S-B10

Expression of Brain-derived Neurotrophic Factor (BDNF) in Normal and Cyclosporine-treated Rat Kidney

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Background: BDNF is originally expressed in central nervous system, but it also expressed in a wide range of non-nerves organs including kidney. Reduction in BDNF expression is thought to be involved in the pathogenesis of a variety of neuropsychiatric and neurological disorders. However, the expression and role of BDNF in diseased kidney has not to be illustrated. The present study examined BDNF and its tyrosine kinase (Trk) receptors expression on kidney in a rat model of chronic CsA nephropathy, and the effect of vasopressin infusion on BDNF expression was also observed in vehicle and CsA-treated rat kidneys.

Methods: Sprague-Dawley rats kept on a low salt diet (0.05% sodium) were treated daily for four weeks with vehicle (olive oil 1 mL/kg s.c.) or CsA (15 mg/kg s.c.). The expression of BDNF TrkB and TrkC was evaluated with immuno-histochemistry, immunofluorescence, and immunoblotting. In addition, urine concentration, histology, oxidative stress (8-hydroxy-2'-deoxyguanosine 8-OHdG), and apoptosis (TUNEL assay) were also compared for different treatment groups.

Results: In VH-treated kidneys, BDNF and TrkB and TrkC were constitutively expressed in the collecting tubules of the outer medulla and cortex, which was confirmed by double immunofluorescence with BDNF and AQP-1 or AQP-2. CsA treatment increased urine excretion and this was accompanied by decreases in the expression of BDNF and TrkB and TrkC. Immunoblotting revealed that CsA decreased BDNF protein expression by approximately of 50%, and this decrease correlated with the number of TUNEL-positive cells ($r=0.778$, $p<0.01$). Infusion of vasopressin reversed all of above parameters.

Conclusion: Our observations suggest that long-term treatment of CsA inhibits BDNF and its receptor expression in the kidney, and that this may be associated with impairment of urine concentration ability. Enhanced apoptotic cell death at least partially accounts for the CsA-induced urinary concentration defect in a rat model of chronic CsA nephropathy.

Key Words: CsA, BDNF, TRK, Apoptosis