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THE BENEFITS OF THE PRONE POSITION IN PATIENTS WITH RESPIRATORY DISTRESS SYNDROME DUE TO COVID-19

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Abstract: In December 2019, we were faced with a rapidly contagious virus that gradually spread around the world: COVID-19. A virus that has mobilized the world in a constant strategy of how to fight it. Among numerous complications, a severe form of COVID-19 is presented by Acute Respiratory Distress Syndrome, leading to intubation by mechanical ventilation and even death in a large number of people. The aim of this study is to review and analyze the benefits and strategies of the prone position in patients with severe acute respiratory distress syndrome due to COVID-19. This is an integrative review, carried out through an online search and the capture of these productions was processed through PubMed and SciELO, totaling 17 articles selected for the study. According to the research, the prone position applied as a protective strategy and not as a rescue, in patients on mechanical ventilation or not, contributed to a better outcome. There is a need for guidance on the indication, staff training and association with all protective behaviors.

Keywords: COVID-19, Acute Respiratory Distress Syndrome, prone position

INTRODUCTION

In December 2019, cases of viral pneumonia of an unidentified form were reported in the city of Wunhan, Hubei province, China. This virus gradually spread around the world in the following weeks. Chinese scientists isolated the causative virus. In January 2020, a new Coronavirus (SARS-CoV-2). Coronaviruses are groups of viruses that have been known since the mid-1960s. In February of the same year, the World Health Organization (WHO) named this pathology covid-19.⁽¹⁾

Being able to infect many animals, especially mammals and birds, until the beginning of the pandemic, six species of coronavirus were known to cause disease in humans. Among these species, four cause symptoms of

the common cold and two others are known to cause severe respiratory syndromes, with mortality rates of around 10 and 35%.⁽²⁾

The disease has spread rapidly and has become a cause for concern due to the high numbers of people infected and dead around the world. According to the latest update on September 3, 2021, 219 million cases of COVID-19 and 4.55 million deaths have been confirmed worldwide. In Brazil, as of August 7, 21 million cases and 588,000 deaths had already been confirmed.⁽³⁾

COVID-19 is characterized by having a broad clinical spectrum, covering asymptomatic infection, mild upper respiratory tract disease and severe viral pneumonia with respiratory failure, multiple organ failure and even death. The most common symptoms at the onset of COVID-19 are fever (98%), cough (76%) and fatigue, while other symptoms include dyspnea (55%), headache, hemoptysis, anosmia, dysgeusia. Gastrointestinal disorders are also observed; diarrhea and vomiting. In its severe form, the clinical characteristics revealed point to the development of Acute Respiratory Distress Syndrome (ARDS), acute heart damage and thrombotic phenomena. Severe symptoms include dyspnea with a respiratory rate greater than or equal to 30 breaths per minute, pulse oxygen saturation of less than 93%, or even a drop in saturation without any obvious respiratory manifestations. It's worth noting that all these symptoms can be associated, partially associated or isolated.

Risk factors contribute to the development of a more serious condition, including hypertension, type 2 diabetes mellitus, respiratory and cardiovascular diseases, immunosuppressants and obesity. Although there is no evidence of severe disease in pregnant women, they are more vulnerable to viral infection.

ARDS is characterized by a rapid onset, with clinical signs of respiratory failure, hypervolemia, lung opacity on X-ray and a

significant drop in the partial ratio of oxygen in arterial blood (PaO₂) to the fraction of inspired oxygen (FiO₂) of less than 300.⁽⁴⁾

In these cases, interventions are recommended which include: mechanical ventilation with protective strategies, increasing the level of end-expiratory pressure (PEEP), alveolar recruitment maneuvers and positioning the patient in the prone position (PP).⁽⁵⁾

Various mechanisms have been proposed since the 1970s to explain the interference of the prone position on patient oxygenation, but only in recent years has it been considered potentially applicable in ARDS therapy. With the aim of increasing oxygenation, respiratory mechanics, alveolar insufflation and ventilation distribution, it homogenizes the pleural pressure gradient, limiting pulmonary hyperinflation. It is useful for increasing lung volume and reducing the amount of atelectasis in the dependent lung.⁽⁶⁾

During PP, the cardiac and mediastinal contents weigh on the dependent region, leading to a reduction in the compressive forces on the upper lung parenchyma and a consequent increase in the area available for gas exchange. In the PP, the collapsed lung volume is influenced by the weight of the lung and heart, and is smaller when compared to the supine position. As perfusion in this region is preserved, the ventilation/perfusion ratio (V/Q) becomes optimized in the PP. In addition, a more homogeneous dispersion of alveolar volume can minimize the possibility of *stretch* and *strain*.

