Beneficial Role of Magnesium Valproate on Renal Complications Associated With Type I Diabetes in Rats

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Objectives: Estrogen is known to exhibit renoprotective role. Valproic acid has been shown to upregulate estrogen receptors in breast and prostate cancer. So, we have studied the effect of 8 week treatment with Magnesium Valproate (MgV, 210mg/kg/day, PO) on renal complications associated with type I diabetes in rats.

Methods: Sprague Dawley rats were made diabetic with STZ (45 mg/kg, IV) and divided in four groups and treatment was given for 8 weeks after which various biochemical, urine and renal antioxidants, prooxidant, histological and immunohistochemical parameters were estimated.

Results: STZ significantly increased blood glucose level and reduced uric acid and creatinine excretion and creatinine clearance; increased serum creatinine, blood urea nitrogen (BUN): Creatinine ratio, uric acid, urinary electrolytes and albumin, urinary albumin:creatinine ratio, total protein and reduced serum albumin levels. STZ diabetic rats also showed significant decrease in antioxidant enzymes superoxide dismutase (SOD) and reduced glutathione and significant increase in malondialdehyde (MDA) and nitrite levels. Diabetic rats also found to have significant increase in collagen level in kidney. Histological analysis showed increased mesangial expansion and glomerular lesions in type-1 diabetic rats and increased expressions of estrogen receptors as evidenced by immunohistochemistry. Chronic treatment with MgV produced significant decrease in blood glucose level and significant increase in serum albumin level, significant reduction in serum creatinine, uric acid, urinary electrolytes and albumin, urinary albumin: creatinine ratio, total protein along with significant increase in uric acid and creatinine excretion and creatinine clearance. MgV treatment also significantly increased SOD and reduced glutathione levels and significantly decreased MDA and nitrite levels along with significant decrease in renal collagen level and attenuated all histological alterations. MgV also increased renal estrogen receptor expressions.

Conclusions: Our data shows that Magnesium Valproate prevents diabetic nephropathy rats possibly mediated through estrogen receptors in kidney.