

만성 사이클로스포린 신증에서 암모니아 수송체 (RhBG, RhCG)의 발현

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Purpose : Chronic cyclosporine nephropathy causes metabolic acidosis associated, but its effects on renal tubular ammonia transport are unknown. This study was performed to evaluate the effect of chronic CsA nephropathy on the ammonia transporter family members, Rh B-glycoprotein (RhBG) and Rh C-glycoprotein (RhCG).

Methods : Sprague-Dawley rats were used. Chronic CsA nephropathy was induced by administering CsA (15 mg/kg per day) subcutaneously for 4 weeks with vehicle (VH; olive oil, 1 ml/kg s.c.) or CsA (15 mg/kg s.c.). Metabolic acidosis was confirmed with decreased total CO₂ concentration in arterial blood (20±0.9 vs. 24±0.4 mmHg, p<0.05) as compared with the VH group. RhBG and RhCG expression were evaluated with immunoblot analysis, immunohistochemistry and real-time RT-PCR. In addition, H⁺-ATPase expression was quantified with immunoblot analysis.

Results : Chronic CsA treatment reduced RhCG protein expression in outer medulla (59±17% vs. 100±25%, p<0.05 CsA vs. VH), but not cortex of CsA-treated kidney. Immunohistochemical analysis was consistent with these findings. H⁺-ATPase expression was significantly decreased in CsA treated kidney compared with the VH group (cortex, 63±7% vs. 100±10%, p<0.05 vs. VH; OM, 75±12% vs. 100±17%, p<0.05 vs. VH). RhCG mRNA expression was unchanged in either the cortex or the outer medulla. In contrast to RhCG and H⁺-ATPase, there were no significant differences in RhBG protein expression, by immunoblot analysis, between CsA and VH, nor were there identifiable changes in the cellular distribution of RhBG. Similarly, RhBG mRNA expression was unchanged.

Conclusion : Long-term treatment with CsA in rats decreases RhCG and H⁺-ATPase expression in parallel in the OMCD. The decrease in RhCG protein expression mediates CsA-induced renal tubular acidosis.