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Neurotoxic Effects of Alcohol and Acetaldehyde During Embryonic Development

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Alcohol drinking during pregnancy results in abnormal fetal development including Fetal Alcohol Syndrome (FAS) in humans and experimental animals. FAS is characterized by two major effects including central nervous system (CNS) dysfunction and multiple anomalies recognizable mainly as a typical face. However, the mechanisms of alcohol-induced embryotoxicity have not been clearly demonstrated. The aim of the present study was to investigate the possible mechanisms underlying ethanol-induced FAS in the developing embryo. First, ethanol-induced developmental abnormalities were investigated in vitro. Post-implantation embryos at gestation day (GD) 9.5 were cultured for 48 hr and observed for morphological changes. Ethanol-mediated changes in proteins regulated apoptosis (p53 and bcl-2), antioxidant (vitamin E and catalase) activities, generation of reactive oxygen species (ROS), and oxidative DNA damage 8-hydroxy-2'-deoxyguanosine (8-OHdG) were measured in embryonic midbrain cells. Alcohol or acetaldehyde significantly induced cytotoxicity in cultured rat embryonic midbrain cells. The levels of p53, bcl-2 and 8-OHdG were concomitantly changed by alcohol and acetaldehyde treatment in midbrain cells. Injured cells induced by ROS were increased by alcohol or acetaldehyde treatment in midbrain cells. Co-treatment with alcohol or acetaldehyde and catalase decreased cytotoxicity in midbrain cells. In post-implantation embryo culture, alcohol or acetaldehyde-treated embryos showed retardation of embryonic growth and development in a concentration-dependent manner. These results indicate that alcohol and its metabolite acetaldehyde induces fetal developmental abnormalities by disrupting cellular differentiation and growth. Data demonstrate that some antioxidants can partially protect against the alcohol-induced embryonic developmental toxicity.

Keyword: alcohol, acetaldehyde, fetal alcohol syndrom