MANAGEMENT OF ACUTE RESPIRATORY DISTRESS SYNDROME

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ABSTRACT

Acute Respiratory Distress Syndrome (ARDS) is a severe medical condition that should be addressed for more researchers and studies since it is associated with high rate of morbidity and mortality. In this work we discuss pathophysiology with clinical manifestations of ARDS in details along with management measures for this condition. In this article we had added some new ideas related to 'low tidal volume ventilation' and 'prone positioning'. For this condition we discuss comparative studies of various treatment options for ARDS.

INTRODUCTION

Acute Respiratory Distress Syndrome (ARDS) is a severe medical condition associated with high morbidity and mortality due to its clinical manifestations. Worldwide, 10% of intensive care unit admissions are due to ARDS; this approximately totals more than 3 million patients annually (Fan et al., 2012). Mortality rates for the disease also remain high; therefore, managing patients with ARDS remains a challenge even after the substantial amount of research done in this area spanning decades. This assignment will focus on the clinical management of patients with acute respiratory distress syndrome. I will discuss how low tidal volume ventilation, the introduction of neuromuscular blocking agents, and nursing management of prone positioning help treat acute respiratory distress syndrome. I will also analyze and suggest recommendations in current management practices.

Keywords – 'Acute Respiratory Distress Syndrome', 'low tidal volume', 'ventilation', 'proning' and 'neuromuscular blockade agents'.

PATHOPHYSIOLOGY

Acute Respiratory Distress Syndrome [ARDS] involves pathology of complicated hypoxia often associated with poor prognosis. According to Isotani et al. (2012), several inflammatory and fibroticevents in the cascade result in ARDS's pathophysiology. An increase in capillary permeability is an indicator of ARDS. Pierrakos et al. (2012) state that capillary endothelium and alveolar epithelium damage in association with defective removal of fluid from the alveolar space results in aggregationof protein-rich fluid inside the alveoli. Thereby creating diffuse alveolar damage with the release of proinflammatory cytokines such as Tumor Necrosis Factor [TNF], Interlukin-1[IL-1] and interlukin- 6[IL-6].

A critical part of the pathogenesis of ARDS is inflammation because of neutrophil stimulation. Along with this, different elements such as endothelium-1, angiotensin-2, and phospholipase A-2 raise vascular permeability and thus destroys microvascular architecture. This enhances inflammation leading to lung damage. Pulmonary hypertension is a critical element of ARDS. It is caused by hypoxic pulmonary vasoconstriction and vascular compression, parenchymal destruction and airwaycollapse (Pierrakos et al.,2012). According to Virani et al. (2019), reduction in surfactant (a lipoprotein that reduces the surface tension in lungs and so keeps the alveoli open and increases gasexchange by increasing the surface area across the alveolar-capillary membrane) production results from damage to alveolar epithelium, atelectasis and reduced pulmonary compliance. Injury to the vascular endothelial cells of the capillary causes cytokines and other inflammatory mediators to be released within the pulmonary system. This result in raised vascular permeability leading to fluid- filled alveoli, causing increased airway resistance, reduced pulmonary compliance and edema in the lungs. The non-compliant fluid-filled alveoli critically compromise oxygenation, causing a mismatch between ventilation and perfusion. This is known as ventilation and perfusion mismatch. Thus, multiorgan failure occurs due to impaired gas exchange which is caused by the body's organ systems and tissue receiving lower than average amounts of oxygen; therefore, oxygen uptake does not meet the body's demand. (Virani et al., 2019).

The condition manifests as rapidly progressive dyspnea, tachypnoea and hypoxia. The 2012 Berlindefinition of ARDS characterizes the condition by "intense lung inflammation leading to increased

Pulmonary vascular permeability, increased lung weight and loss of aerated tissue" (Alessandri et al., 2017). Acute respiratory distress syndrome (ARDS) takes place when pulmonary or extrapulmonary damage leads to the discharge of inflammatory mediators, allowing neutrophil build-up in the lung's microcirculation. Neutrophil build-up can be problematic as it may impair capillary endothelium and alveolar epithelium, bringing about edema of the lungs, hyaline membrane formation, reduced pulmonary function and decreased ventilation. In most cases, ARDS is connected with sepsis or pneumonia (Saguil et al., 2012). According to Michael et al. (2012), ARDS is physiologically characterized by increased vascular permeability leading to edema of the lungs, critical arterial hypoxia and reduced ventilation leading to carbon dioxide build-up.

