Influence evaluation of the pravastatin antioxidant effects on the gelatinolytic activity of metalloproteinases 2 and 9 hypertensive pregnant rats

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Introduction: Hypertensive disorders of pregnancy are the main causes of maternal and fetal mortality, characterized by elevations in maternal blood pressure which may compromise fetal development. The pathogenesis is still unknown, but there are theories that there is a decrease in the plasticity of the vessels of the maternal-fetal interface, placental ischemia accompanied by maternal endothelial dysfunction. Recently, it has been suggested that some endogenous mediators may be related and they seem to participate in the pathogenesis of gestational hypertension, namely: the decrease in the bioavailability of nitric oxide (NO) and the high activity of extracellular matrix metalloproteinases (MMPs). Therefore, this study aims to evaluate the impact of pravastatin on MMPs, since this statin has been shown to increase the bioavailability of NO and has provided antioxidant effects in hypertensive pregnant rats without affecting fetal development. Methods: To achieve this aim, pregnant rats were divided into four groups: normotensive pregnant (Norm-Preg); pregnant rats treated with pravastatin (Preg + Prava); hypertensive pregnant rats (HTN-Preg) and hypertensive pregnant rats treated with pravastatin (HTN - Preg + Prava). Hypertension in pregnant rats were induced by the DOCA-salt model, which consists of the administration of deoxycorticosterone acetate (DOCA) with concomitant replacement of drinking water by saline. The blood pressure of the rats and placentas and pups weights were recorded, as well as gelatinolytic activity of MMP-2 and MMP-9, the metabolites of NO and redox balance were examined. In addition, in order to assess the endothelial function of rats, we performed the technique of vascular reactivity in the abdominal aorta. All procedures for animal experimentation were approved by the Institutional Ethics Committee (protocol no 3902030620). Results: The main effects of pravastatin observed were the decrease in blood pressure, the prevention of intrauterine growth restriction induced by hypertension and the decrease of contraction in the abdominal aorta in group hypertensive pregnant rats treated with pravastatin. Conclusion: We conclude that pleiotropic effects associated with pravastatin treatment against hypertension in pregnancy, prevented intrauterine growth restriction, vascular dysfunction and angiogenic imbalance.

Keywords: gestational hypertension, metalloproteinases, pravastatin.

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