

Abstinence of ethanol promotes changes in smooth muscle of rat aorta artery and alter vascular reactivity

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Introduction: Alcohol Withdrawal Syndrome (AWS) is a short-lasting, but potentially severe complication of alcohol dependence characterizing psychiatric symptoms and changes in autonomous and nervous systems. Even a single moderate dose of ethanol ingestion in non-alcoholic subjects causes significant alterations in cardiovascular system characterizing by changes in heart rate, systolic blood pressure, cardiac output and total peripheral resistance and promotes behavioral changes such as increased anxiety.

Objective: This study aimed to investigate the behavioral and cardiovascular effects associated with AWS and the mechanisms involved in this response. **Methods:** Male *Wistar* rats were divided into three groups: Control: animals received water *ad libitum* for 23 days; Ethanol: chronic treatment with ethanol was started with a solution of 3% ethanol (vol./vol.) being gradually increased every three days to 6% (day 4) and 9% (on day 7), maintaining this concentration up to 21 days; Abstinence of ethanol: the animals were treated the same way as the animals in the ethanol group until the 20th day, and then the ethanol solution 9% was removed and returned the next day (day 21) for only two hours. After that, the animals received only water until the test day (day 23), thereby ensuring the framework of abstinence for 48 hours. Vascular reactivity experiments were performed on isolated thoracic aorta with intact endothelium (E⁺) or denuded endothelium (E⁻). Cumulative concentration-response curves to acetylcholine (ACh), phenylephrine (Phe), sodium nitroprusside (SNP), or KCl were obtained in isolated aortas. The behavioural test was performed in the elevated plus maze (EPM). All protocols were approved by the Ethical Committee (Protocol: 11.1.1212.53.5). **Results:** In E⁻ rings the AWS significantly alter the vascular contraction to Phe (1,14±0,01g, n=12; F_{2;35}= 6,124; p<0,05) and KCl (1,08±0,23g; n=4; F_{2;14}= 4,176; p<0,05) when compared to the respective control groups (Phe=1,76±0,13g; n=10; KCl=1,97±0,19g; n=7). The chronic use of ethanol did not alter Phe or KCl-induced when compared with control or AWS groups. In E⁺ rings did not alter Phe or KCl-induced contraction when compared with control. In the percentage of relaxation AWS promotes significantly alter the vascular relaxation to SNP (139,16±5,13g; n=10; F_{2;26}= 3,892; p<0,05) when compared with control group (117,50±6,04g; n=10) but not alter vascular relaxation induced to ACh (F_{2;32}= 0,8272; p>0,05). We observed that the AWS causes changes in the exploratory behavior of animals tested in the EPM. Animals of group AWS present a significant decrease in percentage of entries (%EOA=19,8±5,4; n=7; F_{2;20}=25,9; p<0,05) and time spent in open arms (%TOA=5,2±2,0; n=7; F_{2;20}=32,9; p<0,05) compared with animals of control group (%EOA=35,7±3,6; %TOA=21,5±5,9; n=7). No differences were found on the number of enclosed arms entries (F_{2;20}=2,8; p>0,05). **Conclusions:** Our results suggest that the AWS promotes changes in vascular reactivity to agents that induce vascular contraction and relaxation and this effect is independent of the endothelium. Our results also suggest that the ethanol withdrawal promotes anxiogenic effects in animals tested in the EPM.

Keywords: Ethanol Abstinence; Hypertension, Vascular Reactivity.

Financial support: CNPq