

"ALLEGATO B"



Correlations between IL-6 serum level and olfactory dysfunction severity in COVID-19 patients: a preliminary study

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Abstract

Background Interleukin 6 (IL-6) is a proinflammatory cytokine that is secreted by cells infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and it is widely recognized as a negative prognostic factor. The purpose of this study was to analyze the correlations between the olfactory scores determined by psychophysical tests and the serum levels of IL-6 in patients affected by coronavirus disease 2019 (COVID-19)

Methods Patients underwent psychophysical olfactory assessment with Connecticut Chemosensory Clinical Research Center test and IL-6 plasma level determination within 10 days of the clinical onset of COVID-19.

Results Seventy-four COVID-19 patients were included in this study. COVID-19 staged as mild in 34 patients, moderate in 26 and severe in 14 cases. There were no significant differences in olfactory scores across the different COVID-19 severity groups. In the patient series, the median plasma level of IL-6 was 7.7 pg/mL (IQR 3.7–18.8). The concentration of IL-6 was found to be significantly correlated with the severity of COVID-19 with a directly proportional relationship. The correlation between IL-6 plasma concentrations and olfactory scores was weak ($r_s = 0.182$) and not significant ($p = 0.12$).

Conclusions In COVID-19 patients, psychophysical olfactory scores did not show significant correlations with the plasma levels of a well-recognized negative prognostic factor such as IL-6. This observation casts some shadows on the positive prognostic value of olfactory dysfunctions.

Keywords COVID-19 · IL-6 · Interleukin 6 · Smell · Anosmia · Cytokine · SARS-CoV-2 · Coronavirus · Cytokine storm

Introduction

Olfactory dysfunctions are one of the most frequent clinical manifestations of coronavirus disease 2019 (COVID-19), affecting more than 70% of patients infected with SARS-CoV-2 [1–5].

Recently, the prognostic value of olfactory disorders has been the subject of heated debate. Although some

researchers have found no correlation between the prevalence of loss of smell and severity of COVID-19 [6–9], many report that olfactory dysfunction is more frequent in mild forms [10–13] and some postulate that this is the price to pay for a more effective immune response against the virus in the olfactory epithelium [14].

Interleukin 6 (IL-6) is a proinflammatory cytokine that is secreted by cells infected with SARS-CoV-2 [15]. IL-6 is one of the factors behind the cytokine storm that occurs in the most severe cases of COVID-19 and serum levels of this cytokine are therefore a widely recognized negative prognostic factor [16–18]. Before the pandemic, only a few authors have investigated the correlation between the severity of chronic olfactory disorders and serum levels of IL-6, noting a statistically significant directly proportional correlation [19, 20]. These results support a hypothesis that IL-6 may play a role in biochemical pathological process underlying

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