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Letter to the Editor

Tocilizumab and remdesivir can be more harmful than beneficial to COVID-19 patients

Josef Finsterer
Neurology & Neurophysiology Center, Vienna, Austria

Corresponding Author: **Josef Finsterer**

We eagerly read the article by Chiu *et al*. about a review of the safety profile of anti-COVID-19 drugs [1]. It was concluded that hydroxy-chloroquine, lopinavir/ritonavir, ivermectin, chloroquine, and favipiravir should not be used for the treatment of COVID-19 patients [1]. On the contrary, tocilizumab, remdesivir, and dexamthasone were recommended for COVID-19 patients under certain conditions [1]. The study is appealing but raises concerns which require discussion.

Several adverse reactions following the use of tocilizumab were not acknowledged. One of the adverse reactions of tocilizumab is bowel ulceration [2]. Another adverse reaction not addressed is pyomyositis [3]. In a single patient lung and liver sarcoidosis-like reactions have been reported following the administration of tocilizumab [4]. There is also one report about tocilizumab-induced lupus [5]. In a 65yo male, treated with tocilizumab for rheumatoid arthritis, pericardial tamponade developed two months after initiation of the treatment [5]. According to an investigation by means of WHO's "VigiBase", tocilizumab increases the risk of reactivating hepatitis-B and tuberculosis [6]. According to this study the mean cumulative incidence of hepatitis-B and tuberculosis was 3.3% respectively 4.3% [6]. In a patient receiving tocilizumab for Takayasu arteritis, pyoderma gangrenosum developed following the anti-IL-6 therapy [7]. There are also indications that tocilizumab can reactivate psoriasis-like eruptions [8]. In a study of 74 patients receiving tocilizumab for COVID-19, 23% experienced late onset infections following tocilizumab use [9]. Bacteriemia and fungemia were also more frequently observed in the cohort receiving tocilizumab as comparted to the control group [9]. In a study of 2433 adverse reactions after tocilizumab reported to the worldwide FDA adverse event reporting system (WAERS), pancreatitis, and lung fibrosis were the most frequent in addition to liver injury [10].

In addition to the most commonly reported adverse reaction of remdesivir, liver injury, the drug potentially triggers a number of other side effects. In a study of the 12 COVID-19 patients in the US treated with remdesivir, three developed vomiting, rectal bleeding without other symptoms, nausea, and gastroparesis [11]. Additionally, remdesivir use can be complicated by kidney damage [12]. This is why remdesivir should not be used in patients with glomerular filtration rate <30 ml/min [13]. When evaluating 2922 adverse reactions to remdesivir reported to the FDA adverse reaction reporting system (FAERS), it was found 16,9% had kidney or urinary complications [12]. In a study of 86 pregnant females with severe COVID-19, treatment with remdesivir caused severe side effects in 16% of the included patients [14]. Side effects observed among these females included anemia, constipation, deep vein thrombosis, dysphagia, arterial hypertension, nausea, and pleural effusion [14], Which of these side effects were truly attributable to remdesivir and which to the COVID-19 infection remains speculative.

Not sufficiently addressed was the issue of combination anti-COVID-19 therapies. Frequently anti-COVID-19 drugs are given together with other amti-COVID-19 medication making it difficult to assess which of the compounds was effective respectively exhibited an adverse reaction.

Overall, the interesting review has several limitations which challenge the results and their interpretation. Adverse reactions of tocilizumab and remdesivir were not comprehensively assessed. Before recommending any compound as an anti-COVID-19 drug it has to be appropriately tested and reviewed for potentially severe adverse reactions not to additionally endanger COVIS-19 patients. If at all, tocilizumab and remdesivir should be applied with caution to COVID-19 patients.

