MP2-1

Inhibition of histone acetylation by curcumin reduces alcohol-induced fetal cardiac apoptosis

Wu X.Y.(1), Yan X.C. (1, 2), Pan B.(1, 2), Liu L.J.(2),Tian J(1)
1 Heart Centre, Children's Hospital of Chongqing Medical University, Chongqing, PR China.
2 Key Laboratory of Developmental Disease in Childhood (Chongqing Medical University), Ministry of Education, Chongqing, PR China.

Background: Prenatal alcohol exposure may cause cardiac development defects. It is known that alcohol could induce cardiac apoptosis and myocardium dysplasia. However the underlying mechanisms are still not clear. Our previous studies suggest that histone modification play a vital role in alcohol induced fetal cardiac development abnormalities. So, the objective of this study was to investigate the effect of histone acetylation regulation mechanisms on alcohol induced cardiac apoptosis.
Methods and Results: C57 pregnant mice were exposed of alcohol by gavage (5μl/g, 56% v/v in saline). TUNEL assay showed positively stained cells were significantly higher in alcohol group. Q-PCR result showed an increase of caspase-3 and caspase-8, and a decrease of bcl-2. Western blotting also showed that, alcohol could raise active-caspase-3 and active-caspase-8, reduce caspase-3 caspase-8 and bcl-2. Meanwhile, alcohol exposure also enhanced acetylation of histone H3K9 in embryonic hearts. ChIP assay showed that alcohol significantly increased the acetylation of histone H3K9 in the promoter of caspase-3 and caspase-8, and decrease acetylation of histone H3K9 in the promoter of bcl-2. The second part was in vitro experiment. We found alcohol (200mM) treatment increased the expression of active-caspase-3, active-caspase-8 and the acetylation of histone H3K9, and also decreased the expression of caspase-3, caspase-8 and bcl-2 in cardiac cells. Then we intervened cardiac cells with curcumin, a HATs enzyme inhibitor. Surprisingly, the up-regulation of active-caspase-3, active-caspase-8 and acetylation of histone H3K9, and the down-regulation of caspase-3, caspase-8 and bcl-2 were reversed. Moreover, annexin-V/PI assay showed that the high apoptosis level that induced by alcohol of cardiac cells were down-regulated after curcumin treating.
Conclusions: This study indicate that histone modification might play an important role in mediating alcohol induced fetal cardiac apoptosis, which is possibly through the up-regulation of acetylation of H3K9 in the promoters of the apoptosis genes. Curcumin could reverse alcohol induced fetal cardiac apoptosis, suggesting curcumin is protective against alcohol abuse during pregnancy.