Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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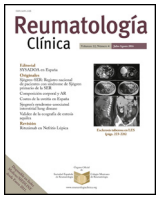

Letter to the Editor

Anakinra as a potential alternative in the treatment of severe acute respiratory infection associated with SARS-CoV-2 refractory to tocilizumab: comment☆

Anakinra, una alternativa potencial en el tratamiento de la infección respiratoria grave por SARS-CoV-2 refractaria a tocilizumab: comentario

Dear Editor,

We have read with interest the article by Figuero-Pérez et al. published in the last issue of your journal suggesting the usefulness of anakinra in severe respiratory SARS-CoV-2 infection refractory to tocilizumab[1] and would like to make some observations.

The clinical course of SARS-CoV-2 infection has three distinct clinical phases[2]. In the initial phase there is viral replication with flu-like symptoms and then some patients progress, between day 6 and 13 of symptom onset, to a hyperinflammatory phase with the development of pneumonia that may progress to respiratory distress syndrome.

The pathogenesis of severe SARS-CoV-2 infection involves dysregulation of the immune response with lymphopenia, increased pro-inflammatory cytokines (IL-1, IL-2, IL-6, IL-7 or TNF alpha) and a decrease in gamma-interferon. This leads to a systemic inflammatory syndrome with elevated acute phase reactants such as C-reactive protein and ferritin[3].

Treatment of this inflammatory phase with drugs such as dexamethasone or tocilizumab has been shown to reduce mortality[4,5].

Anakinra, an IL-1 receptor antagonist, has recently obtained EMA approval for treatment in adult patients with COVID-19 pneumonia and risk of progression to severe respiratory failure based on the SAVE MORE clinical trial which demonstrated a reduction in 28-day mortality and hospital stay in those treated early with anakinra[6].

There is little evidence regarding rescue therapy in patients with poor clinical outcome despite corticosteroids and/or immunomodulators. In an article published by our group[7], we analysed 143 patients with moderate/severe SARS-CoV-2 pneumonia and hyperinflammation treated with various regimens based on the protocols of that date. We observed that in those who had not responded to corticosteroids with or without tocilizumab, treatment with anakinra could be a useful alternative. Our patients received 100 mg/12 h on day 1 if they weighed between 50 and 60 kg, 100 mg/8 h between 60 and 75 kg or 100 mg/6 h if they weighed >75 kg. Subsequently all received 100 mg/12 h from day 2 to day 6. After adjustment for age and clinical severity indices, anakinra administration was associated with a reduced risk of mortality (HR; .518, 95% CI .265–.910, $p = .0437$).

In the case published by Figuero-Pérez et al.[1] we consider that it cannot be suggested that the patient's clinical improvement was due to anakinra when a single dose of 100 mg was administered. Given that the half-life of anakinra is 4–6 h and that of tocilizumab around 6 days, it is likely that the patient's improvement was due to the effect of tocilizumab. There is currently no consensus on the optimal doses of anakinra in this clinical setting, but higher and longer doses have been used in the literature[8,9].

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