High flow therapy in COVID-19 pneumonia

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High-flow therapy (HFT) is a non-invasive form of respiratory support that can lower the intubation rate and mortality in patients with acute hypoxemic respiratory failure (AHRF) (1). Driven by concerns about the exposure of healthcare workers, initial recommendations discouraged the use of HFT in COVID-19 patients (2, 3).

Takeaway messages

✓ Although initial recommendations discouraged the use of high flow therapy in COVID-19 patients, high mortality rates in mechanically ventilated patients resulted in its gradual implementation.

✓ HFT has been used in COVID-19 pneumonia related AHRF with favorable effects on oxygenation and evidence suggests it may decrease the need for mechanical ventilation and its duration.

✓ If appropriate personal protective equipment is used and cohorting precautions are taken, HFT may be applied in COVID-19 patients without leading to a measurable increase in COVID-19 infections in healthcare workers.

However, due to the high morbidity and mortality resulting from early invasive mechanical ventilation (4), the use of HFT was gradually implemented in patients with severe COVID-19 (5). This review looks at the evidence regarding the physiologic effects, the effect on outcomes, the risk of contamination, and the combination of prone positioning (PP) and HFT in patients with AHRF due to COVID-19 pneumonia.

Physiologic effects

The physiologic effects of HFT in acute hypoxemic respiratory failure are well-established, but there is no physiologic data specifically for COVID-19 pneumonia (6-8). HFT is less likely to allow the entrainment of room air during patient inspiration, ensuring more reliable delivery of high FiO2 levels. HFT increases the end-expiratory lung volume, thereby generating PEEP that is responsible for alveolar recruitment and hence reducing regional lung strain. These mechanisms improve oxygenation.

The washout of physiologic dead space by flushing expired air from the upper airway
during expiration improves ventilatory efficiency. HFT reduces the minute ventilation needed to obtain a physiologic arterial CO2 level by decreasing the respiratory rate and anatomical dead space. Therefore, the alveolar ventilation (minute ventilation minus dead-space ventilation) remains stable, whereas the minute ventilation decreases. HFT also reduces the patient’s inspiratory effort and lessens the metabolic work of breathing. Finally, HFT improves respiratory mechanics, i.e., dynamic compliance, transpulmonary pressure, and ventilation homogeneity, and enhances patient comfort and tolerance when compared with conventional oxygen.

Outcomes

In a retrospective observational study (9), intubation rate and mortality were compared between 233 (51%) patients receiving standard oxygen and 146 (39%) patients treated with HFT. The intubation rate was significantly reduced from 75% in the standard oxygen group to 56% in the HFT group. Mortality at day 28 was 30% in the standard oxygen group versus 21% in the HFT group.

A multicenter cohort study (10) compared treatment with HFT and early intubation in 122 patients (61 patients in each group). HFT was associated with an increase in ventilator-free days and a reduction in the ICU length of stay. No difference was observed in mortality; however, analysis showed that patients receiving early intubation had higher SOFA and APACHE II scores and were thus sicker at baseline.

These two studies suggest that COVID-19 patients may benefit from HFT by decreasing the need for mechanical ventilation and its duration, as well as decreasing the ICU length of stay without having a negative impact on hospital mortality. However, there are no randomized controlled trials comparing outcomes in HFT patients with conventional oxygen or early intubation.

Three observational studies provide data from COVID-19 patients treated with HFT. Intubation rates were between 36% (11) and 63% (12), and the time to intubation between 10 h (12) and 2 days (13). Factors associated with successful outcomes with HFT were steroid treatment, low C-reactive protein or D-dimer levels, hypertension, and smoking (12, 13).

Monitoring

Data has shown that patients in whom HFT succeeded had a lower respiratory rate after HFT initiation than those patients who subsequently needed intubation (13-15). In a monocentric prospective observational study, the best cut-off value was 26 breaths per minute after 30 minutes of HFT (15).

