Available online at www.sciencerepository.org

Science Repository

Research Article

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

Yang Liang[1#], Xieguanghui[2#], Wang Zihan[1], Huangguangyao[3], Zheng Bin[1], Zhu Jin Miao[1], Hong Qian[4,5] and Gao Yue[2*]

[1]*Hefei Normal University, Hefei, China*
[2]*Beijing Institution of Radiation Medicine, Beijing, China*
[3]*Department of Pharmacy, Cancer Hospital, Chinese Academy of Sciences, Hefei, China*
[4]*Huaihai Hospital affiliated to Xuzhou Medical University, Xuzhou, Jiangsu, China*
[5]*PLA 71st Group Military Hospital, Xuzhou, Jiangsu, China*
[#]*Contributed equally*

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 μM) decreased amplitude, which has no significant effect on cell index of normal hiPSC-CMs. While ACO 5.0 μM 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 μM. Meanwhile, 0.05- 5 μM 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).

Get access to the full version of this article: http://dx.doi.org/10.31487/j.JSO.2021.02.03

[*]*Correspondence to: Yue Gao, Beijing Institute of Radiation Medicine, No. 27, Taiping Road, 100850, Beijing, China; Tel: 8601066931312; Fax: 8601068214653; E-mail: gaoyue@bmi.ac.cn*

http://dx.doi.org/10.31487/j.JSO.2021.02.03