Multiple arrays of tests such as a blood test, chest x-ray, computed tomography scan, throat and nose swabs, ECG, and airway examination help rule out ARDS from other conditions related to the heart and lungs. ARDS is characterized by fluid-filled air sacs in the lungs, and hypoxemia and hypotension can also be signs of ARDS (Cattamanchi et al., 2018). The Berlin definition of ARDS requires identification of these certain criteria for the diagnosis of this disease. This criteria states respiratory symptoms are related to a clinical insult and presents with a week of this happening, or the patient should present with new worsening symptoms in the last seven days, non-explainable bilateral opacities must be detected in CT scan or chest x-ray, the patient's respiratory failure is unexplained and not described by cardiac failure or fluid overload, and the final indicator is the presence of moderate to severe hypoxemia (Fergusan et al., 2012).

Prone Positioning:

Prone positioning is an approach that involves placing patients on their stomach to help them breathe better and is used in treatment for patients with ARDS (Hadaya et al., 2020). According to Aoyama et al. (2019), prone positioning enhances the ventral-dorsal transpulmonary pressure (difference between alveolar and intrapleural pressure) difference. This enhances gas exchange by lowering dorsal lung compression and therefore improves pulmonary perfusion. Some of the key benefits of this technique involve better drainage of secretions in the lungs, less lung compression by the heart and abdominal organs and more adequate gas exchange in the lungs.

A systematic review by Roxanne Bloomfield et al (2015) composed results from nine randomized trials that consisted of 2165 participants. The results show that prone position breathing was not of benefit for all participators, whereas it proved beneficial for a fraction of the participants. Patients who received early treatment and for lengthened times were found to have reduced mortality; this also included patients with the most critical pulmonary damage. There were also many complications associated with the review. Pressure sores (or ulcers) and blockage or obstruction of the tracheal tube were the most common of these complications. Hypotension and irregular heart rhythms were observed amongst some participants. The early use of prone positioning in patients with ARDS especially in patients with severe ARDS is supported by this review.

A systematic review by Aoyama et al. (2019) found prone position ventilation and venovenous extracorporeal membrane oxygenation (VV ECMO) to have considerably lower mortality in a 28-day period in a meta-analysis of 25 randomized clinical trials. This review "supports the use of prone position ventilation in patients with moderate to severe ARDS." This study ranked VV ECMO the greatest in patients with critical ARDS closely followed by prone position ventilation. This review also recommends the use of prone positioning as a first-line approach for patients with critical ARDS. They also concluded that prone positioning was not superior to any other treatment mechanism in decreasing barotrauma.

Patients suffering from severe ARDS benefited greatly from lying in a prone position for a prolonged time, according to a report by Claude Guerin et al. (2013). The study discovered that the 28-day mortality was 16% and the 90-day mortality 17.4% higher in patients treated in the supine position. However, the number of complications did not vary greatly between patients in the supine or prone group. Such considerable differences in mortality are due to the benefits of prone position ventilation, for instance the recruitment of alveoli that collapsed while in the supine position, reduced ventilator-induced lung injury as stress within lungs is distributed evenly and relief of severe hypoxemia. This paper strongly argues that early application of lengthened prone-positioning sessions undoubtedly lowers mortality.

A systematic review of eight randomized control trials (RCTs) by Munshi et al. (2017) found lesser mortality for patients with moderate to critical ARDS when prone positioning was applied for a long duration of 12 hours or more per day. They indicated that decreased mortality is because of lower ventilator induced lung injury.

Meta-analysis of RCTs of prone position ventilation suggests that it only provides a survival advantage in patients with critical ARDS where the ratio of arterial oxygen partial pressure to fractional inspired oxygen is less than 150 millimeters of mercury Kallet et al. (2015). This comprehensive study also discloses that higher positive end-expiratory pressure (PEEP) (10-13 cm H20), small tidal volume (≤8 mL/kg) and long durations of prone position (>10–12 h/session) enhances the survival rate of patients with ARDS.

Prone position ventilation combined with non-invasive ventilation can also help to steer clear of intubation in patients with moderate ARDS according to an observational study by Ding et al. (2020). 73% of inpatients suffering from mild ARDS avoided intubation. This is due to improved oxygenation in these patients which is due to prone positioning. There are, however, some limitations to the study, with the main one being the small sample size (of only 20 patients).

