



QT Interval Prolongation in COVID-19 Patients on Methadone Treatment

Maryam Sefidgarnia ¹, Susan Salari ² and Kamaledin Alaedini ^{2,*}

¹Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran

²Psychiatry and Behavioral Sciences Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran

*Corresponding author: Psychiatry and Behavioral Sciences Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran. Tel: +98-1133273024, Fax: +98-33285109, Email: k.alaedini@mazums.ac.ir

Received 2020 May 03; Revised 2020 May 10; Accepted 2020 May 11.

Keywords: COVID-19, Methadone, QT Interval

As a result of a widespread infection named coronavirus disease 2019 (COVID-19), there has been a critical request in the world for medications. Up to now, there are no proved effective therapeutic medicines for COVID-19. New medicines and immunizations will take time to be developed and disseminated to patients. Because of variables such as the history of prescription for other infectious diseases, availability, and relatively low cost (1), there has been increasing intrigue about the use of existing medications such as chloroquine (CQ) and hydroxychloroquine (HCQ) as potential treatments for this disease (2) or prophylaxis against COVID-19 (3). For instance, some overviews indicate that hydroxychloroquine is significantly associated with viral load reduction/disappearance in patients with COVID-19, and its impact is fortified by azithromycin (4).

Indeed, even though azithromycin is not approved for the treatment of viral pathogens, there are recounted reports that a few hospitals have started to use azithromycin in combination with hydroxychloroquine (HCQ) or chloroquine (CQ) for treatment of patients with COVID-19 (5). Tragically, these three specified drugs may increase the risk of QT prolongation and ventricular proarrhythmia, especially in severe COVID-19 patients (6).

Nowadays, methadone is one of the foremost popular synthetic opioids in the world with some favorable properties, making it a valuable treatment for both moderate to severe pain and opioid addiction. Unfortunately, this popular drug has multiple cardiac side effects, that the main of which is the prolongation of QT interval and torsade de pointes even at low doses (7). It is vital to note that using more than one proarrhythmic agent is known to extend the chance of significant QT prolongation (6, 8). In this manner, the administration of azithromycin and chloro-

quine/hydroxychloroquine, alone or in combination, for patients on methadone treatment may increase the risk of arrhythmia and death. It implies that the effectiveness of these drugs ought to be weighed against these unfavorable effects, and physicians need to consider the ways of reducing such undesirable impacts. We suggest that the risk of proarrhythmia be minimized by:

- 1) Taking exact drug history (especially for methadone consumption, as individuals may do not tend to report the history of methadone consumption due to social stigma);
- 2) Considering other risk factors such as old age, cardiac disease, diabetes, electrolyte abnormality, hypoglycemia, and renal failure (6);
- 3) Discontinuing unnecessary drugs that prolong QT interval or substitute with other agents with no such side effects (for example, replacement of methadone with buprenorphine);
- 4) Proper education of patients and physicians about this risk.

Footnotes

Authors' Contribution: Maryam Sefidgarnia and Kamaledin Alaedini collected the data and wrote the manuscript. Susan Salari wrote the manuscript. All authors contributed to the preparation of this manuscript, and all of them approved the manuscript for submission.

Conflict of Interests: None.

Funding/Support: None.

References

1. Pereira BB. Challenges and cares to promote rational use of chloroquine and hydroxychloroquine in the management of

- coronavirus disease 2019 (COVID-19) pandemic: A timely review. *J Toxicol Environ Health B Crit Rev.* 2020;**23**(4):177-81. doi: [10.1080/10937404.2020.1752340](https://doi.org/10.1080/10937404.2020.1752340). [PubMed: [32281481](https://pubmed.ncbi.nlm.nih.gov/32281481/)]. [PubMed Central: [PMC7157945](https://pubmed.ncbi.nlm.nih.gov/PMC7157945/)].
2. Gbinigie K, Frie K. Should chloroquine and hydroxychloroquine be used to treat COVID-19? A rapid review. *BJGP Open.* 2020. doi: [10.3399/bjgpopen20X101069](https://doi.org/10.3399/bjgpopen20X101069). [PubMed: [32265182](https://pubmed.ncbi.nlm.nih.gov/32265182/)].
 3. Shah S, Das S, Jain A, Misra DP, Negi VS. A systematic review of the prophylactic role of chloroquine and hydroxychloroquine in coronavirus disease-19 (COVID-19). *Int J Rheum Dis.* 2020. doi: [10.1111/1756-185X.13842](https://doi.org/10.1111/1756-185X.13842). [PubMed: [32281213](https://pubmed.ncbi.nlm.nih.gov/32281213/)].
 4. Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: Results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents.* 2020:105949. doi: [10.1016/j.ijantimicag.2020.105949](https://doi.org/10.1016/j.ijantimicag.2020.105949). [PubMed: [32205204](https://pubmed.ncbi.nlm.nih.gov/32205204/)]. [PubMed Central: [PMC7102549](https://pubmed.ncbi.nlm.nih.gov/PMC7102549/)].
 5. Damle B, Vourvahis M, Wang E, Leaney J, Corrigan B. Clinical pharmacology perspectives on the antiviral activity of azithromycin and use in COVID-19. *Clin Pharmacol Ther.* 2020. doi: [10.1002/cpt.1857](https://doi.org/10.1002/cpt.1857). [PubMed: [32302411](https://pubmed.ncbi.nlm.nih.gov/32302411/)].
 6. Sapp JL, Alqarawi W, MacIntyre CJ, Tadros R, Steinberg C, Roberts JD, et al. Guidance on minimizing risk of drug-induced ventricular arrhythmia during treatment of COVID-19: A statement from the Canadian Heart Rhythm Society. *Can J Cardiol.* 2020. doi: [10.1016/j.cjca.2020.04.003](https://doi.org/10.1016/j.cjca.2020.04.003). [PubMed: [32299753](https://pubmed.ncbi.nlm.nih.gov/32299753/)]. [PubMed Central: [PMC7195336](https://pubmed.ncbi.nlm.nih.gov/PMC7195336/)].
 7. Behzadi M, Joukar S, Beik A. Opioids and cardiac arrhythmia: A literature review. *Med Princ Pract.* 2018;**27**(5):401-14. doi: [10.1159/000492616](https://doi.org/10.1159/000492616). [PubMed: [30071529](https://pubmed.ncbi.nlm.nih.gov/30071529/)]. [PubMed Central: [PMC6244110](https://pubmed.ncbi.nlm.nih.gov/PMC6244110/)].
 8. Tisdale JE, Jaynes HA, Kingery JR, Mourad NA, Trujillo TN, Overholser BR, et al. Development and validation of a risk score to predict QT interval prolongation in hospitalized patients. *Circ Cardiovasc Qual Outcomes.* 2013;**6**(4):479-87. doi: [10.1161/CIRCOUTCOMES.113.000152](https://doi.org/10.1161/CIRCOUTCOMES.113.000152). [PubMed: [23716032](https://pubmed.ncbi.nlm.nih.gov/23716032/)]. [PubMed Central: [PMC3788679](https://pubmed.ncbi.nlm.nih.gov/PMC3788679/)].