Effects of renin system on expression of TGF-β in glomerulonephritis

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Summary

Increased expression of TGF-β and TGF-β receptors (TβR) has been shown to be involved in deterioration of renal function resulted from pathologic matrix accumulation in glomerulonephritis. This study was conducted to explore the effects of renin system on expression of TGF-β and TβR in anti-thymocyte serum (ATS) nephritis. In order to modulate renin expression, rats were fed with low salt diet (chow containing 0.03% NaCl; LS), normal salt diet (chow containing regular 0.39% NaCl; NS), or high salt diet (normal salt diet and 1% NaCl as drinking water; HS). Two mg/kg of furosemide also was injected in LS 7 days before ATS injection and 10 mg/kg of deoxycorticosterone acetate in HS 14 and 7 days before ATS injection. We studied the levels of proteinuria, renal lesions, plasma renin activity, and renal expression of immunodetectable TGF-β1, types I, II, and III TβR, and renin using ELISA, Western blot analysis in isolated glomeruli, and immunohistochemical staining in kidney tissues. The mean arterial blood pressure levels did not differ significantly among the groups. The levels of proteinuria and proliferative glomerular lesions with mesangial matrix accumulation increased transiently after ATS injection in both LS and NS, and were less severe in LS than NS. In contrast, they were markedly severe and persisted in HS. The glomerular TGF-β1 expression was significantly low in LS, whereas glomerular expression of the three TβR increased markedly in HS. Plasma renin activity was significantly higher in LS and lower in HS than NS. Renin expression in the juxtaglomerular apparatus (JGA) did not significantly differ among the groups before ATS injection. Although renin expression in the JGA was less in HS than LS 7 days after ATS injection, no significant difference was noted before and after ATS injection in each group. These data suggest that modulated expression of TGF-β1 and the three TβR induced by HS and LS, respectively, plays an important role in progression and amelioration of ATS nephritis. Although the precise mechanism of modulation of renal TGF-β1 and TβR expression by high or low salt intake is unknown at present, it seems to be independent of renin expression.