COMMENTARY

Respiratory and ventilator management of COVID-19

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Abstract

The current pandemic of COVID-19 has infected around 2.5 million people with more than 125,000 deaths across the globe till date, and numbers are still rising. The causative organism is a virus of corona family. The International Committee on Taxonomy of Viruses (ICTV) named it severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) due to its similarities with the virus was caused SARS outbreak (SARS-CoV). Although most of the patients present with less severe symptoms like rhinitis, cough, fever, and mild flu-like symptoms, it may progress to severe acute respiratory illness, pneumonia or acute respiratory distress syndrome (ARDS) mainly in immunocompromised hosts. Severe infections mainly involve lungs, and compromise its capacity of ventilation. Respiratory and mechanical ventilation is one of the important parts of management.

Keywords: SARS CoV-2, Mechanical management, ARDS, Pandemic, Coronavirus.

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Introduction

Coronavirus disease (COVID -19) was declared a pandemic by WHO on 11th March 2020.[1] It started in Wuhan, China in December 2019. In the next two months, this contagious virus spread all over the globe, severely affecting some most developed countries like USA, UK, Italy, Spain, and France. By this time, in the third week of April 2020, world has seen deaths of more than 125,000 people and the numbers are still increasing day-by-day.

Aetiology

Causative organism for this disease is a virus - severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). These are positive-stranded RNA of large size, measuring up to 30kb in length, with a crown-like appearance (hence the name corona) noted under an electron microscope. Such a unique appearance of the virus is because of the glycoproteins present on the envelope appearing like spikes. The virus is very contagious and spreads from person-to-person through small droplets produced during sneezing and coughing, or even on talking in close contacts.[2]

Pathophysiology

The most commonly affected organ in coronavirus disease (COVID-19) are the lungs. It has been postulated that the interaction of virus with host cell is via an enzyme known as angiotensin-converting enzyme 2 (ACE2). The receptors for enzyme are found in the type II alveolar cells of the lungs. The spikes on surface glycoprotein of the virus connect to ACE2 receptors and gain access to host cell.[3] The viral infection leads to extensive immune reaction in the host labelled as 'cytokine storm'. The effect is extensive tissue damage. It also stimulates the production of acute phase proteins. It is also implicated into the pathogenesis of the cytokine release syndrome (CRS) that is an acute systemic inflammatory syndrome characterised by fever and multiple organ dysfunctions suggest an underlying immunepathology.[4] Involvement of alveoli leads to respiratory failure which is the main reason for mortality in COVID-19.[5] In contrast the pathology of usual acute respiratory distress syndrome (ARDS) is mainly because of increase inflammatory response and increased permeability of alveolar membrane and capillary endothelium, and accumulation of protein-rich fluid inside the alveoli, thereby producing diffuse alveolar damage, with release of pro-inflammatory cytokines, such as Tumor Necrosis Factor (TNF), IL-1 and IL-6.[6]

Latest research about the pathogenesis done by Liu et al and Li et al from China[7] suggested that the key pathogenic molecular step of SARS-CoV-2 is to attack the 1-beta chain of haemoglobin causing dissociation of the porphyrins from iron and releasing iron into the circulation. Thus haemoglobin loses its capacity to bind with oxygen, stopping its delivery to major organs. That is why we observe that severe hypoxia is not corrected with oxygen, and this is coupled with very rapid multi-organ failures. Moreover, the free iron released into the circulation causes oxidative damage to the lungs. Free iron toxicity induces inflammation of alveolar macrophages. Increased serum ferritin level, high

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monocytes, lymphopenia may be the consequences of disturbance of this haeme pathway. Increased iron load and increased haemoglobin production leads to increased blood viscosity with recurrent and diffuse micro and macro circulatory thrombosis leading to high levels of D-dimer in those patients; this explains the cause of sudden deterioration and death in some cases.

Clinical Features

According to WHO, the clinical classification of the COVID-19 is done on the basis of severity of symptoms.[8] Incubation period may vary from 1-14 days. Most of the patients present with less severe symptoms like fever, cough, sore throat, headache and malaise. They are categorised as uncomplicated cases. Some patients may present with pneumonia with symptoms of cough with expectoration, high grade fever and chest pain. If the patient's general condition is stable, it is referred as mild pneumonia. If the patient with above complaints also has respiratory rate more than 30 breaths per minute, or oxygen saturation (SpO_2) <90 % on room air, it is referred to as severe pneumonia. Few of these patients may present with ARDS. It is defined as new or worsening of existing respiratory symptoms after a clinical insult probably within 7 days, with chest imaging showing bilateral opacities which could not be explained with any other disease. ARDS may be classified as mild when ratio of arterial oxygen partial pressure (PaO_2 in mmHg) to fractional inspired oxygen (FiO_2) ($PaO2/FiO_2$) is between 200 to 300 mmHg (with positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) $\geq$5 cm H_2O). Moderate ARDS is when PaO_2/FiO_2 is between 100 to 200 mmHg with PEEP $\geq$5 cm H2O, and severe ARDS is defined when PaO_2/FiO_2 is $\leq$100 mmHg with PEEP $\geq$5 cm H_2O. Few patients may have sepsis, in which life-threatening organ dysfunction is probably caused by a dysregulated host response to infection. A patient in sepsis may present with decrease oxygen saturation below 90%, altered sensorium, breathlessness, decreased urine output, tachycardia, low volume pulse, cold extremities or hypotension. If blood pressure is low despite volume resuscitation and requires vasopressors to maintain mean arterial pressure (MAP) $\geq$65 mmHg it may be labelled as septic shock.

