ROSUVASTATIN-CYTOPROTECTIVE PLEITROPIC EFFECTS DURING EXPERIMENTAL NEONATAL OBSTRUCTIVE NEPHROPATHY

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INTRODUCTION
Congenital obstructive nephropathy is characterized by oxidative stress, decreased proliferation and increased apoptosis. Oxidative stress represents the common denominator of multiple cellular alterations and contributes to tubulointerstitial mechanism damage. Both pro-apoptotic and anti-apoptotic effects of nitric oxide (NO) have been demonstrated. NO has been implicated in apoptosis for unilateral ureteral obstruction (UUO), being a controversial key. Furthermore, induction of the stress response includes synthesis of heat shock proteins (HSPs) been well characterized in injured cells. Hsp70 confers cellular protection by modulating the engagement and/or progression of apoptosis. In agreement, we have demonstrated an association between NO bioavailability and Hsp70 expression in UUO (1). Strategies performed on slowing the progression of chronic kidney disease (CKD) have included increasing evidence for the beneficial, lipid-independent effects of 3-Hydroxy-3-methylglutaryl coenzyme (HMG-CoA) reductase inhibitors (statins). Statins exert beneficial effects upon CKD, including restoration/normalization of endothelial function upregulation of NO, oxidative stress reduction and vascular inflammation. Interest during obstructive nephropathy, rosuvastatin has renoprotective effects in terms of morphology and inflammation, independent of the changes in blood pressure and plasma lipid levels (2).

OBJECTIVE
To determine whether NO associated with Hsp70 expression is involved in rosuvastatin resistance to obstruction-induced oxidative stress and cell death in neonatal obstructive nephropathy experimental model.

MATERIALS AND METHODS
Neonatal rats (n=5) with and without UUO (OC and CC) and Ros treated rats (10mg/Kg/d) for 14 days, were nephrectomized to evaluate in cortexes oxidative stress and heat shock response.

RESULTS
After 14 days of obstruction, oxidative stress markers as lipid peroxidation (MDA) (90±5 vs 70±4 nmol/mL) and NADPH oxidase activity (21682±234 vs. 8200±123 RUF/µg prot/min) increased, whereas hsf1 and Hsp70 expression (0.35±0.04 vs. 0.87±0.05) and lower endogenous nitric oxide levels (67±2 vs. 74±2 nM) decreased. Conversely, Rosuvastatin administration increased hsf1 and Hsp70 expression linked to increase in NO levels with absence of apoptotic response and decreased oxidative stress.

CONCLUSIONS
Roulevastatin exerts cytoprotective effects against oxidative stress through NO restoration and upregulation of Hsp70 in UUO. These effects could be involved on delaying the development and progression of renal injury from obstruction.

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REFERENCES

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