Mini Review

Journal of Iranian Medical Council, Volume 4, Issue no. 2
http://dx.doi.org/10.18502/jimc.v4i2.6458

Rituximab Administration in Coronavirus Pandemic Era: A Mini-Review of Clinical Evidence

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Received: Dec 10 2020
Accepted: Feb 14 2021

Citation to this article:
Shamabadi A, Mahmoudi HR, Daneshpazhooh M. Rituximab Administration in Coronavirus Pandemic Era: A Mini-Review of Clinical Evidence. *J Iran Med Counc*. 2021;4(2):60-3.

Abstract

Rituximab (RTX), as a B cell-depleting agent, is indicated in treating several malignancies and autoimmune diseases. The management of patients currently receiving RTX and patients starting the medication raised concerns in the pandemic era. Theoretically, suppressing the immune response at the beginning of coronavirus disease 2019 (COVID-19) enhances viral replication, but it prevents acute respiratory distress syndrome as the disease progresses. This review aims to investigate the results of RTX administration in patients during the pandemic era. There is insufficient evidence to definitively conclude on the safety of RTX during the pandemic. For this purpose, high-quality controlled cohort studies, as well as registry-based studies, would be helpful.

Keywords: Coronavirus, COVID-19, Neoplasms, Pandemics, Rituximab

Introduction

Subsequent to the widespread outbreak of coronavirus, concerns arose about managing patients' treatment in need of immunosuppressants/immunomodulators. Rituximab (RTX), a CD20 as a B cell-depleting agent, is indicated in treating several cancers and autoimmune diseases (1). The management of patients currently receiving RTX and patients starting the medication raised concerns for therapists in the pandemic era due to the possibility of a flare-up in case that the patient is currently infected and consequently the risk of infection would be increased. Theoretically, suppressing the immune response at the beginning of coronavirus disease 2019 (COVID-19) enhances viral replication, but as the disease progresses, it prevents the cytokine release syndrome causing acute respiratory distress syndrome (2-4). Therefore, therapists in various fields began to share their data and experiences. This review aims to refer to the most significant studies on the topic in different fields and investigate the outcome of patients receiving RTX during the pandemic era. A personal archive on the topic and searches with related keywords in the Scopus and PubMed databases were used to find the studies described.

Discussion

Findings from neurology

Treating patients with a demyelinating disease with B-cell depleting antibodies increases their risk of developing symptoms of fever and cough, fever and shortness of breath, or COVID-19 indicative of lung involvement on Computed Tomography (CT) scans (5). In a retrospective cohort, Langer-Gould *et al* studied 1895 patients with Multiple Sclerosis (MS) undergoing RTX treatment. This study showed that the risk of COVID-19 in these patients is higher than in the non-MS population, but the rate of COVID-19 mortality was unaffected (6).

Findings from oncology

The RTX effect on COVID-19 patients in the oncology setting is also obscure. In a report of 55 COVID-19 cases, using any kind of oncologic treatments such as anti-CD20 agents did not significantly increase mortality rate (7). Among 219 patients with hematologic disorders, four SARS-CoV-2 infected patients were detected and two of them had a history of using RTX in a combination regimen. All four patients had a favorable outcome and completely recovered after medical treatment (8).

Findings from rheumatology

Data regarding the effects of B-cell depleting agents in the rheumatological setting are more controversial. For example, in the study of the global rheumatology alliance registry, patients on biologic treatment had no increased risk of hospitalization due to SARS-CoV-2 infection (9). However, there are two reports of severe clinical course and poor outcome of COVID-19 in patients with Systemic Sclerosis (SSc) (10) and Granulomatosis with Polyangiitis (GPA) (11). The first case of severe COVID-19 and late clinical worsening to severe pneumonia was reported in three patients with SSc who had received RTX. Avouac *et al* recommended providing continuous care for these patients under immunosuppressants due to the fact that RTX is often prescribed off-label in patients with SSc (10). They reported one patient with GPA treated with RTX two months before being infected with COVID-19. The patient developed severe pneumonia, which required supplemental oxygen (11). Meanwhile, in a case-series study in New York, among 86 patients with inflammatory diseases whose COVID-19 was confirmed (59 patients) or suspected (27 patients), only one patient with rheumatoid arthritis had a recent history of using RTX. The patient recovered after treatment with HCQ/azithromycin/lopinavir-ritonavir/tocilizumab and supplemental oxygen (12). Schulze-Koops *et al* reported two elderly patients with erosive rheumatoid arthritis and a history of receiving RTX with fatal outcomes (13). Additionally, in a cohort of 76 patients with rheumatic diseases who received RTX during the past year, 13 patients (17.1%) had suspected or confirmed COVID-19 and the rate of severe disease in cases requiring hospitalization was 61.5% and the mortality rate was 23.1%. This study suggested RTX treatment as a risk factor for unfavorable outcomes in COVID-19 patients with rheumatic diseases (14).

Findings from dermatology

Regarding the indications for the prescription of RTX in dermatology, several reports have been published about the patients receiving the medication during the pandemic. In one teledermatology study of patients with pemphigus vulgaris, five patients with COVID-19 diagnosed by CT scan did not receive RTX within a year

of the pandemic, while no infected case was reported in those who received the medication (15). In another study, none of the 12 patients with an autoimmune bullous disease treated with RTX developed any symptoms of COVID-19 or tested positive (16). In another study, one patient of a cohort of 48 patients with pemphigus who had received RTX had been diagnosed with COVID-19 (17). Kasperkiewicz M recommended avoiding discontinuation or delay in treatment by systematically reviewing reports of patients with autoimmune bullous diseases in need of immunomodulant agents and not just RTX (18). On the other hand, in a retrospective cohort study on 704 patients with an autoimmune bullous disease, 21 cases were diagnosed with COVID-19 by CT scan and/or SARS-CoV-2 RT-PCR. Fourteen of them (66.7%) had a history of receiving RTX within the past year. Each passing month of the last dose reduced the risk of COVID-19 and hospitalization by 38% and 45%, respectively. All three patients who succumbed to COVID-19 received RTX during the past year (19).

Conclusion

RTX has turned out to be the magic bullet for pemphigus treatment and is considered the first-line treatment of this difficult-to-treat disease (20). However, there is insufficient evidence to definitively conclude on the safety of RTX during the pandemic. For this purpose, high-quality controlled cohort and registry-based studies would be helpful. The data derived using high-quality studies could contribute to evidence-based medicine and the preparation of guidelines.

Till then, RTX should be carefully considered on an individual basis for moderate to severe pemphigus after evaluating its risks and benefits (21). In all fields, prescribers should take extra precautions, evaluate the safety and efficacy of extended dosing intervals, and lower doses due to fundamental importance of this medication. Regarding the higher risk of infection, the risk of death and short-term and long-term complications of the disease, patients should be advised on proper adherence to preventive measures (6,22,23). As mentioned earlier, a systematic searching was not applied in this study and all related literature was not investigated. Also, the discussion of vaccines in patients receiving RTX is beyond the subject of this article and should be addressed in future studies.

Acknowledgements

None.

Funding

None.

Conflict of Interest

The authors have no conflict of interest.

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