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LETTERS TO THE EDITORS

# Response to the editorial ''COVID-19 in patients with cardiovascular diseases''. Covid-19 treatment with hydroxychloroquine or chloroquine and azithromycin: A potential risk of *Torsades de Pointes*

*Réponse à l'éditorial, « Response to the editorial ''COVID19 et maladies cardiovasculaires'' »*

*Keywords* Long QT syndrome; Chloroquine; Hydroxychloroquine; Azithromycin; *Torsade de Pointes*
*Mots clés* Syndrome du QT long ; Chloroquine ; Hydroxychloroquine ; Azithromycine ; Torsade de Pointes

A recent editorial in this journal elegantly discussed the influence of cardiovascular diseases on COVID-19 [1]. Another issue is associated with the potential risk of cardiac arrhythmias with chloroquine or hydroxychloroquine (sometimes combined with azithromycin), which are being proposed to treat COVID-19. All three drugs individually can rarely provoke life-threatening polymorphic ventricular tachycardia, often in the setting of marked QT interval prolongation. However, the effects of their combination on this risk, particularly in critically ill patients, are unclear.

Chloroquine blocks $I_{Kr}$ [2] —the main ionic current responsible for ventricular repolarisation— prolongs QT interval duration [3]; as a consequence, it can cause the malignant polymorphic ventricular tachycardia, *torsades de pointes*. The potential of hydroxychloroquine to prolong ventricular repolarisation is less well documented, but cases of QT prolongation and syncope have been reported during chronic treatment [4]. Azithromycin also mildly prolongs QT interval, possibly by different mechanisms [5], so its effect in combination with $I_{Kr}$ blockers is unknown.

Patients with COVID-19 infection have multiple risk factors for this syndrome. Hypokalemia, in the 3.0 — 3.4 mmol/L range, is common. Fever amplifies drug-induced $I_{Kr}$ blockade [6], and an increase in interleukin-6, as seen in COVID-19 infection [7], has been suggested as a mechanism of the QT prolongation associated with inflammation [8].

Until this risk is better evaluated in the context of the current pandemic, we urge physicians to monitor QT interval duration in patients with COVID-19 who are treated with chloroquine or hydroxychloroquine alone or in combination with azithromycin. The following practical measures should be considered:

- record an electrocardiogram before treatment initiation if possible. If rate-corrected QT (QTc, by Bazett's formula, or preferably using the Fridericia formula) is > 500 ms (higher values may be considered if treatment is deemed life-saving in desperate cases), or if the patient is known to have had torsades de pointes or has the congenital long QT syndrome, do not start the drugs;
- avoid any other concomitant non-essential drugs known to prolong QT;
- supplement potassium to > 4 mmol/L;
- if QTc is long (> 480 ms) at baseline, obtain an electrocardiogram again 2—4 hours after the initial dose, and if possible, monitor heart rhythm. Consider stopping therapy if QTc > 520 ms is documented;
- continue to monitor the electrocardiogram as appropriate during treatment (e.g. every other day).

We believe that these simple actions will limit the occurrence of *torsade de pointes*. If it does occur, the patient can be treated with intravenous magnesium and/or isoproterenol and treatment with the offending drug(s) discontinued.

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## Disclosure of interest

The authors declare that they have no competing interest.

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