RESPIRATORY SUPPORT IN COVID-19 PATIENTS

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Abstract

Novel coronavirus disease 2019 (COVID-19) is a pandemic that has become a worldwide challenge. The virus is highly contagious, with very diverse clinical consequences very diverse. It is estimated that if no effective measures are implemented, COVID-19 could plague 90% of the world's population and kill over 40 million people. Despite hard efforts of scientists and clinicians during the last few months, our current knowledge of COVID-19 remains limited. COVID-19 can cause severe respiratory failure requiring a wide range of respiratory support interventions. This review aimed to provide brief guidance for respiratory support management of COVID-19 patients.

keywords: Coronavirus, Respiratory Failure, Mechanical Ventilation.

Introduction

Coronavirus disease 2019 or "COVID-19" also referred to as severe acute respiratory syndrome coronavirus type-2 (SARS-CoV-2) is a viral infection caused by a novel coronavirus from the generation of Coronaviridae.[1] It was first reported in December 2019 in the city of Wuhan, China and then it has spread globally to the extent that the World Health Organization has declared it as a global pandemic in March 11, 2020.

COVID-19 is a flu-like syndrome commonly characterized by fever, cough and dyspnea as well as other symptoms that include malaise, myalgia, diarrhea, sore throat, abdomin al pain, and loss of smell and a variety of other acute neurologic manifestations.[2] The lungs are the most severely affected organ by COVID-19 because the virus enters the host cells via the integral membrane protein angiotensin-converting enzyme 2 (ACE2), which is attached to cellular membranes in the lungs, arteries, heart, kidney, and intestines.[3] The average global mortality rate from COVID-19 has been estimated to be 5-10%.[4]

To date there is no treatment for COVID-19 and currently the management is supportive, where respiratory failure from acute respiratory distress syndrome (ARDS) is the leading cause of mortality.[5] In this review we will highlight the evidenced based respiratory support practices for adult COVID-19 patients in relation to medical gases, noninvasive and invasive ventilatory support, and medication nebulization for direct delivery to the lungs.

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Medical Gases Therapies

Oxygen Therapy

Supplemental oxygen is an essential component of the clinical management of COVID-19 patients.[6] Oxygen can alleviate difficulties of breathing, thereby reducing the work of breathing and the subsequent patient's anxiety as well as it can prevent hypoxemic respiratory failure and death.[6] Oxygen therapy in COVID-19 patients aims to prevent/reverse hypoxemia and maintain peripheral oxygen saturation (SpO2) ≥93%. In spontaneously breathing patients several oxygen therapy devices are available to deliver variable oxygen flow ranges in COVID-19 patients. Low oxygen flows in the range of 2-5 L/min are usually used with oxygen nasal cannulas in children and adults.[7] Moderate oxygen flows (6-10 L/min) are used with simple facemasks while higher oxygen flow rates (10-15 L/min) are needed when using non-rebreather masks with reservoirs.[7] However, these devices do not provide neither high concentrations nor guarantee precise and stable concentrations of inspired oxygen.

Higher and more stable concentrations of inspired oxygen are usually provided with high flow nasal cannula delivery systems, and non-invasive as well as invasive ventilators. However, these devices carry the risk of generating and spreading aerosols that represent risks for health care providers thus requiring and necessitating airborne precautions.[8]

Inhaled Nitric Oxide

When delivered to the lungs in the form of inhaled gas, nitric oxide (NO) can produce selective pulmonary vasodilation and improvement of ventilation to perfusion mismatch as well as reduced spread and density of lung infiltrates in patients with parenchymal diffuse lung diseases such as acute respiratory distress syndrome.[9] A previous pilot study showed that inhaled NO (iNO) at 30 ppm could shorten the time of ventilatory support for patients infected with SARS-CoV.[10] Although evidence supporting the use of iNO in treating COVID-19 is still lacking, similar therapeutic effects of NO can be expected for patients with COVID-19 due to the genetic similarities between the two viruses.[11] Several clinical trials have begun to confirm whether NO inhalation will become an interventional therapy to rescue mechanically ventilated patients with COVID-19 ARDS.[12,13]

