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## Research Article

# Different Proarrhythmic Effects of Aconitine on Healthy and Long QT Syndrome Patients with Human Pluripotent Stem Cell-Derived Cardiomyocytes

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## ARTICLE INFO

## Article history:

Received: 12 August, 2021

Accepted: 28 August, 2021

Published: 14 September, 2021

## Keywords:

Long QT syndrome

aconitine

hiPSC-CMs

## ABSTRACT

Aconitine is the main toxic component in aconite, a traditional Chinese medicine, which was widely used in emergency medicine. Aconitine is highly toxic, and a single dose of 0.2mg can cause malignant arrhythmias/death in adults. Early studies have shown that aconitine can improve arrhythmia in patients by affecting the calcium channel. The dual nature of aconitine therapy and toxicity is puzzling. While cardiac  $Ca^{2+}$  channel opening during repolarization has long been documented in normal human cardiac myocytes, the cellular effects and mechanism of ACO in Long QT syndrome patient remains unexplored. This study aimed to assess the proarrhythmic effects of ACO in healthy and Long QT syndrome patients with human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs). ACO concentration-dependently (0.05 ~ 5.0  $\mu$ M) decreased amplitude, which has no significant effect on cell index of normal hiPSC-CMs. While ACO 5.0  $\mu$ M decreased cell index between 5-30min for Long QT syndrome hiPSC-CMs. Meanwhile, ACO had no significant effect on the amplitude and frequency of calcium transients in normal cardiomyocytes, but it significantly increased the frequency of calcium transients in special cardiomyocytes of LQT disease at 5  $\mu$ M. Meanwhile, 0.05- 5  $\mu$ M ACO significantly shortened the action potential duration of human cardiomyocytes in both normal and LQT groups. Effect of ACO on L-type calcium current was detected in both normal hiPSC-CMs and LQTs hiPSC-CMs; it showed a similar blockage, which suggested that L-type calcium current may not be the major target on the effect of ACO on LQT disease. In conclusion, our data suggest that ACO had different effect on human cardiomyocytes in normal and LQT (hiPSC-CMs).

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