Although prone positioning has several benefits in the treatment of ARDS, there are also numerous complications associated with this treatment mechanism. Skin breakdown, fluid build-up in the face due to increased capillary permeability, brachial plexus neuropathy, obstructed endotracheal tube, slower heart rate, and low blood pressure are the main problems involved (Girard et al., 2014). Patients in the prone position on average are likely to get more pressure ulcers than patients in the supine position.

All in all, the literature supports the early use of prone position ventilation in looking after patients with critical ARDS. This is mostly due to physiological improvements such as improved gas exchange (Scholten et al., 2017) and a decrease in the death rate when the prone position is maintained for a long duration of time (12 hours). According to Albert et al. (2019), benefits or lack of usefulness of prone position ventilation has still not been recorded for patients suffering from mild or moderate ARDS. Therefore, more trials and studies are needed in the treatment of patients with less serious ARDS. Staff involved in treatment must be observant to reduce the instances of complications of prone positioning mentioned above.

Low volume tidal ventilation:

The mortality rate of ARDS remains high (20%-40%) even after 50 years since its first introduction in 1969 (Ochiai et al., 2015). There are many reasons considered to be contributing to the higher mortality rate in patients with ARDS; this includes the lack of knowledge on the pathological process of ARDS and appropriate ventilator support. Since ARDS causes severe impairment in gas exchange, mechanical ventilation is the major supportive and invasive treatment used in these patients. Nevertheless, it can cause more injury to the lungs, including barotrauma, volutrauma, atelectauma, biotrauma etc. (Slutsky et al., 2013). A reduction in ventilator induced lung injury (VILI) is largely associated with a decrease in mortality in patients with ARDS. High inspiratory pressure, respiratory rate and PEEP are some contributing factors of VILI (Gattinoni et al., 2016). To improve outcome in these patients, it is important to establish lung-protective ventilator strategies. There have been many randomized controlled clinical trials (RCTs) and observational studies to understand the best ventilator parameter to be used in order to reduce the harm whilst maintaining good gas exchange (Gattinoni et al., 2016).

Airway pressure release ventilation (APRV), low tidal volume ventilation (LTVV) and high-frequency oscillation ventilation are some of the ventilation strategies used to reduce VILI. High frequency oscillation ventilation is more widely used in children. APRV is an open lung approach which is used in patients who are difficult to oxygenate (Dries et al., 2009). A relatively high continuous positive airway pressure is delivered with unrestricted spontaneous breathing and thus it reduces the patient-ventilator asynchrony (Daoud et al., 2012). It also helps to improve and maintain the alveolar recruitment. However, this mode of ventilation cannot be used in patients who require deep sedation as it demands the patient to breath spontaneously. There are not enough randomized control studies available so far and consequently not enough data to provide evidence on the benefits of APRV and subsequent mortality when compared with other ventilation strategies.

Current evidence suggests that ventilator settings using a low tidal volume (4-6mls/kg) and a high PEEP (Positive End Expiratory pressure) are essential to reduce death. A possible benefit of low-tidal volume ventilation on ARDS patients was first published in 1998 based on a clinical trial on a small group of 53 patients. In that study, Amato et al. (1998) compared the relative efficacy of the protective ventilation strategies using a low tidal volume ventilation with conventional ventilation strategies. However, this study was criticized by some, as the patients who were recruited for this study were extremely ill with multi organ failure. Therefore, mortality could be related to various other factors than the respiratory failure (Bein et al., 2013). Moreover, Fuller et al. (2013) reported that the LTVV is only beneficial if the patients did not manifest ARDS at the time of initial intubation.

A trial conducted by (Brower et al., 2000) in 129 patients revealed that there was a large decrease in mortality when a low tidal volume strategy with plateau pressure less than 30 cm H2O were used. However, this study concentrated more on the efficiency of ventilation strategy and paid little attention to the severity of ARDS in these patients. Terragni et al. (2007) conducted a study in 150 patients, which demonstrated that patients are still prone to get VILI despite the usage of low tidal volume ventilation in case of severe ARDS with more significant lung collapse.

A study by Weiss et al., (2016) in ICU patients from 3 different hospitals from diverse backgrounds indicated that reduction in mortality is associated with early utilization of LTVV in ARDS who met the Berlin definition of ARDS. However, this study also revealed that there had been delays in identifying the syndrome and subsequent delay in commencing LTVV.

