Sulfur Dioxide Effects on Human Atrial Action Potential. In Silico Study

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**Background:** Human exposure to air pollutants agents, like sulfur dioxide (SO₂), has significant effects on the cardiovascular system. Studies have shown that SO₂ blocks the L-type calcium channel and increases the sodium channel (I_{Na}), the transient outward potassium current (I_{to}) and the inward rectifying potassium current (I_{K1}), which implies an action potential duration (APD) decrease, increasing the risk of initiation and maintenance of cardiovascular disease such as atrial arrhythmias.

**Aim:** This study aims to assess the effects of the SO₂ at different concentrations on human atrial action potential, using computational simulation.

**Methods:** Based on experimental data, we developed concentration-dependent equations to simulate the SO₂ effects on I_{CaL}, I_{Na}, I_{to} and I_{K1}. They were incorporated in the Courtemanche model of human atrial cell in a unicellular environment and in a 2D model of atrial tissue. Pacing was applied at a basic cycle length of 1000 ms. The APD at 90% of the repolarization (APD₉₀) and the resting membrane potential (RMP) were measured. S1-S2 cross-field protocol was applied to initiate a rotor. SO₂ concentrations from 0 to 1000 µM were implemented.

**Results:** Our results in a human atrial cell model are in agreement with results from non-human in vitro and in vivo studies. The SO₂ causes the APD shortening and loss of plateau phase of the action potential in a fraction that increases as the concentration increases. For the highest SO₂ concentration (1000 µM), the I_{CaL} peak decreases by 95%, the I_{Na}, I_{to} and I_{K1} peaks increases by 77%, 147% and 96%, respectively, and the APD₉₀ decreases by 81%. The RMP does not show significant changes. In the 2D model, a rotor can be generated from 100 µM of SO₂ concentration.

**Conclusion:** Our results show pro-arrhythmic effects of SO₂ expressed through APD shortening and a rotor generation, during normal electrophysiological conditions.