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Consent for publication: was obtained from the patient

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Code availability: not applicable

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References

1. Chiu MN, Bhardwaj M, Sah SP. Safety profile of COVID-19 drugs in a real clinical setting. Eur J Clin Pharmacol, 2022, 1-21. Doi: 10.1007/s00228-021-03270-2.
2. Bruce-Hickman D, Sajeed SM, Pang YH, Seow CS, Chen W, Gulati Kansal M. Bowel ulceration following tocilizumab administration in a COVID-19 patient. BMJ Open Gastroenterol. 2020; 7:e000484. Doi: 10.1136/bmjgast-2020-000484.
3. Raine C, Hamdulay SS, Khanna M, Boyer L, Kinderlerer A. An unusual complication of tocilizumab therapy: MRI appearances of thenar eminence pyomyositis. Joint Bone Spine. 2013; 80:222. Doi: 10.1016/j.jbspin.2012.10.015.
4. Lambert N, Hansen I, El Moussaoui M, Giot JB, Vercheval C, Lommers É, *et al*. Lung and liver sarcoidosis-like reaction induced by tocilizumab. Br J Clin Pharmacol. 2021; 87:4848-4852. Doi: 10.1111/bcp.14878.
5. Miyahara D, Moriyama Y, Yamazaki Y, Tanii H, Okano Y, Sakurada H. Cardiac Tamponade During Tocilizumab Therapy in a Patient with Rheumatoid Arthritis and Anti-DNA Antibody Positivity. Intern Med. 2021; 60:3245-3249. Doi: 10.2169/internalmedicine.7166-21.
6. Campbell C, Andersson MI, Ansari MA, Moswela O, Misbah SA, Klenerman P, Matthews PC. Risk of Reactivation of Hepatitis B Virus (HBV) and Tuberculosis (TB) and Complications of Hepatitis C Virus (HCV) Following Tocilizumab Therapy: A Systematic Review to Inform Risk Assessment in the COVID-19 Era. Front Med (Lausanne). 2021; 8:706482. Doi: 10.3389/fmed.2021.706482.
7. Borgia F, Sutera D, Spagnolo A, Mazza F, Bertino L, Cannavò SP, Gallizzi R. Onset of pyoderma gangrenosum after tocilizumab therapy for Takayasu arteritis: A new undescribed paradoxical reaction. Br J Clin Pharmacol. 2021; 87:3378-3379. Doi: 10.1111/bcp.14756.
8. Saito Y, Hayashi S, Gonmori T, Hamasaki Y, Igawa K. Interrupting tocilizumab therapy-induced psoriasis-like eruption in a patient with rheumatoid arthritis and Crohn's disease. Int J Dermatol. 2020; 59:e159-e160. Doi: 10.1111/ijd.14809.
9. Pettit NN, Nguyen CT, Mutlu GM, Wu D, Kimmig L, Pitrak D, Pursell K. Late onset infectious complications and safety of tocilizumab in the management of COVID-19. J Med Virol. 2021; 93:1459-1464. Doi: 10.1002/jmv.26429.
10. Gatti M, Fusaroli M, Caraceni P, Poluzzi E, De Ponti F, Raschi E. Serious adverse events with tocilizumab: Pharmacovigilance as an aid to prioritize monitoring in COVID-19. Br J Clin Pharmacol. 2021; 87:1533-1540. Doi: 10.1111/bcp.14459.
11. The COVID-19 Investigation Team. First 12 patients with coronavirus disease 2019 (COVID-19) in the United States [published online ahead of print and peer review March 12, 2020]. medRxiv, 2020. Doi: 10.1101/2020.03.09.20032896
12. Rezaee H, Pourkarim F, Pourtaghi-Anvarian S, Entezari-Maleki T, Asvadi-Kermani T, Nouri-Vaskeh M. Drug-drug interactions with candidate medications used for COVID-19 treatment: An overview. Pharmacol Res Perspect. 2021; 9:e00705. Doi: 10.1002/prp2.705.
13. Silva NAO, Zara ALSA, Figueras A, Melo DO. Potential kidney damage associated with the use of remdesivir for COVID-19: Analysis of a pharmacovigilance database. Cad Saude Publica. 2021; 37:e00077721. Doi: 10.1590/0102-311X00077721.
14. Burwick RM, Yawetz S, Stephenson KE, Collier AY, Sen P, Blackburn BG, *et al*. Compassionate use of Remdesivir in Pregnant Women with Severe Coronavirus Disease 2019. Clin Infect Dis. 2021; 73:e3996-e4004. Doi: 10.1093/cid/ciaa1466.