Review Article

Respiratory Support for Patients with COVID-19 Disease

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Abstract

Covid-19 disease is typified by respiratory symptoms. In severe cases respiratory failure occurs and must be carefully managed. Management can include supplementary oxygen therapy, non-invasive and invasive ventilation. In this article we describe the techniques shown to be effective in this patient group and highlight areas where future research is needed to guide the best.

Keywords: COVID-19, noninvasive ventilation, ventilation

Introduction

COVID-19 is the clinical disease caused by the novel coronavirus SARS-CoV-2. Infection is via the upper respiratory tract and those infected typically present with cough and fever which in severe cases develops into severe dyspnea and significant hypoxemia. The early phases of the pandemic health systems in China and Italy were reporting that 5%–35% of hospitalized patients required intensive care unit (ICU) admission, most commonly due to hypoxemic respiratory failure and up to 5% of all patients in the population diagnosed with COVID-19 would need ICU.[1] Around 5% of hospitalized patients developed acute respiratory distress syndrome (ARDS).[2]

Patients with respiratory failure will require support to promote recovery, from simple supplementary oxygen to more invasive techniques. In this article, we describe and evaluate the techniques which have been used so far to treat COVID-19.

Noninvasive Techniques

Supplementary oxygen

Oxygen is the key treatment in hypoxic respiratory failure and should be administered to all patients with arterial hypoxemia unless contraindicated. More than 75% of patients hospitalized with COVID-19 will require supplementary oxygen.

The World Health Organization currently recommends targeting an oxygen saturation >90%, or 92%–95% in pregnant patients.[3] The Surviving Sepsis Campaign guidelines recommend a maximum target saturation of 96% on the basis of concerns about harms of hyperoxia.[4] Both the recommendations are based on clinical research performed before the COVID-19 pandemic and their applicability is unknown. The "HOT-COVID" international randomized controlled trial currently in progress aims to provide a better guide to target arterial oxygen levels.[5]

High-flow nasal oxygen

In cases where oxygen supplementation via a simple face mask is insufficient to achieve therapeutic targets, high-flow nasal oxygen (HFNO) can be tried. This delivers heated humidified gas via a specially designed nasal cannula, typically at gas flows in excess of 60 L/min. The high gas flow creates positive pressure in the nasopharynx, reducing work of breathing. In a non-COVID-19 population, nasal high flow has been shown to reduce the need for intubation, but no mortality benefit has been demonstrated.[6] In patients with COVID-19, observational studies have shown that the treatment can improve arterial oxygenation, but no patient-centered outcomes have been studied.[7,8]

A significant concern around the use of HFNO was the risk of infection to health workers from aerosolization of virus-containing droplets. This concern has not been borne out

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by laboratory[9] or clinical[7,8] studies and the risk of infection would seem to be negligible.

Continuous positive airway pressure

Continuous positive airway pressure (CPAP) uses either a facemask or hood interface to generate positive pressure in the airways. This can improve oxygenation by opening collapsed alveoli and increasing mean alveolar pressure. Early guidance expressed concern about the use of CPAP as the patient becomes increasingly breathless due to concern about the phenomenon of patient self-induced lung injury.[10,11] This phenomenon was postulated to occur when rapid and vigorous spontaneous respiratory effort leads to high transpulmonary pressures and resultant lung damage. Experience has shown that this does not occur in many patients and the concern was probably exaggerated. CPAP has proven useful to avoid invasive ventilation; one case series showed over half of patients treated with CPAP avoided mechanical ventilation with no deleterious effect on outcome.[12] The RECOVERY-RS randomized controlled trial is currently recruiting and aims to show whether this avoidance of intubation translates into a mortality benefit.[13]

One significant advantage of using noninvasive CPAP is that this treatment can be safely delivered outside of a critical care environment, preserving scarce resource for those patients who need immediate intubation. It is important, however, to have a clear mechanism for transfer of patients who do not respond to CPAP to intensive care when appropriate.

Similar concerns as for HFNO have been expressed about the role of CPAP in spreading viral infection to health-care staff. No evidence has been found of higher infection rates in staff groups looking after patients on CPAP therapy and so it is likely that this risk has been overstated.

One major concern with the use of both HFNO and CPAP is the level of oxygen consumption. Depending on the system used, this treatment can use over 60 L/min of oxygen. This can place an extremely high burden on hospital oxygen delivery systems and it is extremely important to work with medical gas engineers to ensure an adequate supply before using these treatments on a large number of patients. There have been numerous reports from around the world of hospitals running out, or coming close to running out, of oxygen while treating a large number of patients with COVID-19.[14]

Bilevel positive airway pressure

Bilevel positive airway pressure/noninvasive ventilation (BiPAP-NIV) is a treatment modality predominantly used for hypercapnic respiratory failure. Clinical experience in previous respiratory disease epidemics (SARS and Middle East respiratory syndrome) has shown that BiPAP-NIV can be used both safely and effectively in patients with acute respiratory failure.[15] However, experience has shown that the development of hypercapnia in patients without previous respiratory disease is a sign of rapid decompensation and the use of BiPAP-NIV in these patients is likely to only postpone, and possibly render more hazardous, the need for tracheal intubation and mechanical ventilation. BiPAP-NIV should be reserved for those with chronic obstructive pulmonary disease which has been exacerbated by COVID-19 or for those for whom mechanical ventilation is not in their best interests.

Prone positioning

Prone positioning in the awake patient is a new concept which has not been widely tried prior to the COVID-19 pandemic. It can be uncomfortable and is not always well tolerated but in those who can tolerate the prone position for at least 3 h, significant improvement in arterial oxygen content has been observed.[16] The technique may prevent intubation in some patients and is worth trying where safe to do so.

