


Review Article

Supplemental Oxygen therapy and Non-Invasive Ventilation in Corona Virus Disease 2019 (COVID-19)

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Abstract

The world has experienced a pandemic due to novel Severe Acute Respiratory Disease Corona Virus-2 (SARS-CoV2) since December 2019. The clinical spectrum of the disease known as Coronavirus Disease 2019 (COVID-19) is so much wide, starting from an asymptomatic state to paucisymptomatic clinical presentation, pneumonia, respiratory failure to even death. Supplemental oxygen therapy is essential in managing COVID-19. Also, there is sparse evidence regarding use of non-invasive ventilation (NIV) in pandemics like SARS-CoV-2. This study reviews the currently available methods for respiratory support in COVID-19 with a discussion about using these modalities in the COVID-19 pandemic.

Keywords: COVID-19, Oxygen, Respiratory support, Non-Invasive Ventilation, Severe Acute Respiratory Disease Corona Virus-2

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Introduction

Since December of 2019 an outbreak of novel Coronavirus disease 2019 (COVID-19) was reported and WHO declared a pandemic by 11 March 2020. In 28 March of the same year more than 200 countries, territories or areas has been infected with more than 510,000 confirmed cases (1).

The clinical spectrum of this disease could range from asymptomatic, mild upper respiratory tract infection illness, severe viral pneumonia, respiratory failure and even death (2). Most of the reported mortalities are due to alveolar damage and respiratory failure (3). Therefore, at the end of the clinical spectrum, COVID-19 patients require respiratory support. Respiratory support aims to maintain adequate

oxygenation or ventilation to reduce respiratory work and to prevent lung injury. This pivotal role can be achieved by either increasing FiO₂ or helping the mechanical respiratory system of the patient to deliver more oxygen in to the blood stream (4).

Adequacy of oxygen delivery (DO₂) is essential for aerobic metabolism; therefore, "Shock state" is defined by tissue hypoxia. COVID-19 interferes with uptake of oxygen from inhaled gaseous mixture due to alveolar damage with cellular fibromyxoid exudates and interstitial mononuclear inflammatory infiltrates leading to acute respiratory distress syndrome (ARDS) (5). In early stages of ARDS acute oxygen therapy can lay an integral role in treatment of tissue hypoxia. Therefore, understanding basics of oxygen therapy and the devices used are essential for treating patients with

COVID-19.

Non-invasive ventilation (NIV) refers to delivery of positive pressure in to the airway for ventilation support, without invasive endotracheal intubation. NIV has been shown to be effective in acute respiratory failure while avoiding complications of endotracheal intubation especially ventilator associated pneumonia (6). As NIV is proposed as the first line treatment in patients with acute respiratory failure, NIV in COVID-19 patients might be beneficial (7). Besides, NIV is known as aerosol generating procedure, therefore there should be cautions in order to minimize spread of the virus (8).

In this review we have discussed how to maintain oxygenation and the rational use of devices in patients requiring higher FiO₂ and also we have discussed the controversies regarding non-invasive ventilation (NIV).

Supplemental Oxygen Support:

The first line therapy of hypoxemic patient like COVID-19 is administration of supplemental oxygen (9). Oxygen therapy is defined by administration of oxygen at concentrations above room air which is 20.9% (10). There are numerous devices in order to prescribe oxygen. When using these devices some cautions has to be applied in order to gain maximal efficacy for the patient (11). As shown in a multi-center study in Wenzhou, China about 90% of COVID-19 patients required oxygen therapy (12). General principle in providing oxygen for patients with COVID-19 is that higher flow may result in risk of viral aerosolization (8). There are two types of oxygen delivery devices which deliver either the entire (high flow) or partial (low flow) ventilator requirements.

1) Low Flow Oxygen Delivery Devices

Nasal cannula: FiO₂ delivered by nasal cannula depends on minute ventilation and oxygen flow rate, which would be 1-6 liter/min (FiO₂ increases approximately 4% per liter flow from 24% to 44%). This device is simple, comfortable and convenient and prevents rebreathing while allowing talking and eating. It may cause local irritation and dermatitis with higher flow rates and also as the minute ventilation increases the FiO₂ prescribed would decrease (13). When administering oxygen via nasal cannula we should consider that complications like drying of mucosal membrane, nasal trauma or epistaxis could happen

(10).

Simple (Hudson) Mask: At least 5 liter/min of flow rate is required in order to overcome rebreathing, also flow rates more than of 10 liters/min would not be efficient. The FiO₂ provided would be 35% to 60% which also depends on flow rate and minute ventilation. (approximately 4% per liter of O₂) (13).

