Is the Use of Metoprolol Effective in Infusion, in Critical State of Patients with COVID-19?

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Abstract. Acute respiratory distress syndrome is a common disease with high morbidity and mortality. Recently, it has gained relevance due to the pandemic generated by the SARS-CoV-2 infection, in which a large number of patients have required mechanical ventilation and management of the secondary syndrome. COVID-19 has caused more than 540,000 deaths throughout the world as the pandemic continues affecting millions of patients worldwide (Clemente-Moragón et al., 2021), with a clinical presentation ranging from isolated thrombosis to acute respiratory distress syndrome (ARDS) requiring respiratory support, in which infiltration is involving alveolar by activated neutrophils. The beta-blocker metoprolol has been shown to improve inflammation exacerbated in the setting of myocardial infarction (Middleton et al., 2020).

Keywords: COVID-19, metoprolol, respiratory failure, immunity

Introduction

In December 2019, the appearance of a series of pneumonia cases was evidenced in the city of Wuhan, capital of Hubei province, China; some of which were found related to the Huanan wholesale market of shellfish, fish and live animals, this is the probable place of origin of the causative agent of this disease (Clemente-Moragón et al., 2021). This new microorganism belonging to the Beta-coronavirus subfamily was completely sequenced by Chinese scientists on January 7 and named as new coronavirus 2019 (2019-nCoV, for its acronym in English) by the World Health Organization (WHO) on January 12, 2020. Subsequently, the coronavirus study group of the International Committee on Taxonomy of Viruses (ICTV) assigned this agent as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), and the disease it produces was named by the WHO on February 11 as COVID-19 (it is the acronym in English, coronavirus disease 2019). The rapid spread of SARS-CoV-2 on the various continents; with a high number of infected and deceased people, caused the WHO to declare COVID-19 a global pandemic on March 11 (Thompson, Chambers, & Liu, 2017).

It has been documented throughout multiple studies that SARS-CoV-2 infection has had a clinical presentation ranging from isolated thrombosis to acute respiratory distress syndrome (ARDS) requiring respiratory assistance, involving alveolar infiltration by activated neutrophils. The beta-blocker metoprolol has been shown to improve inflammation exacerbated in the setting of myocardial infarction (Zuo et al., 2020). In few studies performed, patients treated with metoprolol spent fewer days on invasive mechanical ventilation, also reducing the content of extracellular neutrophil traps and other markers of lung inflammation.

Intravenous administration of metoprolol to patients with ARDS associated with COVID-19 appears to be a safe and inexpensive strategy that can alleviate the burden of the COVID-19 pandemic (Casey & Ware, 2020).

Methodology

A systematic bibliographic search was carried out in databases such as: pubmed, sciencedirect, Wiley, using the following descriptors such as: COVID-19 and Metroprolol, respiratory failure due to COVID-19, metoprolol in infusion and critically ill patients due to COVID-19 of revision as originals regardless of their year of publication.

Results

SARS-Cov2 infection triggers a multisystemic inflammatory disorder, cytokine-induced hyperinflammation and changes in the white blood cell count. The innate immune response has been linked to the immunopathogenesis of COVID-19. In this sense, neutrophils have been highlighted as essential effector cells in the development of COVID-19. The role of neutrophils in lung tissue during SARS-CoV-2 infection. The neutrophil to lymphocyte ratio (NLR) is elevated in the bloodstream (Clemente-Moragón et al., 2021). Migrated neutrophils contribute to the formation of storm cytokines and release other mediators (Neutrophilic elastase) (Middleton et al., 2020). SARS-CoV-2 infection promotes the release of extracellular neutrophil traps, which can contribute to lung damage (Zuo et al., 2020) and immunothrombosis (Thompson, Chambers, & Liu, 2017). These many steps can be potential therapeutic targets. Similarly, many other cells and mediators are involved in the immunopathology of COVID-19 (Cavalcante-Silva et al., 2021) (Figure 1).

