Electrophysiological effects of malaria and its therapeutic management: a multi-population computational study

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Malaria, a major health issue in tropical regions, has well-documented cardiac involvement. The classical pharmacological treatment is chloroquine, which can also modulate cardiac electrophysiology as a side effect. However, the evolution of cardiac effects during malaria progression across different ages and under treatment remains incompletely characterized. A computational study was conducted to evaluate the effects of malaria and chloroquine on human ventricular electrophysiology across different developmental stages (adult, school-age, preschool, infant, and neonate). Simulations were performed using the O'Hara ventricular action potential model, modified to incorporate malaria-related conditions, including hyperthermia, ionic imbalances, and acidosis. A standard stimulation protocol was applied, and electrophysiological biomarkers, such as action potential duration (APD) and resting membrane potential, were quantified. Malaria conditions induced a slight reduction in APD (1.2–2.9%) and a hyperpolarization of the resting membrane potential (~−5 mV), suggesting decreased cellular excitability due to altered depolarizing currents and ionic gradients. These effects were consistent across populations, although baseline APD values were progressively longer in younger models. Incorporation of a chloroquine model into the malaria-remodeled action potential model, based on concentration-dependent ion channel blockade (INa, IK1, IKr, and ICaL), produced a marked prolongation of APD in all populations, exceeding 100% at high concentrations. This effect is attributed to the inhibition of repolarizing currents, which delays ventricular repolarization and constitutes an electrophysiological mechanism associated with QT interval prolongation and an increased risk of arrhythmias. An age-dependent response was observed: younger populations showed longer baseline APD but lower relative sensitivity to chloroquine. This finding suggests developmental differences in electrophysiological behavior, potentially associated with variations in ion channel expression and conductance scaling. Overall, malaria and chloroquine interact to significantly modulate ventricular repolarization, highlighting the importance of considering both physiological state and age in proarrhythmic risk assessment.