

Randomized trial of an inhibitor of formation of advanced glycation end products in diabetic nephropathy.

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BACKGROUND/AIMS: Pimagedine inhibits the formation of advanced glycation end products and slows the progression of diabetic complications in experimental models. This study was undertaken to determine if pimagedine ameliorates nephropathy in type 1 (insulin-dependent) diabetes mellitus. **METHODS:** This was a randomized, double-masked, placebo-controlled study performed in 690 patients with type 1 diabetes mellitus, nephropathy, and retinopathy. The patients received twice daily dosing with placebo, pimagedine 150 mg, or pimagedine 300 mg for 2-4 years. The primary end point was the time to doubling of serum creatinine; the secondary end points included evaluations of proteinuria, kidney function, and retinopathy. **RESULTS:** Serum creatinine doubled in 26% (61/236) of the placebo-treated patients and in 20% (91/454) of those who received pimagedine ($p = 0.099$). The estimated glomerular filtration rate decreased more slowly in the pimagedine-treated patients with a 36-month decrease from baseline of 6.26 ml/min/1.73 m² as compared with 9.80 ml/min/1.73 m² in the placebo-treated patients ($p = 0.05$), and pimagedine reduced the 24-hour total urinary proteinuria. (The mean reduction from baseline at month 36 was 732 mg/24 h at the low dose and 329 mg/24 h at the high dose as compared with 35 mg/24 h in the placebo group; $p \leq 0.001$.) Fewer pimagedine-treated patients with baseline and end point evaluations (31/324; 10%) as compared with those receiving placebo (16%; 28/179) experienced a three-step or greater progression of the retinopathy (Early Treatment of Diabetic Retinopathy Study) score ($p = 0.030$). Three patients receiving high-dose pimagedine but none receiving low-dose treatment developed glomerulonephritis. **CONCLUSIONS:** While this study did not demonstrate a statistically significant beneficial effect of pimagedine on the progression of overt nephropathy resulting from type 1 diabetes, it is noteworthy in providing the first clinical proof of the concept that inhibiting advanced glycation end product formation can result in a clinically important attenuation of the serious complications of type 1 diabetes mellitus. Copyright 2004 S. Karger AG, Basel

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