Although it is mainly provided during invasive mechanical ventilation, previous studies have shown that iNO can be delivered to spontaneously breathing patients using either non-rebreather masks or high flow nasal cannula.[14,15]

Inhaled Heliox

Heliox is a premixed mixture of oxygen and helium that has no pharmacological effects on airway smooth muscles. However, heliox generates less resistance than atmospheric air when passing through the airways of the lungs, and thus requires less effort by a patient to breathe in and out of the lungs.[16] In that sense, COVID-19 with underlying obstructive lung diseases (e.g., asthma, chronic obstructive lung disease) might benefit from short trials of inhaled heliox to decrease the work of breathing, decrease oxygen consumption and alleviate patient's anxiety. Inhaled heliox is mainly delivered to spontaneously breathing patients using a non-rebreather mask.

High Flow Nasal Cannula Oxygen (HFNCO) Therapy

The utilization of HFNC in COVID-19 patients has been largely debated as it relates to its benefits and harms both for patients and healthcare providers.[17] The physiological benefits of HFNCO are improved oxygenation, decreased anatomical dead space, decreased metabolic demand of breathing, decreased production of carbon dioxide, superior comfort and improved work of breathing, positive nasopharyngeal and tracheal airway pressure and better secretion clearance.[18]

A case series of 138 COVID-19 patients from Wuhan, China showed that 4 (11%) of the patients admitted to the ICU were successfully treated with HFNCO.[19] Similarly, in other case series of 191 COVID-19 patients, 41 (21%) were successfully treated with HFNCO (33 in ICU and 8 in non-ICU).[20]

More evidence and reports are suggesting that in patients with mild to moderate ARDS and in negative pressure rooms, HFNCO could be a viable initial alternative to mechanical ventilation.

One potential concern about the use of HFNCO in COVID-19 patients is that it could aerosolize the respiratory tract pathogen and expose healthcare providers and other patients to risk of transmission. Using evidence from several recently published studies, the WHO concluded that HFNCO does not create widespread dispersion of exhaled air particularly at flows ≤30 L/min, and therefore, should be associated with low risk of transmission of respiratory viruses.[21] They recommended wearing a standard medical face mask if a medical provider is within 2 m of the patient. However a recent study showed that the 2-m distance zone might not be enough and as such it is highly recommended that COVID-19 patients on HFNCO are kept in single-occupancy rooms with either negative pressure or high-efficiency particulate air filtration systems and possibly wearing a standard medical face mask, and that healthcare workers caring for those patients wear full airborne personal protective equipment (i.e. N95 masks or equivalent, gown, gloves, goggles, hair covers and face shields).[22]

Noninvasive Ventilation

Suspected COVID-19 patients and asymptomatic positive polymerase chain reaction (PCR) test patients with abnormal arterial blood gases (i.e., hypoxemia and/or hypercapnia) may benefit from noninvasive positive pressure ventilation (NIPPV) to prevent early intubation.[21] Moreover, the scarcity in ventilators or the preference to reserve them for more critical patients add to the necessity of using non-invasive equipment. Unfortunately, the use of masks and other patients' interfaces during NIPPV has the potential to generate dispersal jets containing droplet or aerosolized viral particles and increase risk of transmission to other patients as well as health care workers.[23]

NIPPV should be avoided as long as possible; however, whenever indicated, important rules should be followed during its use in COVID-19 patients:

1- Use well-fitted oronasal interface (or helmet) with minimal handling and manipulation. Avoid any disconnection.

2- Avoid the use of vented masks, nasal masks, or nasal pillows.

3- Use negative pressure isolation rooms (if available).

4- Use an approved compatible viral filter on the expiratory limb (for dual-limb circuits) or before exhalation port (proximal to the patient) in a single-limb circuit.

5- Wear full approved-quality personal protective equipment when managing these patients.

