

Pathophysiological aspects of COVID-19 and use of non-invasive ventilation. Is it possible?

Aspectos fisiopatológicos do COVID-19 e uso de ventilação não invasiva. É possível?

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According to the World Health Organization (WHO), in June 2020 the confirmed cases of COVID-19 caused by the coronavirus (SARS-CoV-2) had already exceeded seven million worldwide. Declared a pandemic state on March 11, 2020, health teams are faced with strategic plans for variable conducts¹ especially in the indication and handling of non-invasive ventilatory support.

The lethality rate of those infected is determined by the combination of intrinsic characteristics (comorbidities, age, immune system) and offer/availability of therapeutic resources². However, when considering mortality in hospitalized patients in a series of 5,700 cases admitted to 12 hospitals in New York was found that the age group between 20 and 50 years is larger than expected with a 10% increase in people between 20 and 30 years³. In addition, the disease has milder characteristics in the first week that worsens later, with death increased exponentially between the 12th and 24th day, mischaracterizing an acute process⁴.

Comorbidities are proportionally associated with the severity of the outcomes. To facilitate clinical

management and perform risk stratification, a group of Chinese researchers developed the CALL Score, which calculates according to comorbidities, age, lymphocyte value and LDH (lactate dehydrogenase). A score below 6 indicates a lower probability of progression while higher than 9 points, the opposite⁵. A worse prognosis was demonstrated in hospitalized patients with hypertension, diabetes and coronary heart disease, advanced age, high SOFA (Sequential Organ Failure Assessment) score (organ dysfunction) and high D-dimer values. SARS-CoV-2 was detectable until death and in survivors, with its longest duration being 37 days. The median release of the virus into the airways was at least 14 days, reaching 60 days^{6,7}.

The increase in lethality stimulates the search for effective means of treating the infection. Several indications and contraindications have been applied in the management of these patients, especially in relation to the use of non-invasive ventilation (NIV). This editorial seeks to address doubts about virus transmission, precautionary measures and how much these factors can influence the application of NIV.

The use of NIV can promote improvement in oxygenation and peripheral oxygen saturation, decrease in respiratory work and significant reduction in the need for intubation and mortality, when applied with safety criteria, in the appropriate manner and continuous monitoring. In a sample of 138 hospitalized, it was observed that dyspnea starts on the 5th day after infection, hospitalization on the 7th and ARDS on the 8th. High-flow oxygen therapy, NIV and invasive mechanical ventilation are applied in the ICU⁸. However, doubts remain about when to use NIV in confirmed cases of COVID-19. The key point of all discussions about the use of mechanical ventilation, whether invasive or not, revolves around the high risk of contamination by the virus.

In an official note, the National Health Surveillance Agency (ANVISA) created specific guidelines on the handling and disposal of waste used and especially, the importance of hand hygiene and the correct use of personal protective equipment (PPE) by health professionals, they are: cap, goggles or face protector, mask (surgical or respiratory protection - n95, depending on the procedure performed), waterproof long-sleeved apron and procedure gloves⁹.

Aerosol-generating procedures can increase contagion and include orotracheal intubation, NIV and manual ventilation after intubation. Tracheal aspiration, bronchoscopy, use of nebulizers, administration of oxygen therapy, high-flow nasal cannula, mask manipulation (oxygen therapy or NIV interfaces), defibrillation, chest compressions, insertion of a nasogastric tube and collection of pulmonary secretion. The most consistent transmission is strongly related to orotracheal intubation or tracheostomy, due to the need for long-term proximity to the patient's airway. The data found regarding contamination during the application of NIV were not strong enough to establish certainty to justify the veto to the procedure¹⁰. RNA samples from the SARS-CoV-2 virus were found in bedroom furniture, personal items and a particle dispersion corridor. The results lead us to ponder the potential for contamination of the genetic material found in aerosols, since in the cases mentioned, the samples did not grow in cultures¹¹.

In the first COVID-19 case confirmed in California, 121 professionals maintained contact with the patient, of these, 43 developed symptoms for 14 days after exposure and three had a confirmed result

of infection, despite not using the recommended PPE. In another hospital, of the 146 professionals involved in the care of contaminated people, none became infected, despite the use of PPE to care for patients on invasive ventilation with closed suction circuit since their admission. These findings lead us to believe in the efficiency of barriers in preventing contamination¹². Another case of a Chinese NIV patient who tested positive for SARS-CoV-2 at the time and after extubation is noteworthy. More than 35 professionals were involved in aerosol procedures, using a surgical mask, not the n95 mask, intended for use in these situations. All were followed up and none of them showed symptoms or positive results in the collections of oropharyngeal swab¹³. This leads us to conclude that there is still a need for more striking studies on the contamination of health teams.