In view of the above, and in the face of the current pandemic, questions have been raised about the effectiveness of PP as a protective strategy and therapeutic resource with early or rescue management.

OBJECTIVE

The aim of this study is to review and analyze the benefits and strategies of the prone position in patients with severe acute respiratory disease syndrome due to COVID-19.

MATERIAL AND METHOD

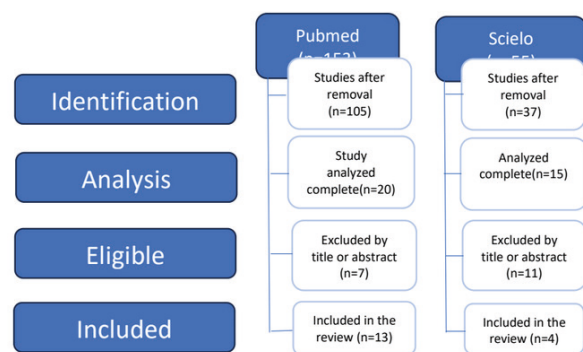
Integrative literature review study. It is a method that provides the synthesis of knowledge and the incorporation of the applicability of the results of significant studies into practice. This is a study carried out by means of a bibliographic survey and based on the author's experience of carrying out an integrative review.

To prepare this review, the following methodological procedures will be followed: formulation of the review question and objectives; establishment of criteria for selecting articles; categorization of studies; evaluation of the studies included in the integrative review; data analysis and presentation of the results.⁽⁸⁾

The study was carried out through an online search and the data was captured using PubMed and SciELO. The keywords used in the databases were "COVID-19, SARS-CoV-2, ARDS and prone position, with the Boolean operator "AND". This search resulted in 153 from PubMed and 55 from SciELO.

The inclusion criteria for these studies in this review were meeting the eligibility criteria (those articles that addressed the worsening of ARDS infection due to COVID-19 and the contribution of prone positioning), articles in English, a sample of more than 50 patients. The exclusion criteria were case report study design, reviews on the mechanism of infection and the virus, articles in languages other than English and neonatal and pediatric studies. Figure 1 shows the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) diagram based on reading the titles and abstracts: 183 articles were eliminated, leaving 25 articles.

Of these 25 articles, 5 were reviews of the virus and its mechanism of infection, and were disregarded. Finally, 3 studies emphasizing neonatal respiratory mechanics were eliminated. As a result, this review consisted of 17 articles analyzed by the author.



RESULT

In April 2020, Parisa Ghelichkhani and Maryam Esmaeili described that among the treatment methods introduced for the management of ARDS patients, the prone position can be used as an adjunctive therapy to improve ventilation in these patients. It should be prescribed together with low tidal volume (6ml per kg of body weight) and infusion of neuromuscular blockers (cisatracurium for 48 hours). These 3 treatment strategies together lead to improved oxygenation and survival in ARDS patients.⁽⁹⁾

Recently, in a multicenter observational study, Guérin et al. showed that only 13.7% of ARDS patients were placed in the prone position. Even in patients with severe ARDS, the rate of use of this technique was 32.9%. In the aforementioned study, 2 main reasons were given for the reluctance of doctors to use this treatment method: 1- Based on the judgment of doctors in most cases, hypoxia in patients with severe ARDS is not severe enough to justify the use of the prone position. 2- Most patients with ARDS have hemodynamic instability, which prevents the doctor from deciding to use the prone position.⁽¹⁰⁾

Altiney et al, in an August 2021 study of patients receiving mask oxygen therapy in intensive care units because of acute respiratory failure due to COVID-19 pneumonia, applied the prone awake position (PPA) to a certain group of patients. The values of PaCO₂, PaO₂, pH, SpO₂ and PaO₂/FiO₂ ratios were recorded at the beginning and 24 hours later. Patient demographics, comorbidities, need for intubation, days without ventilation, length of stay in the intensive care unit and short-term mortality were recorded. Among the patients who met the study criteria and were observed after the 24th hour, the median SpO₂ value of the PPA group was 95%, the median PaO₂ value was 82 mmHg, while the SpO₂ value of the non-PPA group was 90% and the PaO₂ value was 66 mmHg (p = 0.001, p = 0.002). There was no statistically significant difference between the groups in the length of stay in the intensive care unit and days without ventilation, but short-term mortality and the need for intubation were lower in the PPA group (p = 0.020, p = 0.001).⁽¹¹⁾

