiological benefits of HFNO are numerous and include washing out carbon dioxide from the naso- and oropharynx, decreasing the work of breathing, and improving mucociliary clearance. HFNO can provide a fraction of inspired oxygen (FiO_2) of up to 1.0 and generate a low level of positive end-expiratory pressure (PEEP) because of the high flow rates that are applied. From a patient point of view, the nasal interface is comfortable, which makes it acceptable even for claustrophobic patients to use for prolonged periods of time, compared with the tight-fitting face masks required with continuous positive airway pressure, bilevel positive airway pressure or non-invasive ventilation, which are often impeded by air leaks and skin injury. The clinical conditions and settings in which HFNO has been applied are diverse and include hypercapnic and hypoxaemic respiratory failure, pre-oxygenation before intubation and respiratory support after extubation, acute heart failure, bronchoscopic procedures, and the palliative management of patients with respiratory failure, where escalation to invasive mechanical ventilation is deemed futile.[2] A major benefit to healthcare institutions is the ease of use and scalability of HFNO, since minimal training is required to be proficient in its use and it can be provided anywhere in the hospital, even outside intensive care units (ICUs).

One of the conditions in which mechanical ventilation is still the mainstay of treatment, as opposed to HFNO, is acute respiratory distress syndrome (ARDS). ARDS is characterised by severe inflammation of the alveolar epithelial-capillary endothelial barrier caused by direct or indirect pulmonary injury, resulting in diffuse protein-rich interstitial and alveolar oedema, hyaline membrane formation, surfactant dysfunction and pulmonary microvascular thrombosis.[3] These pathophysiological changes lead to severe ventilation/perfusion mismatching, increased shunt fraction, increased dead-space ventilation, poor lung compliance and severe hypoxaemia. As per the Berlin definition,[4] ARDS is clinically recognised by new or worsening respiratory symptoms, bilateral pulmonary opacities, respiratory failure that is not fully explained by cardiac failure or fluid overload, and a partial pressure of arterial oxygen (PaO_2)/FiO_2 ratio ≤300 while providing a PEEP level of at least 5 cm H_2O. In resource-poor as well as non-ICU settings, the Kigali modification of the Berlin definition,[5] which uses a peripheral oxygen saturation/FiO_2 ratio ≤315 with no requirement for PEEP as a defining criterion for severe hypoxaemic respiratory failure, may be more practical. In view of the pathophysiological changes resulting in diffuse alveolar flooding, ARDS was traditionally considered to be a condition of poor lung compliance in which HFNO, which does not provide high levels of PEEP, would have a minor role.

Non-invasive means of providing oxygen increased substantially during the COVID-19 pandemic, when ICU resources were completely overwhelmed by patients with severe acute hypoxaemic respiratory failure (AHRF). HFNO was extensively used outside the ICU in South Africa (SA). A previous study from Western Cape Province in SA reported on the utility and feasibility of HFNO therapy in patients with severe COVID-19.[6] In the current issue of *AJTCCM*, Audley *et al*.[7] add to the body of knowledge by reporting on the outcomes in 744 patients with severe COVID-19 who were managed with HFNO during the first and third waves of the pandemic. These were patients with severe AHRF, with median PaO_2/FiO_2 ratios of 57.9 and 64.3 mmHg during the first and third waves, respectively, who were managed in high-care wards. HFNO failed in 58.5% and 49.7% of the patients died, with no differences in outcomes observed between the first and third waves. The authors conclude that despite significant differences in patient age, comorbidities and healthcare personnel experience with HFNO, there were no differences in outcomes between the waves. New insights into subgroups of ARDS may partly explain why HFNO is more beneficial in some patients with severe AHRF than in others. Studies using chest computed tomography (CT) images of patients with ARDS during the COVID-19 pandemic assisted in categorising patients into different phenotypes: those with focal patchy areas of consolidation with high lung compliance and limited recruitable lung, and those with bilateral dependent pulmonary consolidation, low lung compliance and potentially more recruitable lung.[8] From a clinical point of view, it is often difficult to recognise these phenotypes at the bedside without resorting to special investigations such as CT or electrical impedance tomography, but the different phenotypes may partly explain the efficacy of HFNO in approximately half of patients with severe COVID-19 and ARDS.