The severity of the symptoms is associated with immune status of the patient. Those with comorbid diseases like diabetes, history of malignancy, diseases with known immune-suppression, morbid obesity, and old age may get severe disease with pneumonia with ARDS or sepsis and shock. Mortality increases with associated comorbids.

Treatment

Treatment protocol is mainly based on symptomatic management. If the patient is having viral pneumonia, hypoxia, ARDS, sepsis, septic shock, he or she should be admitted in ICU and all the staff should deal with the situation with extreme precaution using personal protective equipment (PPE). WHO recommends if a patients present with low oxygen levels, severe respiratory distress and shock, he should be urgently started on supplemental oxygen to maintain SpO_2 above 94%.[8] Mode of oxygen delivery should be through face mask with reservoir bag as oxygen delivery through nasal cannula may increase the likelihood of spreading droplets.[9] There is a debate on using High Flow Nasal Oxygen (HFNO) over conventional oxygen delivery system considering aerosol generations. It is experienced that some patients with hypoxaemic respiratory failure with no evidence of hypercapnia, HFNO could be tried in early stages as it may prevent or delay intubation.[10]

Non-invasive Ventilation

It is not recommended to use non-invasive ventilation routinely in COVID-19-induced ARDS. It may lead to delay in planning of intubation, may causes high failure rates, and most importantly, it increases the risk of droplet spread due to aerosolization if mask fitting is not appropriate and there is high leak through mask.[11] Non-invasive ventilation may be considered an effective strategy for the patients who present early in their disease especially hypercapnic respiratory failure, e.g. chronic obstructive pulmonary disease (COPD).[10]

Invasive Ventilation

Lung protective mechanical ventilation as used in standard care for ARDS is used to overcome acute respiratory failure due to ARDS caused by COVID-19. Lung protective strategy is applied in ARDS to prevent barotrauma. The tidal volume is kept low (4-6 ml/kg of predicted body weight), PEEP is generally kept high (mostly up to 15 cm H_2O), and the upper limit of plateau pressure is limited below 30 cm H_2O. Occasionally, intentional rise in PCO_2 (permissible hypercarbia) is allowed as it may decrease the chance of volu-trauma.[13]

Sedation is generally required for controlled ventilation. It is recommended to keep the patients under sedation which allows proper functioning of ventilator and prevent dyssynchrony. Deep sedation is continued until desirable oxygen level are achieved although it is good clinical practice to hold sedation daily in morning round to assess the sensorium and mental status of the patient. Use of neuromuscular blockade agents are not generally recommended, unless the patient has significant worsening hypoxia or hypercapnia and in situations where the patient's respiratory drive cannot be managed

with sedation alone resulting in ventilator dys-synchrony and lung de-recruitment. There were a lot of studies regarding prone positioning during mechanical ventilation but still not much evidence suggest that it is beneficial over normal position. Still it can be tried in some patient with refractory hypoxia not improving on maximum ventilator parameters. Whenever it is used in cases of refractory hypoxemia it should be under strict hospital guidelines which include using appropriate PPE by entire medical personal and take utmost precaution to minimise the risk of adverse effect like accidental extubation and breaking of the circuit.[8,12]

Intravenous fluid plays a vital role in the management of ARDS due to COVID-19. If patient is not in shock, intravenous fluid conservative therapy can be give with planning of negative balance of 0.5 to 1.0 litres per day. However if the patient is in shock, fluid balance is must. Extreme precaution is to be taken in patients with acute kidney injury, especially if it is associated with oliguria. ARDS lung is very much prone for secondary bacterial infection. It is advisable to cover the patient with appropriate antibiotics when on mechanical ventilator.[13] Recommendation regarding glucocorticoid use is controversial in ARDS; it is recommended for refractory shock however in case of COVID-19-induced ARDS, recommendation is against it as it can be harmful in viral pneumonias.[14]

Extracorporeal membrane oxygenation (ECMO) may be considered in patients with COVID-induced ARDS not responding on mechanical ventilation despite all the measures including prone positioning. Currently, no such recommendation is available pertaining use of ECMO in COVID-induced ARDS because of less experience. However in future, constructive guidelines may be postulated once we gain little more experience in using ECMO in COVID-induced ARDS.

Conclusion

Although it is a systemic disease, as involvement of lung carries the burden of mortality, respiratory management which may or may not include mechanical ventilation is of utmost importance in the treatment of COVID-19. Management of acute hypoxemic failure due to severe pneumonia or ARDS is difficult. It is even more difficult in case of COVID-19 as data and research related to it is very little. Further studies are ongoing for strengthening the treatment protocol for COVID-induced ARDS.

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