Hepatocyte growth factor, vascular endothelial growth factor, glial cell-derived neurotrophic factor and nerve growth factor are differentially affected by early chronic ethanol or red wine intake

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ABSTRACT

Ethanol intake during pregnancy and lactation induces severe changes in brain and liver throughout mechanisms involving growth factors. These are signaling molecules regulating survival, differentiation, maintenance and connectivity of brain and liver cells. Ethanol is an element of red wine which contains also compounds with antioxidant properties. Aim of the study was to investigate differences in hepatocyte growth factor (HGF), vascular endothelial growth factor (VEGF), glial cell-derived neurotrophic factor (GDNF) and nerve growth factor (NGF) in brain areas and liver by ELISA of 1-month-old male mice exposed perinatally to ethanol at 11 vol.% or to red wine at same ethanol concentration. Ethanol was administered before and during pregnancy up to pups’ weaning. Ethanol per se elevated HGF in liver and cortex, potentiated liver VEGF, reduced GDNF in the liver and decreased NGF content in hippocampus and cortex in the offspring. We did not find changes in HGF or NGF due to red wine exposure. However, we revealed elevation in VEGF levels in liver and reduced GDNF in the cortex of animals exposed to red wine but the VEGF liver increase was more marked in animals exposed to ethanol only compared to the red wine group. In conclusion the present findings in the mouse show differences in ethanol-induced toxicity when ethanol is administered alone or in red wine that may be related to compounds with antioxidant properties present in the red wine.

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1. Introduction

Growth factors are signaling molecules that are able to influence survival, differentiation, maintenance and connectivity of different cells, including brain and liver cells (Allen and Dawbarn, 2006; Levi-Montalcini, 1987; W. Sun et al., 2002). Prominent growth factors playing critical roles in the physiopathology of brain and liver cells are nerve growth factor (NGF) and hepatocyte growth factor (HGF). Vascular endothelial growth factor (VEGF) and glial cell-derived neurotrophic factor (GDNF) have also been found to be produced by and acting upon brain and liver cells (Burke, 2006; Maharaj et al., 2006). Prenatal ethanol intake is known to cause a plethora of behavioral, biochemical and structural effects in postnatal life in the liver and brain (Addolorato et al., 1997; Niccols, 2007). However, the mechanisms throughout which these deleterious effects occur, as well as the effects induced in the constitutive concentration of these important signaling molecules are not known. It has been shown that acute and chronic ethanol treatment enhances the production of reactive oxygen species, lowers cellular antioxidant levels, and increases oxidative stress in many tissues, especially the liver and the brain. Ethanol-induced oxidative stress plays a major role in the mechanisms by which ethanol produces liver and brain injury (Dey and Cederbaum, 2006). Using a mouse model of early ethanol administration (Fiore et al., 2009) the aim of the present study was to investigate differences in toxicity due to early (perinatal and postnatal up to weaning) chronic ethanol or red wine consumption (at same ethanol concentration, 11%) on the levels of HGF, VEGF, NGF and GDNF in the liver, and brain.

2. Materials and methods

2.1. The mouse model of ethanol and red wine administration

CD-1 outbred female mice were housed singularly in Plexiglas cages (33 cm × 13 cm × 14 cm) under standardized conditions with pellet food (enriched...