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Sara Auld, Emory University
Mark Caridi-Scheible, Emory University

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Delivering care from an unstable evidence base: the evolving care of COVID-19 through the lens of high-flow nasal oxygen

Sara C. Auld, MD, MSc1,2,3, Mark Caridi-Scheible, MD1,4
1Emory Critical Care Center (ECCC), Atlanta, GA
2Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, Department of Medicine, Emory University School of Medicine, Atlanta, GA
3Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA
4Department of Anesthesiology, Emory University School of Medicine, Atlanta, GA

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On March 6, 2020, the first patient diagnosed with COVID-19 at our institution was admitted to the Emory Serious Communicable Disease Unit (SCDU), which was initially established for the care of patients with Ebola and other special pathogens. The demand for ICU beds quickly outstripped the SCDU capacity: within days we converted ordinary ICUs to receive the influx of COVID patients. Our teams struggled with fear, anxiety, and uncertainty about our safety and that of our families. We struggled much more wondering about the best care for our patients.

Our institutional guidelines initially recommended against the use of both non-invasive positive pressure ventilation (NIPPV) and high-flow nasal oxygen, also referred to as heated high-flow nasal cannula and high-flow nasal cannula. This recommendation emerged from a desire to avoid unnecessary staff exposure to aerosolized viral particles. Global guidance in March, 2020 similarly cautioned against high-flow nasal oxygen, out of concern for limited efficacy and high failure rates.[1] During those early weeks, patients under our care who remained hypoxemic or tachypneic despite a 100% non-rebreather mask were promptly intubated. As believers in the robust data supporting the use of high-flow nasal oxygen who have been using it as part of our armamentarium to care for patients in the last several years, [2, 3] we could not dismiss our nagging doubt that we may have been doing a disservice to our patients by withholding this modality. Upon further review of evidence demonstrating minimal additional air dispersion as compared to traditional face masks,[4] our institutional guidelines were relaxed on March 25, 2020 to allow for the use of high-flow nasal oxygen.
It was at this time that we initially were assigned to review, ‘High flow nasal oxygen in COVID-19 patients with acute hypoxemic respiratory failure: A multi-center, retrospective cohort study,’ by Xia and colleagues [5]. They reported their experience caring for 43 patients with COVID-19 who were treated with high-flow nasal oxygen at three tertiary-care hospitals in Wuhan, China in the earliest days of the outbreak. Just under half of patients in their cohort failed high-flow nasal oxygen, requiring escalation to either non-invasive or invasive mechanical ventilation. Patients who failed were older, more commonly male, and had a lower oxygen saturation on admission. They were also more likely to have an increase in their respiratory rate and a decrease in their ROX index (ratio of oxygenation = [SpO₂/FiO₂]/RR) after initiation of high-flow nasal oxygen. As has been reported in other settings (6), patients with failure of high-flow nasal oxygen had a high mortality rate (65%), whereas no patients died among those who did not require escalation of their respiratory support. While this was not a randomized trial of high-flow nasal oxygen use, it offers some reassurance to providers that there is a role for this modality in the treatment of COVID-19 and identifies clinical risk factors for treatment failure.

The early experience of Xia and colleagues from Wuhan felt like a life-line in March, when the manuscript first reached our hands. Several months later, many of us have cared for our own patients with COVID-19 and these early data no longer feel novel. Yet it is important that they are published and read. In reviewing and publishing this report, the editors have faced the “challenge of discerning signal amidst noise,” steadily walking the fine line between expediting critical reporting and ensuring a thorough and comprehensive review process (7).

Surprisingly, there are few data to guide our use of high-flow nasal oxygen in COVID-19. As of July 9, 2020, a search of the terms “high-flow nasal oxygen” and “high-flow nasal cannula” on LitCovid, a curated hub of articles related to COVID-19 in PubMed, revealed 37 articles written in English, out of more than 30,603 total articles. Thirteen of those articles were reviews or guidelines, three reported on the use of high-flow nasal oxygen in periprocedural settings, ten were observational studies that reported the use of high-flow nasal oxygen in their cohorts but did not explicitly focus on the modality, eight were small case series of fewer than ten patients—leaving just three articles reporting on patient outcomes in the context of high-flow nasal oxygen use, two of which examined the use of high-flow nasal oxygen in conjunction with awake prone positioning (8–10). We found an additional pre-print manuscript reporting, similar to Xia and colleagues, that the ROX index was predictive of failure of high-flow nasal oxygen and the need for invasive mechanical ventilation, with greater mortality in the group that progressed to invasive mechanical ventilation (11).