In April, an interesting question was raised on the subject in *The Lancet*, initially pointing out that the fear of high transmissibility makes the teams exclude the possibility of non-invasive ventilatory measures, and also raises the pertinence of giving up the non-invasive resource as a practice in a limited resource scenario¹⁴. It is also important to mention that shortly after the pandemic state was declared, WHO made available a Guideline in which they do not restrict, but consider the use of NIV in a well-selected population of patients with hypoxemia^{14,15}.

The biggest concern of health professionals regarding NIV in confirmed cases of COVID-19 is the use of the open ventilation circuit. In these cases, air leakage is assumed, whether intentional or not, caused both by the need to use the exhalation valve in the circuit and by the fixation of the mask on the patient's face, thus increasing the spread of the virus in the environment, due to the dispersion of aerosols. Based on this principle, the recommendations suggest that patients are in contact precautions, droplets and aerosols; preferentially - not necessarily - in rooms with negative pressure, since these act by reducing the chance of infection, since the internal pressure of this room will remain lower than the external, preventing air currents^{16,17}.

In an attempt to attenuate a possible aerosolization, attention should be paid to the details of the ventilator circuit assembly, preferably opting for double branch circuits and high efficiency antibacterial/antiviral filters (both in the expiratory branch of the mechanical ventilator and proximal to the patient). As for the available interfaces, the good fit also minimizes the

generalized dispersion of exhaled air¹⁴⁻¹⁶. There is a preference for the Helmet® (non-ventilated mask), which can reduce the possibility of contamination. However, patients using NIVs separated into groups were evaluated for the effectiveness of the conventional face mask compared to the Helmet® interface (transparent hood that covers the patient's head and has a rubber collar on the neck). There was a significant reduction in intubation and mortality rates in the helmet group. It is worth noting that the use of the helmet provides leakage reduction and allows for higher adjustments of positive end-expiratory pressure (PEEP), enhancing alveolar recruitment and decreasing respiratory work¹⁷⁻²⁰. However, the full face mask also has minimal leakage and allows greater airway pressurization²¹.

In Spain, researchers drew up a clinical consensus with recommendations on non-invasive respiratory support (NIV and oxygen therapy with a high-flow nasal catheter) in adult patients with acute respiratory failure secondary to SARS-CoV-2 in an attempt to optimize clinical support, assist in identify the indication and describe the high risk processes of NIV failure, so that they are avoided. The results suggest application of NIV to patients with PaO₂/FiO₂ greater than 100 and without multiple organ failure (APACHE severity score less than 20). The use of NIV should be performed after careful evaluation for at least 30 minutes, not exceeding 60 minutes in these cases. If the patient does not present evident clinical improvement, such as decreased ventilatory discomfort, it is recommended to discontinue the attempt of non-invasive support, especially if the patient progresses with a minute volume greater than 10l/min, tidal volume above predicted 9ml/kg, respiratory rate above 25ipm, need for positive end-expiratory pressures greater than 10cmH₂O or need for high FiO₂ (increased to 50%). This set of signs shows severity that indicates the need for invasive ventilation. According to the Brazilian Mechanical Ventilation Guidelines, in a hypoxemic population, the success rate of NIV to prevent orotracheal intubation and other complications may be 50%^{16,21,22}. Another study suggests that the attempt at NIV should be indicated when the PaO₂/FiO₂ ratio is greater than or equal to 150 mmHg²³.

Some studies document the feasibility of performing NIV in patients with COVID-19 with good results in those who met the criteria for testing and using the

interface with mild and moderate ARDS submitted for five days to treatment with NIV associated with prone position. There was a significant improvement in peripheral oxygen saturation, increased oxygenation ratio and decreased respiratory rate. This is a therapeutic suggestion to be considered, where a positive response was observed in 80% of patients². Recently, a meta-analysis that included 25 studies involving 3,804 patients with acute hypoxemic respiratory failure, suggests the Helmet® interface as the most advantageous. The use of NIV was able to reduce mortality and orotracheal intubation, when compared to other oxygen therapy administration interfaces²⁰.

Controlled and randomized studies, systematic reviews with meta-analysis and more robust evidence are still needed, but NIV, in some confirmed cases of COVID-19, has been showing good results in clinical practice in several countries, including Brazil, in reports by physical therapists who are on the front line. The use of NIV and the correct use of PPE are fundamental to avoid contamination of the assistant team. In short, NIV should not be seen as an absolute restriction, it even seems to be a good indication for treatment, especially in a low-resource scenario, provided that it is performed safely, with careful monitoring and not delaying the indication for orotracheal intubation.

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