A remaining question is why patients who failed HFNO died despite escalation to mechanical ventilation. There may be several reasons, but one possibility could be that positive-pressure ventilation in an already inflamed lung worsens lung damage by means of ventilator-induced lung injury, despite applying lung-protective ventilation strategies, thereby resulting in poor outcomes in ventilated patients. Another possibility is that a delay in timeously recognising failure of HFNO to decrease the work of breathing within the first few hours of application may worsen alveolar inflammation by increased negative pleural and thereby transpulmonary pressures, thus contributing to patient self-inflicted lung injury. Failing to recognise and act on a lack in clinical improvement timeously makes HFNO a double-edged sword. The expanding array of conditions for which HFNO has been found to be beneficial opens the possibility of managing more and more patients with severe hypoxaemic respiratory failure outside the ICU, such as in high-care or even general wards. The challenge, however, is that failure to monitor patients on HFNO adequately may result in a delay in timeous intubation and mechanical ventilation, thereby worsening outcomes. It is important for clinicians practising in settings with scarce ICU resources to be well versed and comfortable in using non-invasive means such as HFNO for managing AHRF. We should, however, remain vigilant and beware of becoming complacent in our monitoring of patients while they are on HFNO, since a delay in escalating care can have detrimental outcomes for patients and give HFNO a bad reputation. A trial of HFNO in patients with severe AHRF to assess

for a response to treatment makes sense; however, a very low threshold for intubation and mechanical ventilation should be maintained for patients who fail to respond to HFNO within the first few hours.

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1. Nishimura M. High-flow nasal cannula oxygen therapy in adults. J Intensive Care 2015;3(1):15. https://doi.org/10.1186/s40560-015-0084-5
2. Nishimura M. High-flow nasal cannula oxygen therapy in adults: Physiological benefits, indication, clinical benefits, and adverse effects. Respir Care 2016;61(4):529-541. https://doi.org/10.4187/respcare.04577
3. Bos LDJ, Ware LB. Acute respiratory distress syndrome: Causes, pathophysiology, and phenotypes. Lancet 2022;400(10358):1145-1156. https://doi.org/10.1016/S0140-6736(22)01485-4
4. Ferguson ND, Fan E, Camporota L, et al. The Berlin definition of ARDS: An expanded rationale, justification, and supplementary material. Intensive Care Med 2012;38(10):1753-1582. https://doi.org/10.1007/s00134-012-2682-1
5. Riviello ED, Kiviri W, Twagirumugabe T, et al. Hospital incidence and outcomes of the acute respiratory distress syndrome using the Kigali modification of the Berlin definition. Am J Respir Crit Care Med 2016;193(1):52-59. https://doi.org/10.1164/rccm.201503-0584OC
6. Calligaro GL, Lalla U, Audley G, et al. The utility of high-flow nasal oxygen for severe COVID-19 pneumonia in a resource-constrained setting: A multi-centre prospective observational study. EClinicalMedicine 2020;28:100570. https://doi.org/10.1016/j.eclinm.2020.100570
7. Audley G, Raubenheimer P, Symons G, et al. High-flow nasal oxygen in resource-constrained, non-intensive, high-care wards for COVID-19 acute hypoxaemic respiratory failure: Comparing outcomes of the first v. third waves in South Africa. Afr J Thorac Crit Care Med 2023;30(1):e1151. https://doi.org/10.7196/AJTCCM.2023.v30i1.1151
8. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? Crit Care 2020;24(1):154. https://doi.org/10.1186/s13054-020-02880-z

Afr J Thoracic Crit Care Med 2024;30(1):e151. https://doi.org/10.7196/AJTCCM.2024.v30i1.151