In summary, early recognition and application of ventilation with low tidal volume (4-8 ml/kg predicted body weight), high respiratory rate (Up to 35BPM), inspiratory pressure less than 30cm

H2O and inspiratory-expiratory ratio less than 1 are associated with a better survival rate (Munshi et al., 2017). It also emphasizes the need for titrating the PEEP in order to maintain oxygenation.

Neuromuscular blocking agents:

Neuromuscular blocking agents (NMBAs) are a popular choice of treatment used to treat patients with ARDS as nearly half of patients with ARDS are treated with an NMBA (Torbic et al., 2019). This is because NMBAs are thought to reduce inflammation; it also decreases the oxygen demand for the body. As oxygen demand is reduced, heart rate also lowers, reducing cardiac output. NMBA's work by blocking the acetylcholine receptors on the postsynaptic neurone, thereby blocking the transmission of nerve impulses and inducing reversible muscle paralysis, thus inhibiting spontaneous breathing (Bourenne et al., 2017). A recent study specified that a 48-hour infusion of an NMBA might decrease the intensive care unit (ICU) death in patients with moderate to severe ARDS (Tao et al., 2018). Besides, NMBA also helps in reducing the risk of barotrauma, and it claims not to aggravate the chances of critical care induced myopathy (Neto et al., 2012; Alhazzani et al., 2013).

The two main NMBAs currently used in intensive care units (ICU's) are Atracurium and Cisatracurium, both of which are non-depolarizing NMBAs. These NMBAs work by competing with acetylcholine for the acetylcholine receptor, binding to it and inhibiting transmission of nerve impulses. The drug of choice for continuous infusions is Cisatracurium in most of the critical care units (Zheng et al., 2020). Cisatracurium works by eliminating ventilator desynchrony and consequently lowering the chances of VILI. This research suggests that Cisatracurium provides positive results for patients suffering from ARDS. Observation of NMBAs for severely unwell patients requires using the train of four (TO4) assessments; the clinical assessment of triggering on ventilator, shivering, and peripheral nerve excitation and stimulation (Murray et al., 2016).

A comparative study by Moore et al. (2017), comparing the clinical effects of Cisatracurium versus atracurium, discovered there were no differences in clinical outcomes between the two NMBAs. Patients who were treated with Cisatracurium and atracurium had very similar improvement of PaO2 /FIO2; as well as ICU stay length days and number of days not using a ventilator was likewise similar. However, a slight contrast was found with the inpatient mortality rates, with patients treated with Cisatracurium having a 12% less mortality rate than patients being treated with atracurium. However, one of the problems that can be said about this study is the disproportionate number of people treated with each NMBA. While 58 subjects were treated with Cisatracurium, only 18 were treated with atracurium.

Whilst favorable outcomes of NMBAs, such as improved oxygenation are known (Grawe et al., 2016). Side-effects, such as continued neuromuscular weakness, have also been recorded (Warr et al., 2011). As NMBAs paralyze the diaphragm in the treatment of ARDS, NMBAs linked with sedation could be accountable for the development of lung atelectasis.

A study by Chang et al. (2017) concluded that using NMBAs in moderate to critical ARDS remarkably lowers mortality. This is due to the beneficial effects of NMBAs, such as facilitating patient-ventilator synchrony and providing protection from VILI.

The literature supports NMBAs in patients with severe to moderate ARDS. NMBAs are the preferred pharmacological treatment option in ARDS primarily due to their mortality benefit in patients with moderate to severe ARDS. According to Torbic et al. (2019), they offer the most benefit when used early before the lungs progress to the fibrotic (thickening/scarring) period of ARDS.

Conclusion:

Although Acute Respiratory Distress Syndrome was discovered and described in the late 1960s, it carries on to be associated with high mortality and morbidity. The Berlin 2012 definition of ARDS has made it easier to diagnose the condition. Still, the management and treatment of patients with ARDS are not standardized and is dependent on the Physician. Several reviews and randomized controlled trials support the use of early prone position for a long duration due to the mortality improvement in patients with ARDS. Low tidal volume ventilation also lowers death in patients with ARDS as well as reducing the chances of ventilator-induced lung injury. Neuromuscular blocking agents have also shown improved oxygenation in patients therefore reducing the rates of mortality in patients. Whilst treatment is available for ARDS more research needs to be done to make a standardized treatment plan for acute, mild and severe ARDS, as well as trying to make a patient-centred approach.

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