Invasive ventilation

In patients with respiratory failure refractory to noninvasive techniques, or with a reduced level of consciousness, tracheal intubation and mechanical ventilation will be necessary. The risks of baro-and volutrauma are significant and significant harm can be caused by failure to be attentive to the principles of lung protective ventilation. Patients with COVID-19 needing mechanical ventilation meet the Berlin definition of ARDS[17] and the standard ventilatory principles of ARDS management should be followed.

Lung protective ventilation

Trials of ventilation in ARDS have shown the importance of limiting tidal volumes to 6–8 ml/kg ideal body weight and plateau pressures to <30 cmH_2O.[18] These principles hold in COVID-19 respiratory failure and are most important to avoid iatrogenic lung damage. Permissive hypercapnia may be necessary to allow low tidal volume ventilation, although this is not completely benign and should be avoided if not necessary.[19]

Early commentators suggested two distinct phenotypes in COVID-19: a type L with high lung compliance and a type H with low lung compliance.[11] It was suggested that type L lungs could be ventilated with higher tidal volumes without risk of lung injury. Further experience has shown that these two types represent extremes of a continuum where patients with high initial compliance will rapidly progress to poor compliance without careful attention to lung protective measures.

There is no good evidence as to which ventilator mode should be used in ARDS; we would recommend that ICUs use whichever mode they are used to using to provide lung-protective ventilation. Recent years have seen interest in airway pressure release ventilation (APRV), but there is no strong evidence of benefit to this mode as yet[20] and no information at all on its use in COVID-19. ICUs experienced in the use of APRV may wish to consider its use in COVID-19 patients.

Positive end-expiratory pressure

Positive end-expiratory pressure (PEEP) is almost always

necessary in mechanically ventilated patients to splint lung units open and improve ventilation-perfusion matching; it can recruit collapsed lung and improve respiratory system compliance. However, higher PEEP increases intrathoracic pressure, reducing venous return and hence pulmonary perfusion. High PEEP may cause alveolar overdistension which will reduce lung compliance and may worsen ventilator-induced lung injury.

There is no proven method of choosing the ideal PEEP.[4] It should be adjusted for each patient depending on the FiO_2 and arterial oxygen saturation.

Sedation and paralysis

Adequate sedation and analgesia is necessary to alleviate pain and distress associated with intubation and ventilation. It should be titrated to minimize respiratory effort to maximize ventilator synchrony. Adequate sedation will reduce oxygen consumption and carbon dioxide production, thus reducing the demand on the respiratory system. Neuromuscular blocking agents may be useful in refractory hypoxemia although there is no good evidence of an improvement in mortality.[21]

Fluid management

Trials of fluid management in ARDS have shown improved outcomes with a conservative fluid strategy[22] and this should be the aim in ventilated patients with COVID-19. It is important, however, not to render these patients hypovolemic with over-aggressive diuresis; significant fever can lead to high unmeasured fluid losses and this should be replaced. Patients with COVID-19 have a higher rate of renal failure needing renal replacement than other viral pneumonias;[23] the risk of this may be reduced by targeting euvolemia.

Prone positioning

In patients with refractory hypoxemia despite FiO_2 >0.6 and appropriate PEEP, prone positioning is useful to improve arterial oxygen content. Trials in ARDS prior to the COVID-19 pandemic have shown a mortality benefit if the prone position is used for more than 16 h per day.[24] Prone positioning requires at least five members of staff and carries risks of accidental dislodgment of airway devices and vascular lines, as well as skin, tissue, or eye damage from pressure. It is important to have trained in and practised prone positioning before using it in a clinical setting, and attention to pressure points and regular repositioning are the keys.

Inhaled pulmonary vasodilators

Inhaled pulmonary vasodilators such as nitric oxide and prostacyclin have been shown to increase arterial oxygen content but not to carry a mortality benefit in ARDS.[4] Some national guidelines have suggested their use in selected refractory cases in centers with experience in using these agents.[25]

Extracorporeal membrane oxygenation

Patients who are refractory to all of the above invasive ventilatory and related interventions should be considered for extracorporeal membrane oxygenation (ECMO). Early reports from China showed that ECMO could be used in these patients, but that the mortality was high.[26] Despite this, many health systems expanded ECMO capacity and defined more rigorous criteria for offering the treatment.[27] Later reports have shown significantly better outcomes with high rates of recovery and hospital discharge.[28]

ECMO should be offered to patients who meet standard referral criteria. It should only be performed in centers who are experienced in the use of ECMO for severe respiratory failure.

The role of extracorporeal carbon dioxide removal is unknown. There are case reports of its successful use[29] in COVID-19, but it is a therapy which still has an uncertain role. The ongoing REST randomized controlled trial[30] aims to answer the question of its effectiveness in ARDS, although it is not a COVID-19-specific trial.

Conclusions

COVID-19 is a new disease with a mortality rate considerably higher than previous common viral pneumonias. Although the disease is mild in most sufferers, many infected people will require admission to hospital and critical care with respiratory failure.

Despite initial concerns about COVID-19-related ARDS being in some way special or novel, experience has shown that it can be treated in the same way as ARDS from other causes. Noninvasive respiratory support has been shown to be safe, with an infection risk lower than feared and one that can be mitigated by use of appropriate personal protective equipment. Noninvasive techniques can be effective and avoid intubation in a significant proportion of patients.

When intubation and invasive ventilation is necessary, attention to the principles of lung-protective ventilation is the key to avoiding further harm. Failure of lung-protective ventilation should trigger consideration of referral to a respiratory ECMO center.

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Conflicts of interest

There are no conflicts of interest.

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