Reservoir bag (non-rebreather mask): this device is a facial mask combined with a reservoir bag with capacity of 600 to 1000 mL and a one-way valve connecting these two. These add-ons enable delivering higher concentrations of oxygen about 85-90% with flow rate of 15 liter/min. The mentioned bag and valve is designed so that they could stop rebreathing of expired gas. Flow must be sufficient to keep reservoir bag from deflating upon inspiration (13).

2) High Flow Oxygen Delivery Devices

Facial mask with Venturi valve: These devices have the benefit of overcoming rebreathing due to high flow rates provided by Venturi valves operating by Bernoulli principle of jet gas mixing. They are capable of providing low concentrations of O₂ (24-30%). But higher flow rates and wider oxygen jet they can provide FiO₂ as high as 60%. Their oxygen concentration do not depend on minute ventilation hence it depends on oxygen flow rate which is indicated by each valve and should be followed by the manufacturer's preference (14). The nozzles are color coded for desirable concentrations of 24% blue, 28% white, 35% yellow, 40% red and 60% green (10).

High Flow Nasal Cannula: These relatively new systems allow humidification and heating the oxygen provided for the patient while delivering variable flow rates between 1 to 60 Liter/min. Actual FiO₂ delivered by these devices is not stable. It depends on the flow rate, respiratory rate, peak inspiratory flow rate and also method of breathing (higher with mouth-open breathing than mouth-closed breathing) (11). Their FiO₂ could range from 24% when using low flows up to more than 70% with high flow rates. although it has not yet been described any contraindications, but in cases NIV is contraindicated you should reconsider its use (15).

There are limited data regarding use of HFNO in pandemics, hence a retrospective cohort study in

Table 1: Pros and Cons of NIV in COVID19 patients with respiratory failure.

Pros	Cons
Non-invasive method	Need personnel protection equipment
Effective in non-severe respiratory failure	Need airborne isolated room
Low rate of mortality	Ineffective in severe respiratory failure
Lower ventilator associated pneumonia (VAP)	Barotrauma

Wuhan, China, reported mortality of 28% in first month of outbreak. In that study about 20% of patients receiving HFNO, survived (2, 8). Although early invasive ventilation is proposed in some studies, a cohort study of Influenza A epidemic showed HFNO decreased invasive mechanical ventilation by 45% (8, 16). Clinical data of 60 severe cases gathered in Jiangsu, China, concluded that early NIV and HFNO combined with prone ventilation can delay intubation and improved hypoxia in COVID-19 patients (17).

The risk of aerosol production when using HFNO depends on duration of use, flow rate, patient cooperation and sealing of the interface. A well fitted interface would minimize aerosol generation (18). On the other hand, personal protective equipment (PPE) are a critical point when using HFNO (16). Also negative pressure ventilation rooms are ideal when performing aerosol generating procedure and if not applicable normal room with strict door policy should be used (8).

These results are suggesting that if mechanical ventilation became scarce, using HFNO would be a necessity in order to provide adequate oxygenation for these patients (19). Patient selection in this situation would be critical. Patients with higher risk factors and severe illness, that suggests inevitable mechanical ventilation, would not benefit from HFNO (8).

Non-Invasive Ventilation

Some devices are designed to help ventilation and drive force. They can be either invasive also known as intubation, or non-invasive ventilation (NIV). NIV divides in to two groups;

Continuous positive airway pressure (CPAP), this mode delivers high pressure oxygen by a tight fitting mask, attached to a ventilator, in all the times during respiration. This cannot ventilate patients, it could keep airways and alveolus open during ventilation. Its use has been verified in sleep apnea and heart failure. Pressure assigned by this device is

analogous to positive end expiratory pressure (PEEP).

Bilevel positive airway pressure (BiPAP): This mode delivers two different airway pressures, which are inspiratory (IPAP) and expiratory (EPAP). EPAP is analogous to PEEP on CPAP and IPAP is a higher pressure which helps to increase inspiratory effort of the patient (22). Initial pressure setting for EPAP is 3 cmH₂O and for IPAP is 10 cmH₂O. Then it should up titrate in 10-30 minutes to achieve adequate chest expansion, IPAP shouldn't exceed 30 cmH₂O (23).

