

GW23-e2701

CARVEDILOL PREVENTS THE ETHANOL-INDUCED VENTRICULAR ARRHYTHMIAS BY MODIFYING THE GAP JUNCTION REMODELLING IN RATS

doi:10.1136/heartjnl-2012-302920a.290

Jinyao Liu, Izumi Takase, Ayako Hakucho, Xu Liu, Atsuya Fujimiya, Jinyao Liu.
Department of Legal Medicine, Yamaguchi University Graduate School of Medicine

Objectives Our previous studies showed carvedilol blocked the abrupt termination of an ethanol regimen promoted the cardiac sympathetic predominance and the life-threatening ventricular arrhythmias in rats. However, the mechanisms by which they do are unclear. Cardiac gap junctions provide the pathway for intercellular current flow, enabling coordinated action potential propagation and contraction. Cell-to-cell coupling is provided predominantly by connexin 43 (Cx-43) channels and its remodelling is supposed to contribute to the abnormal conduction properties and arrhythmias in ventricle. This study was designed to demonstrate the gap junction remodelling, cardiac sympathetic nervous system activity, and the effects of carvedilol on them in rats.

Methods Seven-week-old male Wistar rats were pair-fed with a control or 5 g/dl ethanol liquid diet for 48 days and then subjected to 1-day withdrawal, and 1-day withdrawal with 7-day carvedilol (can block the sympathetic nervous system via β_1 , β_2 , and α_1 adrenergic receptors) pretreatment. Cardiac sympathetic nervous system activity and gap junction remodelling were evaluated based

on the heart rate variability, Western blotting, and reverse transcriptase PCR analyses.

Results The results showed that carvedilol inhibited the acute ethanol withdrawal (ie, having followed 48-day continuous ethanol treatment) induced the cardiac sympathetic predominance and gap junction remodelling, as evidenced by the increases in lower-frequency power in heart rate variability, down-regulation of Cx-43 mRNA and protein expressions, and down-regulation of phosphorylated Cx-43 protein expressions.

Conclusions We concluded that acute ethanol withdrawal followed 48-day continuous ethanol treatment may trigger the cardiac sympathetic predominance, which then induct the gap junction remodelling, finally leading to the occurrence of the ventricular arrhythmias. Carvedilol might prevent the acute ethanol withdrawal induced ventricular arrhythmias by modifying the gap junction remodelling via blocking the sympathetic nervous system activity.