NIPPV can be applied either in continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) modes. For hypoxemic respiratory failure, CPAP is usually started at 10 cmH_20 pressure and an FiO_2 of 0.6, with potential to increase to 12-15 cmH_2O and FiO_2 1.0 as per the target SpO2. For hypercapnic respiratory failure, BiPAP is recommended with a pressure gradient between the inspiratory and expiratory pressures enough to achieve a tidal volume of approximately 5 mL/Kg.[24]

Invasive Mechanical ventilation

COVID-19 patients who meet the criteria for acute respiratory distress syndrome (ARDS) are admitted to the ICU because of acute hypoxemic respiratory failure and the need for advanced respiratory support modalities.[25,26] Once considered as ARDS, the severity of COVID-19 patients is classified according to the

Table 1
Oxygenation for ARDS severity as per the Berlin definition

	Mild	Moderate	Severe
Oxygenation	200<PaO2/FiO2≤300 with PEEP≥5cmH2O	100<PaO2/FiO2≤100 with PEEP≥5cmH2O	PaO2/FiO2≤100 with PEEP≥5cmH2O

Berlin definition of ARDS (Table 1).[27]

Studies from the USA and Italy have reported high percentages of intubation and use of invasive mechanical ventilation (85%-94%) in COVID-19 patients admitted to the ICU.[25,28,29]

There is strong evidence that inappropriate strategies of mechanical ventilation can be detrimental and contribute to the increased mortality rates in ARDS patients.[30] Accordingly, severe intubated COVID-19 patients should be ventilated with lung protective strategies that aim at reducing/eliminating all forms of ventilator induced lung injuries (e.g., barotrauma, volutrauma, atelectrauma, biotrauma, and myotrauma). However, several reports have indicated that COVID-19 ARDS are not one but rather two phenotypes with different characteristics.[31,32] “Type H” COVID-19 ARDS is characterized by high elastance (i.e., low lung compliance), high lung weight, high lung recruitability, and high right-to-left shunt while “Type L” COVID-19 ARDS is characterized by low elastance (i.e., high lung compliance), low lung weight, low lung recruitability, and low ventilation-perfusion ratio.[31,32] Since two phenotypes of COVID-19 ARDS have been identified, it is essential that strategies for mechanical ventilation should not only be protective but also formulated to the specific phenotype of COVID-19 ARDS.[31,32]

“Type H” COVID-19 ARDS

Twenty to thirty percent of total COVID-19 ARDS patients develop “Type H” ARDS.[31] In these patients and due to the high lung elastance (i.e., low lung compliance), high lung weight, high potential for lungs recruitability, mechanical ventilation settings should be selected in a way to respect the protective lung strategy and baby-lung ventilation (Table 2) by preventing alveolar overdistension with the use of low tidal volume and low driving pressures, eliminating cyclic opening and closing of the alveoli by using moderate to high positive end expiratory pressure (PEEP) and minimizing stresses and strains on alveoli.[33,34] Strong evidence recommends the early and short use (24-72 hours) of neuromuscular blockade to facilitate such protective mechanical ventilation strategy.[26,33,34]

“Type L” COVID-19 ARDS

These patients should not be ventilated in a similar strategy as “Type H” ARDS and classical ARDS patients. Although early intubation is crucial to avoid transformation to “Type H” ARDS, these patients need to be ventilated with liberal tidal volume to prevent reabsorption atelectasis, hypoventilation, hypercapnia and the need for using high respiratory rates with low PEEP because of the low potential of lung recruitability and the need to avoid hemodynamic compromises (Table 2).[31,32] In these patients, respiratory rate should not exceed 20 breaths/min[35] and prone positioning should be considered more as a rescue maneuver to facilitate the redistribution of pulmonary blood flow rather than for opening collapsed areas.[35]

Oxygen Supplementation

As previously mentioned, the target peripheral oxygen saturation should be between 90-96% as higher fraction of inspired oxygen (FiO2) is associated with a

