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RESEARCH ARTICLE

NON-INVASIVE OXYGENATION METHODS IN PATIENTS WITH COVID-19

***Paulo López Reymundo, Irina Chávez Requena, Alejandro Castro Serrano, Diego Ramírez Urízar, Víctor Villalobos Álvarez and Roberto Jiménez Contreras**

Department of Critical Care, "Dr. Mario Shapiro" ABC Medical Center, Mexico City

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ABSTRACT

Since the start of the COVID-19 pandemic, the most frequent complications of this infection include pneumonia and Acute Respiratory Distress Syndrome. Hypoxemia and increased work of breathing are determining factors in adopting various non-invasive oxygenation therapeutic strategies in patients with COVID-19. It is important to know and describe the different modalities of non-invasive oxygen therapy, in order to preserve oxygenation and adequate respiratory work, the strategies described in the literature include: conventional nasal cannulas, high-flow nasal cannulas and non-invasive mechanical ventilation coupled with other support measures such as prone position, administration of schemes with steroids, immunomodulators and inhaled nitric oxide. Non-invasive oxygenation strategies by different methods are essential tools for the treatment of patients with moderate-severe COVID-19 pneumonia. It is necessary to evaluate the device to be used, since this disease has heterogeneous characteristics according to severity and time of evolution.

INTRODUCTION

Last December 2019, in the city of Wuhan, the disease due to the betacoronavirus COVID-19 was declared. This virus causes pneumonia with acute respiratory failure (ARF) conditioning the Severe Acute Respiratory Syndrome by Coronavirus-2 (SARS CoV-2).(1) Initial treatment of hypoxemia and ARF focuses on the administration of oxygen through nasal cannulae or mask. If gas exchange deteriorates progressively and oxygen demand increases, an indication for high-flow devices or non-invasive mechanical ventilation (NIMV) should be considered.(2)

Pathophysiology: The main manifestation of COVID-19 is hypoxemia, which can progress to Acute Respiratory Distress Syndrome (ARDS), defined by a partial pressure of arterial oxygen (PaO_2)/Fraction of inspired oxygen (FiO_2) ratio of less than 300mmHg.(3) Three areas have been descriptively characterized in the presentation of ARDS: 1) The lung zone with the greatest damage, which includes the dependent regions (with alveolar collapse and pleural effusion). 2) The intermediate zone (distinguished by partial collapse). 3) The less dependent areas where there is integrity of the alveolocapillary unit.(4)This affects pulmonary perfusion (Q) or ventilation (V), leading to a V/Q mismatch. (5)(6)

Mechanisms of cell infection and spread: How SARS CoV-2 spreads to the lower respiratory tract is unclear, but there are two theories:

- Microaspiration of SARS CoV-2 particles causes spread from the oropharynx to the lungs.
- The microparticles are transported directly to the lower part of the respiratory tract by the air flow, without going through the upper part.(7)

COVID-19 ARDS: COVID-19 ARDS is often associated with near-normal compliance of the respiratory system. Compliance may vary depending on the predominant pathological mechanism and time of evolution. Gattinoni et al. proposed two phenotypes of COVID-19 ARDS: type H, characterized by high elastance, high lung weight, and high recruitability; and type L, characterized by low elastance, low V/Q ratio, low lung weight, and low recruitability. (10)

High-Flow Nasal Cannula in COVID-19: Most affected patients can receive non-invasive respiratory support until pulmonary recovery. Spinelli et al. recommend oxygen therapy with High-Flow Nasal Cannula HFNC to administer positive pressure in the airway, with the consequent decrease in respiratory drive by clearing out carbon dioxide (CO_2)of the upper airway and improvement in oxygenation and lung compliance, without generating greater lung damage. HFNC have aroused interest as a system that is capable of offering high flow rates ranging from 30 to 60 liters/min of heated and humidified gas at a controlled oxygen concentration (13). Physiologic response to therapy includes increases in airway pressure, end-tidal lung volume, and oxygenation that are likely to be optimal at higher flow rates (50-60 L/min), while effects on airway bye washin out dead space and reduced work of breathing (WOB) can be obtained with intermediate flows (20-45 L/min) (14).

Corresponding author:** ***Paulo López Reymundo,
Department of Critical Care, "Dr. Mario Shapiro" ABC Medical Center, Mexico City.