The ROX (Respiratory rate-OXygenation) index is calculated from the respiratory variables that assess respiratory failure and can thus be used to predict the need for invasive
ventilation. It represents the ratio of SpO2/FiO2 to RR. In acute hypoxemic respiratory failure due to non-COVID-19 pneumonia, the ROX index identified patients at low risk of HFT failure with a cut-off value of 4.88 measured after 12 hours of HFT (16). In COVID-19 patients, five retrospective studies (12, 14, 17-19) showed that patients with a successful outcome had a higher ROX index, but the cut-off point for values associated with success varied between 5.55 after 6 hours (17) 3.67 after 12 hours (18).

**Contamination**

The majority of studies on HFT in COVID-19 are either experimental or carried out on healthy subjects and therefore do not reflect real life. The World Health Organization commissioned reviews to examine the evidence on the use of HFT: Six simulation studies and one crossover study on non-COVID-19 patients were analyzed; HFT did not increase the risk of aerosol dispersion in comparison to typical patient breathing with violent exhalation; aerosol production levels and particle number concentrations found with HFT were similar to those with nasal prongs, non-rebreather masks, and spontaneous breathing (20). HFT with a surgical mask on the patient’s face could thus be a reasonable practice that may benefit hypoxemic COVID-19 patients (21).

Half of the environmental swab samples taken from the isolation room of a COVID-19 patient receiving HFT and non-invasive ventilation (NIV) showed positive results. However, all air samples were negative. Viable viruses were identified on one quarter of the sites. These findings highlight the need for use of personal protective equipment (22).

The incidence of COVID-19 infections before and after the implementation of HFT/NIV was measured in a US hospital. Results showed that use of HFT in a COVID-19 patient, when associated with the use of appropriate personal protective equipment and cohorting precautions, did not lead to a measurable increase in COVID-19 infections in healthcare workers (23).

**HFT combined with prone positioning**

Awake PP may improve the mismatch of ventilation-perfusion and open the atelectatic lungs by means of adequate sputum drainage. Two descriptive studies reported data from COVID-19 patients treated with HFT combined with PP. In the study of 10 patients (24), PaO2/FiO2 was higher after PP. PaCO2 increased, but remained under the physiologic values (hypocapnia is usually observed in spontaneously breathing COVID-19 patients). None of the patients required intubation. In the other study of nine patients (25), PP was applied twice daily with a median of 5 (3-8) procedures per subject. The median duration was 2 (1-4) hours. SaO2 and PaO2 increased after PP. PaCO2 decreased in the study, but patients were hypercapnic at the beginning. Two patients required intubation.

In a prospective multicenter, adjusted cohort study (26), 199 patients received HFT and 55 of these (28%) were pronated. The use of PP as an adjunctive therapy to HFT did not
reduce the risk of being intubated: 82 (41%) patients required intubation, 60 (41%) in the HFNO group and 22 (40%) in HFT + PP group. The time from HFT to intubation was longer in the HFT + PP. Mortality was not affected by the use of PP. In the HFT + PP group, there was a strong trend towards a delay in intubation of 2 days; mortality was similar in both groups. In this study however, PP was indicated by medical criteria and not applied uniformly. The authors were unable to determine whether clinicians had used PP as standard practice for COVID-19 patients or as a rescue strategy. PP was only considered for analysis if the duration was > 16 h/day and results could not be extended to patients pronated for shorter periods of time, but this did not suggest a worse prognosis in the case of delayed intubation.

**Conclusion**

HFT has been used in COVID-19 pneumonia related AHRF with favorable effects on oxygenation. Those patients who failed with HFT had a higher mortality rate because they were sicker at baseline. The ROX index may be used as a predictor of intubation, but the optimal cut-off is open to debate. If used with the appropriate protective equipment and precautions, HFT was shown not to increase contamination or infection of healthcare workers. The combination of HFT and PP requires further investigation.

Ventilators from Hamilton Medical offer high flow oxygen therapy as a standard or optional feature*. No additional device or ventilator is required and the therapy can be alternated with noninvasive ventilation as needed by changing the interface and simply switching modes. The HAMILTON-H900 humidifier now also offers a special high flow oxygen therapy mode with dedicated settings to support high flow oxygen therapy for all patient groups.

* Not available in all markets or on all ventilator models

**References**


