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 Editors

The effect of potential therapeutic agents on QT interval in patients with COVID-19 Infection: The importance of close monitoring and correction of electrolytes

The novel coronavirus, which had initially led to pneumonia of unknown etiology in a series of patients in China's Hubei province in December 2019, has now precipitated a global health crisis [1]. With the number of infected individuals rising across the globe, identification of effective therapeutic strategies and management of their potential side effects has become of paramount importance. In the absence of solid evidence based on randomized controlled trials supporting a specific treatment, many healthcare professionals have resorted to the off-label use of different medications with a wide range of side effects. Hydroxychloroquine, lopinavir/ritonavir (Kaletra), and azithromycin are among these medications with anecdotal reports supporting their effectiveness in the treatment of this infection. However, all three of these medications are known to cause QT interval prolongation and therefore increase the risk of sudden cardiac death [2–4]. Furthermore, stress, fever, and electrolyte disturbance can make these individuals prone to arrhythmia. Abnormalities in potassium and magnesium levels are known to affect the QT interval [5]. Therefore, effective countermeasures to manage QTc prolonging effects of the treatments used in patients with COVID-19 infection could play a substantial role in the final outcome of the disease.

Herein, in a retrospective observational study, we report on the effectiveness of implementing the strategy of keeping potassium and magnesium levels above 4 mEq/L and 3 mg/dL respectively in preventing QT prolongation through supplementing these electrolytes in 13 patients diagnosed with COVID-19 infection according to positive SARS-CoV-2 PCR results or typical chest CT findings treated with one or a combination of these medications. On admission, baseline QTc assessment was done and at the same time treatment for COVID-19 was initiated unless QTc $\geq$ 460 ms. QTc was calculated using Bazett's formula. The mean $\pm$ SD pretreatment QTc was 417 $\pm$ 22 ms. At the same time baseline values for potassium and magnesium were measured and monitored in addition to providing supplementary doses of these electrolytes throughout the treatment in order to keep their levels above the mentioned thresholds suggested by the national protocol for the treatment of patients with COVID-19 infection. The QTc intervals were assessed every other day in order to monitor for QT prolongation. After a week of treatment, the QTc increased by an average of 14 (95% CI -7 to 35) ms, which was not statistically significant (Fig. 1). There was no incidence of arrhythmia or sudden cardiac arrest among the studied individuals.

Considering that our study had a minimum power of 80% for detecting a QTc prolongation of $\geq$ 30 ms, our findings provide supporting evidence for close monitoring and correction of the electrolytes during the treatment of patients with COVID-19 infection, particularly in those treated with medications that prolong the QT interval. We believe that our preliminary data can pave the way for randomized controlled trials investigating the efficacy of this intervention in a broader study population.

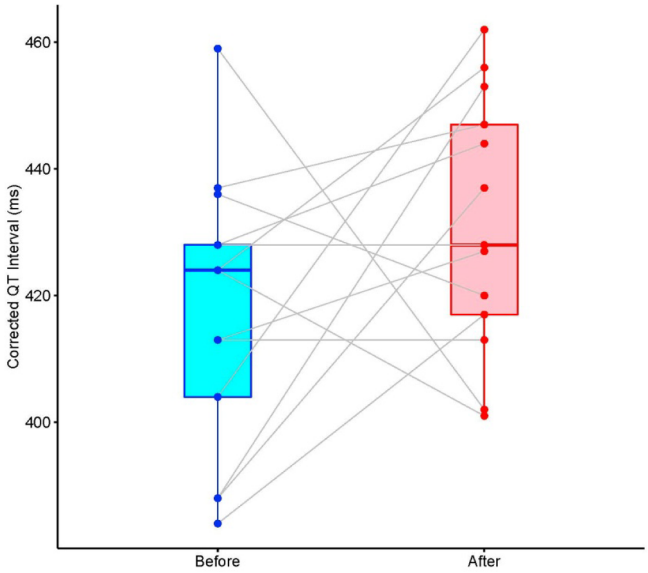

Fig. 1. . Box plot of corrected QT interval before and after treatment in patients with COVID-19 infection.

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Ethics Statement

Compliance with Ethical Standards

This investigation was conducted in accordance with the ethical principles and recommendations outlined in the Declaration of Helsinki.

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Prior Presentation

This manuscript has not been presented earlier.

Ethical approval

Ethics approval was waived for this observational study by the local ethics committee.

Informed consent

Written informed consent was obtained from all study participants.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Parham Habibzadeh[a,1], Mohsen Moghadami[b,2], Kamran Bagheri Lankarani[b,3,*]
[a] *Shiraz University of Medical Sciences, Shiraz, Iran*
[b] *Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran*
E-mail address: Lankaran@sums.ac.ir (K.B. Lankarani).

[*] Corresponding author at: Distinguished Professor of Medicine, Director Health Policy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
[1] https://orcid.org/0000-0002-2086-0425
[2] https://orcid.org/0000-0001-8015-0313
[3] https://orcid.org/0000-0002-7524-9017