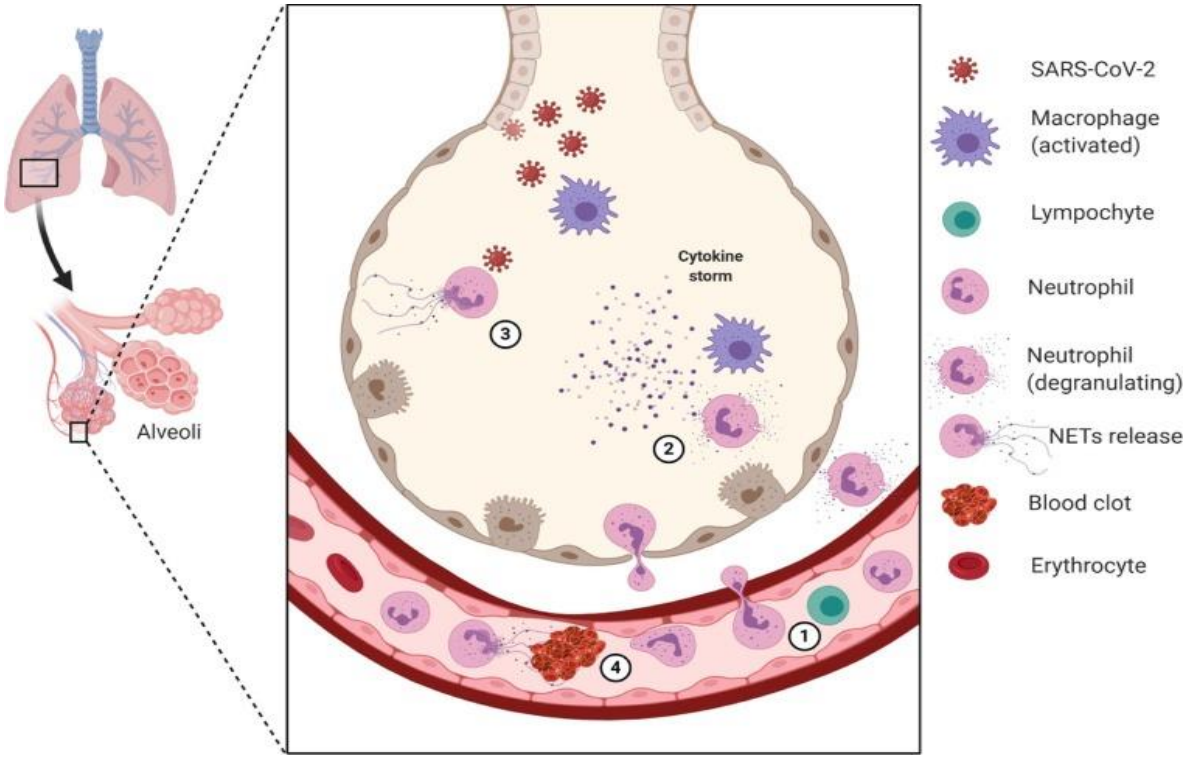

Figure 1. Release of extracellular neutrophil traps

Pilot trials with a total of 20 COVID-19 plus ARDS patients on invasive mechanical ventilation were randomized to metoprolol (15 mg daily for 3 days) or control (no treatment). All patients underwent bronchoalveolar lavage (BAL) before and after metoprolol / control. The safety of metoprolol administration was assessed by invasive electrocardiographic and

hemodynamic monitoring and echocardiography. Showing that the administration of metoprolol had no side effects. At the beginning of the study, the neutrophil content did not differ between the groups. In contrast, patients randomized to metoprolol had significantly fewer neutrophils on day 4. Metoprolol also reduced the content of extracellular neutrophil traps and other markers of lung inflammation. Oxygenation improved significantly after 3 days of metoprolol treatment at baseline and on day 4, while it was unchanged in control subjects. Patients treated with metoprolol spent fewer days on invasive mechanical ventilation than those in the control group.

Discussion

A trial of metoprolol in critically ill patients with COVID-19 published in the Journals of the American College of Cardiology shows that intravenous administration of metoprolol to patients with ARDS associated with COVID-19 was safe, reduced exacerbated lung inflammation and improved oxygenation. With studies showing that treatment with intravenous metoprolol (15 mg / day) for three days "significantly reduced the infiltration of neutrophils in the lungs and improved the oxygenation of patients" (Zuo et al., 2020). Clarifying that the basis of treatment lies in the early identification of the precipitating injury for its correction and the recognition of comorbidities that may impede recovery if they are not treated optimally. The start of oxygen therapy is recommended when oxygen saturation (SatO2) is less than 90%, to achieve goals of equal to or greater than 92% (Middleton et al., 2020). However, applying this strategy will reduce the admission of COVID-19 patients to the intensive care unit, reducing the risk of complications, in addition to being a safe and economical strategy that can alleviate the burden of the COVID-19 pandemic (Ashbaugh et al., 1967).

Conclusion

There are not many studies on patients treated with metoprolol infusion, however outgoing research shows that in patients who used the beta blocker spent fewer days on invasive mechanical ventilation, the content of extracellular neutrophil traps and other traps was also reduced. markers of lung inflammation. Intravenous administration of metoprolol to patients with ARDS associated with COVID-19 appears to be a safe and inexpensive strategy that may alleviate the burden of the COVID-19 pandemic but does not yet compromise many outstanding results compared to other significant strategies.

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