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COMMENTARY

Tocilizumab Improves Survival in Critically Ill Patients with COVID-19

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The pandemic caused by COVID-19 continues to be the main objective of hundreds of scientific societies and world organizations, to mitigate the impact it has generated on the human race, and to seek a solution definite eradication. Recent research on the pathophysiological process generated by this disease in humans has identified key molecular aspects for the creation of vaccines, or the specific use of some medicines that can control the inflammatory process produced at the multi-systemic level, and thus reduce morbidity and mortality rates [1,2]. As this virus has a strong tropism towards the lungs, bilateral diffuse alveolar lesion, and production of fibromyxoid exudate have been observed [3], various local immune response pathways have been evaluated, to find a target to regulate the inflammatory response, and to prevent multisystem complications [4]. Xu, et al. [2] made an invaluable finding, in which they show that during the inflammatory response there is a decrease in CD4+ and CD8+ T lymphocytes, but an increase in Th17 lymphocytes [2]. The latter is mainly stimulated by interleukins 6 (IL-6) and 23 (IL-23) [5]. These results were corroborated by Liu, et al. [6], who conducted a study in which 40 cases of COVID-19 patients were analyzed, arguing that severe cases have a sustained decrease in T lymphocytes, compared to moderate cases [6]. Besides, it was found that in severe cases there is a disproportionate increase of IL-2, IL-6, IL-10, and interferon-gamma, at peripheral level [6].

These observations have allowed drugs with specific targets for these molecules to be proposed, Tocilizumab being one of them. This drug is an IgG1-type recombinant anti-IL-6R monoclonal antibody that binds to IL-6 membrane receptors, inhibiting signal transduction [7]. It was initially released as an effective rheumatological therapeutic agent for rheumatoid arthritis and systemic juvenile idiopathic arthritis [8], however, it is postulated as a potential weapon for COVID-19.

Several studies have been carried out, finding favorable results in the fight against this disease with the use of this drug. Zhao, et al. [9] performed a systematic review and meta-analysis, where it was found that Tocilizumab decreased mortality in critically ill patients compared to the control group (19.5% vs. 28.3%; OR, 0.47; 95% CI, 0.36-0.60; $P < 0.00001$), concluding that this agent was effective [9]. Similar outcomes were found by Malgie, et al. [10] and Lan, et al. [11], supporting a reduction in mortality of 12% and 7.8% respectively [10,11]. It should be noted that in the study by Lan, et al. [11], there was no significant difference between the risk of admission to the Intensive Care Unit between the two groups, nor any difference between the need for mechanical ventilation [11] however, the socio-demographic and clinical characteristics of these groups, where the patients who medically intervened suffered from a more severe condition, must be taken into account.

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Another systematic review and meta-analysis that included 6279 patients showed that overall mortality was reported to be lower in the group in which Tocilizumab was used compared to the control group (Risk Difference (RD): -0.06, CI: -0.12 - -0.01, p = 0.03), and unlike the study by Lan, et al. [11], if the need for mechanical ventilation in the intervened group was lower (RD: -0.11, CI: -0.19 - -0.02, p = 0.01) [12]. Specifically, there is strong evidence on the quantitative impact of Tocilizumab on IL-6, as published by Antwi-Amoabeng, et al. [13], where the patients with COVID-19 exhibited average IL-6 values of 376.6 (148-900.6) pg/mL before treatment [13]. After treatment, these values decreased on average to 71.1 (31.9-122.8) pg/mL (p = 0.002), as did the C-reactive protein, which was on average 140.4 mg/L (P < 0.0001) before the intervention, and subsequently decreased these values to 24.6 mg/L on average [13]. This supports that Tocilizumab is a therapeutic agent with potential in critically ill patients with COVID-19, controlling the hyperinflammatory state, product of the cytokine storm.

The TOC-COVID study [14], a randomized, double-blind, placebo-controlled clinical trial, is currently being conducted to evaluate the efficacy and safety of Tocilizumab in patients with severe COVID-19 disease [14]. It is necessary to wait for the results of this study, to corroborate the outcomes that the evidence shows today, and to be able to certainly affirm that there is a therapeutic weapon capable of reducing the need for mechanical ventilation and mortality by COVID-19.

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Conflict of Interest

None.

Authors Contribution

All authors have contributed for this manuscript.

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