Innovative Journal of Medical and Health Science
Received 12 Jan 2021 | Revised 25 Feb 2021 | Accepted 26 Mar 2021 | Published Online 13 Apr 2021

DOI: https://doi.org/10.15520/ijmhs.v11i05.3293
I Jour Med Health Science 11 (05), 1672–1674 (2021)
ISSN (O) 2589-9341 | (P) 2277-4939 IF:1.6

LETTER TO THE EDITOR

Anti-COVID-19 drugs rather than SARS-CoV-2 exacerbate myasthenia

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Keywords: SARS-CoV-2, COVID-19, myasthenia, neuromuscular transmission, side effect, chloroquine, azithromycin

1 | LETTER TO THE EDITOR

With interest we read the article by Zupanic et al. about eight patients with known myasthenia gravis (MG) who experienced an infection with SARS-CoV-2 [1]. Four patients experienced exacerbation of MG during the infection while the remaining four patients did not experience worsening of MG during the infection with SARS-CoV-2. Three patients required mechanical ventilation and two oxygen supplementation. Six responded favourably to intravenous immunoglobulins (IVIG) [1]. One patient died [1]. It was concluded that the outcome of MG patients experiencing exacerbation of MG during an infection with SARS-CoV-2 is fair and that these patients profit from IVIG [1]. The study is appealing but raises the following comment and concerns.

The main shortcoming of the study is that the diagnosis MG was confirmed by elevated acetyl-choline receptor (AchR) antibodies in only half of the patients [1]. In two patients the antibody status was "unknown" and two further patients were negative for AchR antibodies [1]. Since the diagnosis remains unconfirmed in four patients they need to be excluded from the evaluation.

Since myasthenia may not only exacerbate due to an infection but also due addition of myotoxic drugs or increase of the dosage of already used drugs, it is crucial to know the entire medication the eight included patients were taking at the time of admission and the entire medication these patients received during hospitalisation. Several drugs given as an anti-COVID-therapy can potentially exacerbate MG. Furthermore, patients requiring ICU treatment, including mechanical ventilation, are usually exposed to drugs that are potentially myasthenia-toxic. Thus we should know if they received calcium, mag-

Supplementary information The online version of this article (https://doi.org/10.15520/ijmhs.v11i05.3293) contains supplementary material, which is available to authorized users.

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nesium, antibiotics, opiates, or chloroquine. From azithromycin, frequently given to COVID-19 patients, it is well-known that it can exacerbate MG [2] or even trigger the development of a myasthenic crisis [3]. There is also evidence that chloroquine, another frequently applied anti-COVID-19 medication, particularly in the first months of the pandemic, can trigger the development of MG [4]. Chloroquine is generally recommended not to be used in MG patients.

A further shortcoming is that exacerbation in four patients was not substantiated by carrying out repetitive nerve stimulation, single-fibre electromyography (SF-EMG), or edrophonium tests. Documentation of exacerbation of myasthenia by means of these tests is crucial as particularly worsening of respiratory function due to myasthenia often cannot be delineated from respiratory insufficiency due to the SARS-CoV-2 infection. It is also crucial that serum titers of causative antibodies against the acetyl-choline receptor (AchR), muscle-specific kinase (MUSK), titin, LRP4, or agrine are determined to substantiate if SARS-CoV-2 increased these serum levels during exacerbation/crisis or not.

Exacerbation of MG in SARS-CoV-2 positive patients may not only be managed by application of intravenous immunoglobulins (IVIG) but also by modification of the established myasthenia treatment or by plasmapheresis, or addition of a new immunosuppressive regimen.

We do not agree with the notion that the case series reported in the index article is the largest of COVID-19 patients with myasthenia. In a recent publication, 380 COVID-19 patients with myasthenia had been reported [5].

Overall, the interesting study has several shortcomings, which should be addressed before drawing final conclusions. It is crucial to delineate if the doctor or the virus is responsible for exacerbation and to avoid that myasthenia patients experiencing a SARS-CoV-2 infection receive medication that potentially worsens myasthenia. In case of respiratory failure, investigations for delineation between respiratory failure due to myasthenia or due to SARS-CoV-2 pneumonia should be carried out.

Declarations

Acknowledgement: none

Statement of ethics: was in accordance if ethical guidelines

Conflicts of interest: none

Funding sources: no funding was received

Author contribution: JF: design, literature search, discussion, first draft, critical comments, final approval, FS: literature search, first draft, discussion, critical comments, final approval, FS: literature search, discussion, critical comments, final approval

Informed consent: was obtained

The study was approved by the institutional review board

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How to cite this article: Finsterer J., F.A.S. **Anti-COVID-19 drugs rather than SARS-CoV-2 exacerbate myasthenia**. Innovative Journal of Medical and Health Science. 2021;1672−1674. https://doi.org/10.15520/ijmhs.v11i05.3293