Janet O Adeola et al, in July 2021 carried out a review which found that prone positioning is well documented to improve oxygenation and cardiac function in patients with ARDS and can confer greater survival, with benefits that outweigh the risks, such as facial edema, endotracheal tube displacement and intra-abdominal organ dysfunction in obese patients. The use of this technique in COVID-19 requires prolonged sessions unprecedented in the treatment of ARDS patients.⁽¹²⁾

Jacob Rosen et al, in a multicenter randomized trial in June 2021, with adult patients with confirmed COVID-19, on high-flow nasal oxygen or non-invasive ventilation for respiratory support and a PaO₂/FiO₂ ratio ≤ 20 kPa were randomly assigned to a protocol targeting 16 h of prone positioning per day or standard care. The primary endpoint was intubation within 30 days. Secondary endpoints

included duration of prone positioning to awakening, 30-day mortality, ventilator-free days, length of hospital and intensive care unit stay, use of non-invasive ventilation, organ support and adverse events. Of the 141 patients assessed for eligibility, 75 were randomized, of whom 39 were allocated to the control group and 36 to the prone group. Within 30 days of enrollment, 13 patients (33%) were intubated in the control group versus 12 patients (33%) in the prone group (HR 1.01 (95% CI 0.46-2.21), $P = 0.99$). The median duration of prone was 3.4 h [IQR 1.8-8.4] in the control group compared to 9.0 h per day [IQR 4.4-10.6] in the prone group ($P = 0.014$). Nine patients (23%) in the control group had pressure sores compared with two patients (6%) in the prone group (difference - 18% (95% CI - 2 to - 33%); $P = 0.032$). There were no other differences in secondary outcomes between the groups.

Liu and colleagues demonstrated for the first time that the deformations suffered by the lung parenchyma inside the rib cage vary depending on body position. The authors showed that the position causes regional changes in pleural pressures, imposing a gradient along the gravitational axis of the lung, which is more homogeneous in this position when compared to the supine position.

Similarly, Petrone and colleagues, seeking to understand the behavior of the lung parenchyma during the prone position, showed that the heart “rested” on the lung parenchyma during the supine position, decreasing transpulmonary pressures in the regions just below the mediastinum, which was not seen during the prone position, since this allowed the heart to “rest” on the sternal region.

Klaiman et al demonstrated that the prone position in the first hours of ventilation significantly improves gas exchange and oxygenation, reducing the mean airway pressures required for ventilation, and can cause a significant improvement in survival.

But can we predict which patients will or won't respond? A small number of studies have looked at predictors of response. Chatte et al, in 1997, found that the level of PEEP applied, the length of mechanical ventilation prior to the maneuver and the fraction of inspired oxygen were predictors of response: higher PEEP levels (13.1 +/- 5 vs 7.9 +/- 4.3), longer mechanical ventilation time (5 +/- 8 vs 8 +/- 10) and higher inspired oxygen fractions (0.93 +/- 0.1 vs 0.71 +/- 0.16) are found in responder patients, i.e. patients who have had an increase in PaO₂ greater than 20 mmHg. Other factors such as age, SAPS (score), LIS (lung injury score) and tidal volume were not significant.⁽¹⁷⁾

The use of the prone position is related to a faster reduction in IMV parameters, such as inspiratory pressure and respiratory rate. In addition, it has been shown that the prone position can reduce the incidence of post-extubation atelectasis by up to half when compared to the supine position, without affecting any of the physiological parameters or causing adverse effects during the weaning process⁽¹⁸⁾.

Some randomized controlled trials in adults with ARDS in the prone position were unable to demonstrate a reduction in mortality; however, these trials included mild ARDS, short duration in the prone position and did not use low tidal volumes⁽¹⁹⁾.

More recently, a systematic review with meta-analysis evaluated adult patients who used the prone position compared to the supine position and who received a protective ventilation strategy. The hypotheses evaluated in this review were:

- Longer daily time in the prone position could optimize lung protection
- The prone position is more beneficial in patients with more severe hypoxemia
- The effect of the prone position on oxygenation was also analyzed in order to obtain data on the average PaO₂/FiO₂ ratio on the first, second and third day after randomization for each treatment group⁽¹¹⁾.