In adults with ARF due to COVID-19 who do not improve with conventional oxygen therapy, escalation to non-invasive positive pressure devices such as HFNC is recommended before starting support with NIMV. In turn, it can help avoid the risks associated with invasive mechanical ventilation (IMV) such as delirium and cognitive impairment, weakness, and secondary infections (15). HFNC oxygen therapy should be initiated in a setting that has personnel trained to monitor the patient's clinical course and to recognize early signs of failure. There is the ROX index (iROX) that analyzes the respiratory rate (RR), partial oxygen saturation (SpO2) and FiO2 with the following formula: iROX= ([SpO2/FiO2]/RR) and predicts their failure. An RR<29 rpm at the second hour of treatment and an FiO2 <0.59 and iROX >5.98 at 8 hours are associated with success. Failure of this entails the need for mechanical ventilation (MV) with increased length of stay and mortality in the intensive care unit (ICU) (16).

NIMV in COVID-19: NIMV decreases the workload of the respiratory muscles, this may be benign or, failing that, increase lung damage. At the beginning of the pandemic, its use was not recommended due to the high risk of infection by aerosolization, and for this reason, it was contraindicated. As the pandemic reached its peak, the use of non-invasive devices became widespread. There are protective measures to prevent aerosolization, such as the administration of NIMV in a single room, preferably with negative pressure, as well as the placement of antiviral/antibacterial high-efficiency particulate air (HEPA) filters (17). Continuous positive airway pressure (CPAP) is an NIMV modality that administers positive pressure throughout the respiratory cycle, improves lung mechanics but can lead to poor CO_2 elimination, causing rebreathing, preventing a decrease in respiratory drive (18). Three Italian guidelines (Sorbello, Lazzeri et al. 2020) and one German guideline (Kluge et al. 2020) suggest that helmet NIMV should be the first choice among various interfaces. (19). Better helmet tolerance and reduced room contamination could also improve treatment and increase safety, and offers less resistance to the patient's respiratory effort compared to a mask (20).

Prediction of NIMV failure in COVID-19: In the absence of an indication for advanced airway management, the response to NIMV has been assessed with the HACOR scale for predicting failure, including level of consciousness assessed by Glasgow, heart rate (HR), RR, acidosis, and arterial oxygen saturation (SaO_2)/FiO_2. The highest score is 25 points, this scale is applied one hour after NIMV placement, a score ≥5 is equivalent to 81.8% diagnostic certainty for failure. In case of obtaining a lower score, it is still evaluated at 6, 12, 24 and 48 hours later (22)

Prone position in COVID-19: The prone position improves oxygenation in non-intubated patients with ARDS due to moderate to severe COVID-19, an increase in SpO2 of 84% to 94% has been reported in the first 5 minutes of prone position (23). Other benefits have been described, such as greater and better distribution of the tidal volume when prone in the dorsocaudal regions, since part of the lung is freed from the overload of the heart and abdomen. Lung perfusion continues to be preferentially distributed in the dorsal regions, with an improvement in the V/Q ratio (26). The PROSEVA study is one of the most relevant studies in terms of prone position and mechanical ventilation in which improvement in mortality of patients with ARDS and oxygenation less than 150 mmHg was evidenced, having a mortality of 23% vs 41% HR 0.44 (95% CI, 0.29-0.67) in those patients in supine opposition (25).

Inhaled nitric oxide (iNO) and NIMV in COVID-19: ARDS presentsincreased pulmonary vascular resistance secondary to increased shunts and hypoxic pulmonary vasoconstriction. Therefore, the use of nitric oxide is indicated as a selective vasodilator, reducing pulmonary arterial hypertension and improving gas exchange. Currently, the use of iNO has been proposed for spontaneously ventilated patients with respiratory failure who do not respond to conventional oxygen therapy (HFNC, NIMV) and in the prone position (27). Despite the pathophysiological appeal of iNO as adjuvant therapy to improve oxygenation in hypoxemic ARF related to COVID-19, there are still insufficient trials and the results are controversial with little evidence. Given the cost of this therapy, it is important to take this consideration into account when it is indicated (28)(29).

CONCLUSION

The importance of an adequate assessment and selection of a respiratory assistance device in patients with ARFdue to COVID-19, associated with other strategies to optimize management, are beneficial, and can even prevent the progression of respiratory failure and avoid complications. In case of no respiratory improvement, it is not recommended to prolong oxygen therapy with non-invasive devices because we condition the delay of IMV and increase mortality, for this reason we must individualize each therapeutic strategy. We do not have any clear recommendations on the use of iNO in patients with COVID-19. Regarding the investigations carried out, only improvement has been seen in terms of oxygenation and decrease in WOB. Although, more studies with greater statistical power are required to endorse this rescue therapy.

Prolong oxygen therapy with non-invasive devices in the absence of improved oxygenation leads to delayed intubation with increased mortality. Therapy should be individualized according to the patient.

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