Other new modes of delivery can have been proposed not limited to proportional assist ventilation (PAV), average volume assured pressure support (AVAPS) and assist/control modes (24). Contraindications of NIV are facial anomalies, recent upper gastrointestinal surgery, nausea and vomiting, airway obstruction, inability to protect airway, life threatening hypoxia, confusion and agitation, patient refusal, bowel obstruction, and unstable hemodynamics.

In a retrospective cohort by Zhou in Wuhan at first month of the outbreak of coronavirus disease 2019 among 191 patients, about 30% of patients had dyspnea described by respiratory rate more than 24/min. More than half of them supported with invasive ventilation and less than half of them were supported by non-invasive ventilation the mortality rate between these two groups was 92% in NIV compared with 96% in intubated patients (2). Xiabo Yang and colleagues (18) describe 52 patients with COVID19 that was admitted in Wuhan, China, 29 patients needed mechanical ventilation that 76% of whom required invasive mechanical ventilation although 24% of whom continue their treatment by non-invasive mechanical ventilation. Mortality rate among intubated group was 86% versus 57% in NIV group. These mortality rate in other study on 29 patients was 79% in intubated patients versus 86% in patients supported by non-invasive ventilation (17). Mortality rate was higher in patients with invasive

mechanical ventilation. The exact cause of death is unclear. Intubated patients might have more severe respiratory symptoms and organ failure but this difference in several studies might be due to the method of oxygen supply in COVID patients.

Oxygen therapy is one of the main supportive therapies in critically ill patients because most of them suffered from organ failure due to hypoxia. Regardless of oxygen supply method, early oxygen therapy is recommended in various studies (17). Invasive mechanical ventilation is recommended in some studies. But almost all patients had limited life expectancy after intubation. therefore, more effort are required in order to evaluate this concept (25). On the other hand, sometimes supportive therapy by NIV is not a choice because of some inevitable reasons like when there is lack of ventilator, fear of contamination and uncertainty about intubation(19, 26).

In some studies, it is not recommended to use non-invasive mechanical ventilation for patients with COVID-19 (9, 18, 27). The main reasons for their concerns are both evidence in support for their beneficial aspects, and also the safety properties of these devices (8, 16). First of all, there are many concerns about wide spread dispersion of the virus as it was high in other viruses like Middle East Respiratory Syndrome (MERS) (26). Regardless of the belief that NIV is an aerosol generating procedure, reports show that this method is using all over the world in treatment of COVID-19. There are many suggestions about using high level of personal protection equipment and standard hospital structures to make effective negative pressure room during treatment with NIV(27) (8). Jonathan Chun-Hei Cheung et al., insist on doing aerosol generating procedures just in airborne infection isolated room and with double glove technique (27).

The other disadvantage of non-invasive ventilation is delayed emergent intubation that may expose the staffs with not enough person protection equipment. Patients with non-invasive ventilation are also at the risk of large tidal volume and barotrauma due to high transpulmonary pressure. In patients with severe respiratory failure beneficial of oxygen therapy by NIV is still questionable. It seems to be better not to use NIV for severe respiratory failure (8). On the other hand, in recent studies there are evidences in beneficial

usage of non-invasive mechanical ventilation in non-severe form of respiratory failure in patients with corona virus. These publications suggest that acceptable interface fitting mask while using NIV has low risk of transmission and cannot create wide spread dispersion (28). The other important point in using this method is that the patients need close monitoring to evaluate if treatment failure would happen or not (26). Other advantages of NIV versus intubation are higher acceptance of patients and health care providers .In some cases with respiratory failure NIV could decrease the rate of intubation and its complications like ventilator associated pneumonia (20, 21). Advantage and disadvantage of respiratory support by NIV is shown in Table 1.

Conclusion

Early oxygen support is advised in every patient with COVID-19, in order to achieve maximal benefit basic principles of oxygen support should be implemented. Each patient should be considered unique and the appropriate oxygen support device should be selected. HFNO has been shown to be effective in maintaining oxygenation while it may not have major impact on clinical outcome. HFNO should be used with caution due to its ability to spread the virus, therefore PPE, negative pressure ventilation rooms or strict door protocols and avoidance of positive pressure ventilation rooms are mandatory. There is concern about viral spread through aerosolization by NIV. This concern is questionable as recent studies did not find any differences between viral spread of NIV versus coughing in patients suffering from COVID-19. Also NIV has been shown to reduce VAP and decrease rate of invasive ventilation in mild to moderate cases. Therefore, its use is recommended in non-severe respiratory failure cases with appropriate PPE.

Acknowledgment

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

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