One of the adverse effects of the prone position for a patient with ARDS is the potential increase in intra-abdominal pressure and the concomitant changes in perfusion in important organs, such as the liver. ⁽¹²⁾

The prone position results in greater homogeneity in the ventilation/perfusion ratio, since there is a reduction in pulmonary shunt - more lung areas are recruited compared to the supine position, which has perfused but less ventilated areas ⁽¹³⁾.

Patients on mechanical lung ventilation, sedated and curarized, have reduced diaphragmatic muscle tone, and the abdominal contents cause a caudal deviation in the posterior portion of the diaphragm, leading to atelectasis in this region. When the prone position is instituted, there is a reduction in this deviation and, consequently, in the areas of alveolar collapse ⁽¹⁶⁾.

Overall, it seems that the studies on the efficacy of the prone position in ARDS patients clearly point out that the correct selection of the patient, the timely start and the duration of placing the patient in this position can affect the efficacy of this treatment method. The available meta-analyses show that the prone position can reduce mortality in ARDS patients when performed in the first hours of the disease, in patients with severely impaired oxygenation and for a long time. The suggested minimum duration of the prone position is 12 hours a day ⁽¹⁷⁾.

The improvement in oxygenation during prone ventilation is multifactorial, but occurs mainly through a reduction in pulmonary compression and improved pulmonary perfusion. CT image modeling data has shown that the asymmetry of the lung shape leads to a greater gravity gradient of induced pleural pressure when in the supine position compared to the prone position. Although prone is indicated in patients with severe ARDS who are not responding to other ventilation mo-

dalities, this technique has changed from a rescue therapy for refractory hypoxemia to an initial lung protection strategy aimed at improving survival in severe ARDS, especially given the current COVID-19 pandemic ⁽¹⁸⁾.

Several interventions for ARDS have been evaluated in this period in particular, prone positioning is one of the few therapeutic interventions for patients with severe ARDS that has demonstrated improved oxygenation and a survival benefit. Prone positioning outside intensive care (ICU) is safe and can decrease respiratory rate and improve oxygenation with early application potentially delaying the need for intubation in COVID-19 patients. physiologically, prone positioning can improve ventilation and perfusion matching, but studies have not associated physiological changes with clinical outcomes, especially in COVID-19. ⁽¹⁹⁾

Prone positioning may not be successful in all cases (10). Oxygen saturation or arterial gas levels should be closely monitored to assess responsiveness. If the patient cannot tolerate the position, right or left lateral positions can be tried. In addition, shorter prone position sessions can be considered for patients with mild or moderate ARDS (e.g. 2 hours in awake pregnant women). Prone positioning for intubated patients with severe ARDS is usually performed for at least 16 hours a day. Potential complications of prone positioning include edema facial and skin breakdown; pressure ulcers; dislodgement of the endotracheal tube, lines or drains; and worsening oxygenation or hemodynamic instability ⁽²⁰⁾.

The etiology of ARDS can also play a role in the response to the prone position. Although ARDS becomes a uniform pathology in advanced stages, in early stages it can originate from different etiologies. From previous data obtained in studies on alveolar recruitment maneuvers, we know that the response in PaO₂ can be different depending on whe-

ther the primary insult is pulmonary or extrapulmonary. Although both types of ARDS respond positively to the prone position, 63% of patients with extrapulmonary ARDS and only 29% with pulmonary ARDS have a significant response after one hour in the position. The time spent in the prone position also needs to be longer in pulmonary ARDS, around two hours, or sometimes longer, for there to be a response, while in extrapulmonary ARDS the PaO₂ may not differ between the first thirty minutes and the following two hours. This can be explained by the fact that alveolar/interstitial edema and compression atelectasis, which are more prominent in extrapulmonary ARDS, give way more easily to changes in transpulmonary pressure than the consolidation caused by epithelial damage and exudative inflammation found in pulmonary ARDS. Although extrapulmonary ARDS seems to have a better response to the prone position, mortality among patients in this group remains higher, regardless of whether the prone position is used or not ⁽⁽²¹⁾⁾.

CONCLUSION

It is indisputable that the prone position in patients with ARDS due to COVID-19 can reduce mortality and ventilation time. However, this strategy alone is not enough; it must be associated with other protection protocols for it to be of real benefit.

Prone positioning is a non-pharmacological strategy that should be part of the toolbox in every ICU that manages ARDS patients. Its use requires an understanding of the indications and risks, along with proper health system planning through the development of protocols, procedures and well-trained staff.

Replication of the results and scaling of the intervention are important, but prone positioning could represent an additional therapeutic option in patients with ARDS due to COVID-19.

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