Table 2
Key mechanical ventilation settings in COVID-19 patients

	Type H	Type L
VT (mL/Kg) of IBW	4-6 mL/Kg	6-8 mL/Kg
PEEP (cmH2O)	≥10 cmH2O	5-10 cmH2O
Ppl (cmH2O)	≤28cmH2O	≤30cmH2O
DP (cmH2O)	≤15cmH2O	≤15cmh2O
RR (br/min)	20-30 br/min	≤20 br/min
FiO2 (%)	Least for SpO2 89-93%	Least for SpO2 89-93%

VT: tidal volume; IBW: ideal body weight; PEEP: positive end expiratory pressure; Ppl: plateau pressure; DP: driving pressure = Ppl-PEEP; RR: respiratory rate; FiO2: fraction of inspired oxygen; SpO2: pulse oximetry oxygen saturation higher mortality and as such FiO2 should be titrated to the minimum in order to maintain a PaO2 between 60-80 mmHg.[34]

Prone position

A very important adjunct to mechanical ventilation in ARDS patients is placing patients in the prone position. Prolonged prone position (16 hours per day) for patient with severe ARDS improves oxygenation and decrease mortality.[36] As for COVID-19 ARDS, and especially for Type H, reports and experts opinion have recommended prone positioning as a potential treatment strategy for refractory hypoxemia in intubated and non-intubated COVID-19 patient.[26,35]

Aerosol Therapy

In COVID-19 patients, aerosol therapy is an essential part of treatment. However, delivering aerosolized medications to patients with COVID-19 has been a real concern for caregivers and healthcare professionals who are at risk of transmission along with other patients to unintended inhalation of aerosols that have been released from the aerosol device during patient expiration. Several measures have been recommended for efficient aerosol therapy with minimal risk for corona virus transmission.

In COVID-19 patients who are awake, spontaneously breathing and can perform specific breathing techniques with inhalers, clinicians should consider using pressurized metered-dose inhalers with spacers and/or dry powder inhalers for aerosol drug delivery instead of nebulizers.[37] When using spacers, viral filters must be attached at the distal port of the spacer. It is preferred to use facemask instead of mouthpiece to reduce dry wastage and improve delivery efficiency. Administering aerosol therapy in negative pressure rooms can further decrease the risk of viral transmission.

Secondary inhalation of emissions released from the patients with COVID-19 using HFNC is a real concern. It leads to the risk of distribution of aerosolized virus because HFNC does not have a closed circuit, unlike ventilators. If aerosolized medications need to be delivered through HFNC, surgical mask should be placed on the face of infected patients during HFNC. The use of vibrating mesh nebulizers (VMN) is highly recommended for patients on HFNC.[37]

In COVID-19 patients receiving either CPAP or BiPAP support, it is preferred to use a vibrating mesh nebulizer placed between the exhalation valve and patient's interface.[37]

In intubated and mechanically ventilated COVID-19 patients, it is vital to keep the ventilator breathing circuit intact and prevent the transmission of the virus. Therefore, delivering aerosolized medications via jet nebulizer or pressurized metered dose inhalers will not be appropriate due to the breakage of the circuits for the placement of the device on the ventilator circuit before aerosol therapy. As such it is preferred to use VMN in COVID-19 mechanically ventilated patients since the VMN can stay in line for up to 28 days, and the reservoir design can allow the addition of medications without requiring the ventilator circuit to be disconnected. It is recommended to place the vibrating mesh nebulizer on the dry side of the active humidifier as this will improve the efficiency of the treatment and further reduce retrograde contamination from the patient.[37]

Conclusion

COVID-19 may progress incredibly quickly leading high fatality rates. Although the pulmonary pattern of critically ill patients with COVID-19 has been defined as ARDS, it does not always represent or even resemble ARDS. Two distinct phenotypes have been already identified. Understanding the characteristics of each phenotype is essential for more efficient guidance and interventions with respiratory support therapies. Further studies are warranted to provide additional insight on the respiratory management of patients with severe COVID-19.

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