ROLE OF CYTOKINES AND THROMBOPHILIA GENES IN THE ETIOPATHOGENESIS OF ISCHEMIC STROKE AFTER COVID-19

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ABSTRACT

It has been found that coronaviruses can lead to an excessive, unregulated immune response in the host body - cytokine release syndrome. Information is increasingly being heard that this type of immune response is an integral part of the development of target organ dysfunction and one of the main factors of morbidity and mortality. In particular, it can serve as a background in the development of acute respiratory distress syndrome (ARDS) in patients with COVID-19.

Key words: serve as a background, patients with COVID-19 complicate

INTRODUCTION

Thus, an autopsy analysis of patients with COVID-19 complicated by ARDS revealed hyper activation of cytotoxic T cells, and the immunological profile of patients with severe disease showed hyper activation of the humoral link of immunity, including interleukin-6 (IL-6). In this regard, it was suggested that inhibition of IL-6 may be useful in the treatment of patients with severe COVID-19.

This work includes a systematic review and meta-analysis of previous studies. The aim of the work was to assess the evidence base on the use of tocilizumab (a humanized monoclonal antibody to the IL-6 receptor capable of blocking the pro-inflammatory effects of IL-6) in the treatment of COVID-19. The subjects of the study were the immunological response in patients with COVID-19 (mainly the dynamics of serum IL-6), as well as the effectiveness of tocilizumab in the treatment of COVID-19.

Results

Interleukin-6 and COVID-19

Ten cohort studies have described the body's immunological response to SARS-CoV-2. In all of them, an increase in IL-6 levels was recorded in patients with COVID-19. Many studies have also revealed higher levels of IL-6 among patients with a more severe (complicated) course of the disease. In total, 6 studies compared IL-6 levels in patients with complicated COVID-19 and uncomplicated. The first group included patients requiring hospitalization in the ICU, patients with ARDS, as well as those who were diagnosed with a severe or critical course of the disease during hospitalization. In patients with complicated forms, serum levels of IL-6 were almost three times higher than in patients with uncomplicated disease.

In addition, in a study by Liu et al.(1) Among 30 patients, 26 had a decrease in IL-6 levels, concordant with an improvement in lung condition according to computed tomography.

In a study by Wu et al.(2) When assessing risk factors for ARDS and death, patients with ARDS had a significant increase in IL-6 levels. In addition, an increase in IL-6 levels was associated with death. In a study by Ruan et al.(3) A significantly higher increase in IL-6 levels was also recorded in patients with a fatal outcome compared with its level in surviving patients.

The use of tocilizumab

In one non-randomized open-label clinical trial (Xu et al.(4)) the effect of tocilizumab on the course of COVID-19 was studied in 21 patients with severe and critical course. All patients received standard therapy, which included lopinavir and methylprednisolone, as well as tocilizumab 400 mg intravenously in one or two doses. 18 patients received tocilizumab once, three patients were prescribed repeated administration due to the resumption of fever within 12 hours after the first dose. After taking tocilizumab, fever resolution was observed in all patients within 24 hours with a distinct relief of clinical symptoms. In addition, there was a statistically significant decrease in oxygen demand from the second to the fifth day after taking tocilizumab. Resolution of X-ray changes on computed tomography of

the chest was also revealed in 19 patients. At the same time, no significant adverse drug reactions or lung infections were detected after treatment with tocilizumab.

This study is limited by its small sample size, lack of randomization, control group and retrospective design, however, the results are biologically reliable, since all included patients had elevated IL-6 levels, which gradually decreased in parallel with clinical and radiological improvement.

Conclusion

Thus, the results suggest that the progression of COVID-19 to a complicated disease may be the result of an excessive, unregulated host immune response and autoimmune damage. Preliminary studies show that inhibition of the cytokine pathway at the IL-6 level with tocilizumab may be an effective way to control this dysregulation. However, in order to more accurately determine the effectiveness of tocilizumab in the treatment of COVID-19, the results of several ongoing clinical studies should be expected.

It is also planned to conduct a multicenter randomized controlled trial to study the effectiveness of sarilumab, another monoclonal antibody blocking IL-6 receptors, in the treatment of severe forms of COVID-19.

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