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

Tocilizumab in COVID-19: Beware the risk of intestinal perforation

Dear Editor,

Zhang et al. [1] discussed the use of tocilizumab, a monoclonal anti-IL-6 receptor antibody, in the treatment of cytokine release syndrome associated with severe COVID-19. Although tocilizumab may be beneficial in selected COVID-19 patients with a counter-productive hyperinflammatory phenotype, the efficacy and safety of such treatment is unknown. Tocilizumab is primarily used for rheumatological conditions, including rheumatoid arthritis and giant cell arteritis. Rheumatologists have extensive experience using tocilizumab; however, this may not be the case for intensivists, infectious disease specialists, and other physicians treating critically ill COVID-19 patients. Therefore, we would like to highlight a rare but feared complication of tocilizumab: intestinal perforation [2]. The mechanism for intestinal perforation in patients receiving tocilizumab is not fully understood, but prior diverticulitis has been noted as a risk factor [2].

The human host receptor of SARS-CoV-2 is angiotensin-converting enzyme 2 (ACE2), which is highly expressed in the intestines [3]. Intestinal viral replication is likely considering the ACE2 expression, gastrointestinal symptoms and presence of SARS-CoV-2 RNA in fecal samples [4,5]. Some gastrointestinal symptoms, such as abdominal pain, are associated with increased disease severity [5].

Furthermore, critically ill COVID-19 patients may have altered hemodynamics, potentially leading to intestinal hypoperfusion that can compromise intestinal mucosal integrity. More studies are required to evaluate whether these variables influence the risk of intestinal perforation with tocilizumab in critical COVID-19 cases; however, clinicians should be aware of the potential for this adverse event. Lastly, as tocilizumab attenuates the acute phase response, intestinal perforation may not necessarily cause significant C-reactive protein (CRP) elevation and may initially go unnoticed in sedated and ventilated patients.

Declarations

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References

[1] Zhang C, Wu Z, Li J-W, Zhao H, Wang G-Q. The cytokine release syndrome (CRS) of severe COVID-19 and Interleukin-6 receptor (IL-6R) antagonist Tocilizumab may be the key to reduce the mortality. Int J Antimicrob Agents 2020:105954. https://doi.org/10.1016/j.ijantimicag.2020.105954.
[2] Strangfeld A, Richter A, Siegmund B, Herzer P, Rockwitz K, Demary W, et al. Risk for lower intestinal perforations in patients with rheumatoid arthritis treated with tocilizumab in comparison to treatment with other biologic or conventional synthetic DMARDs. Ann Rheum Dis 2017;76:504–10. https://doi.org/10.1136/annrheumdis-2016-209773.
[3] Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci 2020;12:1–5. https://doi.org/10.1038/s41368-020-0074-x.
[4] Lin L, Jiang X, Zhang Z, Huang S, Zhang Z, Fang Z, et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. Gut 2020. https://doi.org/10.1136/gutjnl-2020-321013.
[5] Henry B, Olivera M, Benoit J, Lippi G. Gastrointestinal symptoms associated with severity of coronavirus disease 2019 (COVID-19): a pooled analysis. Intern Emerg Med 2020. https://doi.org/10.1007/s11739-020-02329-9.

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