Hydroxychloroquine's influence on hypoxic and hypokalemic ventricule: An in-silico perspective

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Hydroxychloroquine (HCQ) has been widely used, irrespective of pre reported cardiotoxicity. This demands further investigation on the mechanisms of HCQ interaction under hypoxia without and with a pro-arrhythmic comorbidity like hypokalemia in the ventricular tissue as well as its effects when excited with premature beats (PBs) to understand the possibility of arrhythmic occurrence. This is made possible by configuring a 2D transmural anisotropic ventricular tissue model consisting of endocardial, midmyocardial and epicardial myocytes for *mild* and *severe* hypoxia, hypokalemia and HCQ conditions. Results show that along with a QT interval reduction, low amplitude or T-wave inversion is observed in *mild* and *severe* hypoxia conditions respectively. No significant adverse effect of HCQ is observed in both cases. Under hypokalemia, *mild* hypoxia creates notched T-waves. Including HCQ has the effect of increasing the QT interval and T-peak. In presence of PBs, arrhythmia is generated only in presence of hypokalemia. Further, *severe* hypoxia causes inverted T-waves and a shortened QT-interval in hypokalemic comorbid configuration. In presence of PBs, reentry is created only in addition of hypokalemia. When treated with HCQ, no notable changes occurred. This in-silico ventricular model indicates that HCQ treatment has no significant adverse effect in presence of hypokalemia and hypoxia, except in the combination of mild hypoxia with hypokalemia condition where it initiated a re-entrant arrhythmia pattern. These results could help guide treatment with HCQ.