IJAE
Vol. 117, n. 2 (Supplement): 187, 2012
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Effects of stereoisomers of thioctic acid on rat renal vasculature microanatomy

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Metabolism of oxygen by cells can generate potentially dangerous reactive oxygen species (ROS). Endothelial cells lining vascular luminal surface are an important site of signalling molecules and a ROS target during ischemia, inflammation and other pathological conditions. Targeted delivery of ROS modulating enzymes conjugated with antibodies to endothelial surface molecules provide site-specific interventions of endothelial ROS. Excessive ROS cause pathological activation of endothelium including exposure to cell adhesion molecules. Intercellular adhesion molecule-1 (ICAM-1) is a member of the Ig superfamily and is also found on the surface of several other cell types, including endothelial cells. These molecules [e.g., ICAM-1, vascular cell adhesion molecule 1 (VCAM-1) and platelet-endothelial cell adhesion molecule-1 (PECAM-1)] exposed on activated endothelium represent attractive targets for delivery of drugs and imaging probes to pathological sites in the vasculature.

This study has investigated the effect of different stereoisomers of the antioxidant thioctic acid on the endothelium of rat kidney vasculature. Twenty-week-old spontaneously hypertensive rats (SHR) and normotensive Wistar Kyoto rats were treated for 2 weeks with a daily dose of 12.5 nM/kg racemic (+/-)-, (+)- or (-)-thioctic acid. Kidney vascular microanatomy was Investigated by ICAM-1, VCAM-1 and PECAM-1 immunochemistry and immunohistochemistry. .

Treatment with thioctic acid significantly improved renal vascular endothelium status by preventing the ICAM and VCAM adhesion. (+)-Thioctic acid elicited the most sustained effect, (+/-)-thioctic acid was less effective and (-)-thioctic acid worsened activity of the compound.

The above data suggest that (+)-thioctic acid, the naturally-occurring enantiomer of the compound, is probably the only form of it able to interfere with endothelial adhesion mechanisms in renal vasculature. The comparatively lower activity of racemic (+/-)- thioctic acid is likely determined by the negative impact of (-)-thioctic acid on the parameters under investigation. Analysis of vascular intercellular adhesion mechanisms could represent an interesting approach for investigating specific vascular disorders and also other pathologies in which vascular involvement plays an important role.

Keywords: Antioxidants, thioctic acid, rat kidney, adhesion factors.