Effect of hydroxychloroquine on the cardiac ventricular repolarization

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Introduction

Hydroxychloroquine has been suggested as possible treatment for **SARS-CoV-2 infection**. The WHO advised against use of hydroxychloroquine for SARS-CoV-2 infection, as **no clinical benefit** was shown. Also, studies reported **QTcF-prolongation** after treatment with hydroxychloroquine, mediated by **hERG channel** inhibition. QTcF-prolongation has been associated with Torsade de Pointes and cardiac death.

Aim

Analysis of the **concentration-dependent effects** of hydroxychloroquine on the ventricular repolarization, quantified as:

- QTcF-prolongation
- T-wave morphology: Morphology Combination Score (MCS)

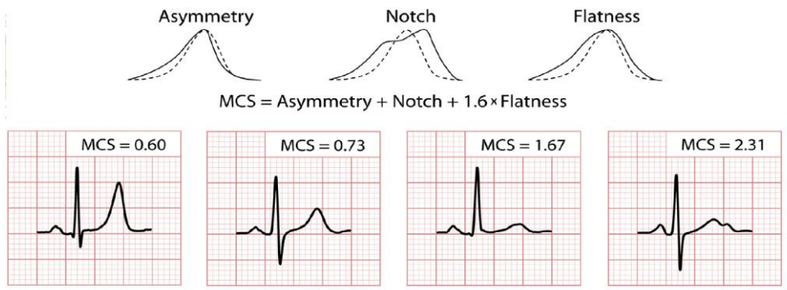
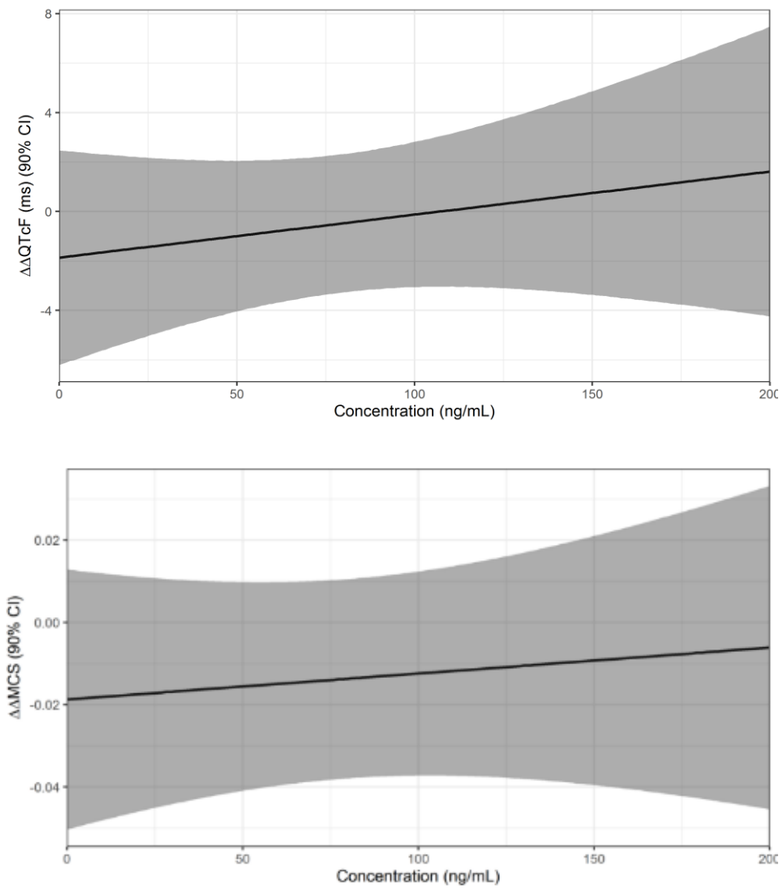


Figure 1: Morphology Combination Score and quantification

Methods

- **Design:** randomized, placebo-controlled trial
- **Inclusion**: 20 young (≤30) and 20 elderly (65-75) healthy male subjects
- **Dosing**: 2400mg hydroxychloroquine in 4 days
- **Analysis**: concentration-effect analysis of ECG interval durations and MCS



Results

- **Cmax**: 200 ng/mL
- No significant effect of **age group**
- **No significant associations** between hydroxychloroquine plasma concentration and measures of ventricular repolarization
  - QTcF-interval (*p=0.25)*
  - MCS *(p=0.34)*

Conclusion

- Hydroxychloroquine **does not appear to increase** the risk of **QTcF-induced arrhythmias** in the studied dosing regimen.
- The dosing level is **not sufficient to induce hERG-channel inhibition.**
- We hypothesize that the observed QT-prolongation in SARS-CoV-2 patients is caused by other factors than hydroxychloroquine use.

Figure 2: Concentration-dependent effect of hydroxychloroquine on ΔΔQTcF-interval and ΔΔMCS, corrected for baseline measurements and placebo

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