The role for high-flow nasal oxygen in critically ill patients with COVID-19 remains unclear. While several reports have found that patients who received high-flow nasal oxygen had higher mortality than those who did not, these observational studies cannot account for confounding by indication, whereby the sickest patients would have been those most likely to receive high-flow nasal oxygen in the first place (9, 12). The same uncertainty holds for NIPPV. While there are hospitals that have used NIPPV in the care of patients with COVID-19 (13,14), (including a hospital in Singapore where 20 healthcare workers wore a...
simple surgical mask while caring for an NIPPV patient who was later found to have COVID-19—and none became ill (15), our institutional guidelines still recommend against non-invasive ventilation because of concern for aerosol generation with leakage around the face mask.

Anecdote is not evidence. Observations are not proof. The patient phenotypes and clinical trajectories are changing. Yet the continuing flow of COVID-19 patients demands that we choose treatment in the face of distressing uncertainty. So what can we do? We start with what we know—or at least what we think we know—about best practices for viral pneumonia, ARDS, and general critical care. Inevitably, some of our choices will eventually be proven “wrong.” It is for precisely this reason that reports such as that of Xia—and of our own (16)—must be written, reviewed, and published.

We started our COVID-19 response by consolidating current best practices in non-COVID critical care and management of respiratory failure into pragmatic guidelines. In ordinary circumstances, we would wait for evidence to accumulate and then modify our practice. History tells us that circumspection is ordinarily best: the history of critical care is littered with good intentions that were ineffective or frankly harmful (17). Prudence asserts equipoise, awaiting evidence that is large-scale, rigorous and undeniable. The onward global march of COVID-19 denies us this equipoise. The number of infected patients’ lives at stake grows ominously with every passing day. This is not business as usual. We cannot wait. They cannot wait.

How has our healthcare system moved forward? We have paid close attention to every patient’s evolution, assembled subject matter experts, formed working groups, shared and analyzed internal data, reviewed the emerging (albeit limited and imperfect) literature, and week by week (sometimes day by day) integrated that new knowledge into our institutional guidelines. When new avenues of uncertainty arose, from how to handle higher than normal rates of ventilator dyssynchronies to unprecedented rates of filter clotting for patients on continuous renal replacement therapy, we pivoted our efforts to assess, evaluate, and respond. We formed a microcosm, sharing observations, reviewing experience, and challenging our own logic and outcomes. We collated ideas and data, digested them, put them up for debate, and attempted to place them in perspective as we made changes in practice. Absent the sort of evidence that comes from randomized, controlled trials, we did the best we could with what we had.

Observational comparative studies like the one of high-flow nasal oxygen by Xia et al are reassuring. Each provides additional data in what remains a largely data-free zone, supporting cautious, ongoing changes in our practice. These small adjustments are slow moves towards perfect care. Increments are preferred to big changes in these parlous times. We understood that the Xia report was not a perfect study, that there was selection bias for administration of high-flow nasal oxygen, that the sample size was somewhat limited, among other potential critiques. Yet the Xia study informed our own decision to incorporate high-flow nasal oxygen into our care. While the Xia study did not provide a definitive answer to high-flow nasal oxygen use, it allowed us to take one more step towards rigorous practice. With publication of their peer-reviewed revised report, Xia and colleagues now
create more confidence for readers that high flow nasal oxygen is an appropriate choice for some patients with COVID-19.

Only nineteen weeks ago, we admitted our first COVID-19 patient. We have just admitted our 580th. She will receive more informed care that is shaped by local and global experience. Like Xia and colleagues, we have written, submitted, revised, and ultimately published in Critical Care Medicine. By continuing to submit our reports of experiences to peer-review, we—and the authors of the other 30,602 papers—join an invisible college. We do so in hope of informing the best care today, and of delivering even better care tomorrow.

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References


