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# Response to: 'Tocilizumab Rescue Therapy in Severe COVID-19 Pneumonia' (Ir Med J; Vol 114; No. 3; P289)

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Dear Sir,

We read with interest the data presented by Nurdin et al. on their experience with using tocilizumab as a rescue therapy in patients admitted to the intensive care unit with severe COVID-19 pneumonia. Following the results of their study the authors suggest that tocilizumab may have a role in the management of COVID-19 pneumonia. This conclusion appears to be largely based on the finding of markedly reduced C-reactive protein (CRP) serum levels as well as defervescence of fever following administration with tocilizumab.

The authors rightly conclude that, based on their data, it is difficult to attribute clinical benefit to tocilizumab use but that it may be of benefit in reducing the hyperinflammatory response. We would like to raise a word of caution about correlating a reduction in CRP levels with a positive clinical response to tocilizumab. Tocilizumab is a recombinant humanised monoclonal antibody that inhibits interleukin-6 (IL-6) from binding to its receptor (IL-6R)[1]. IL-6 is an inflammatory cytokine produced in response to infections and tissue damage and it has a key role in cytokine release syndrome (CRS). CRS is a recognised complication of COVID-19 and is associated with high mortality. Patients hospitalised with severe COVID-19 have been shown to have increased levels of IL-6, potentially attributable to CRS[2]. It is on that basis that IL-6 inhibitors are currently being used as experimental treatment options in patients with severe COVID-19.

After IL-6 is synthesized in the initial stage of inflammation, it moves through the bloodstream to the liver and induces hepatic synthesis of acute phase proteins including CRP[3]. Therefore, inhibition of IL-6 leads to a rapid reduction in CRP serum levels. Due to its mechanism of action, administration of tocilizumab in patients with COVID-19 is associated with a reduction in CRP serum levels regardless of clinical outcome and can suppress CRP response for up to three months post administration[4, 5].

In conclusion, while the study presented is interesting and further studies are warranted to evaluate the use of tocilizumab in patients with COVID-19, using CRP as an indicator of clinical efficacy is not advisable. The reason for this is that a significant drop in serum CRP levels is an expected finding following the use of tocilizumab and does not always correlate with a better outcome. Clinical parameters should be used to monitor response to treatment, such as oxygen requirements and the need for other organ supports, radiological progression, length of hospital stay and survival. A normal CRP should not be used to outrule bacterial superinfection; the use of additional biomarkers such as procalcitonin should be considered.

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