

Combined AGE inhibition and ACEi decreases the progression of established diabetic nephropathy in B6 db/db mice.

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The accumulation of advanced glycation end products (AGE) is a key factor in diabetic nephropathy (DN). Pyridoxamine inhibits AGE formation and protects against type I DN. Herein we tested: (1) whether C57BL6 db/db mice as a model of established type II DN resembled patients treated with drugs which inhibit angiotensin II action; (2) whether pyridoxamine was effective as a single therapy; and (3) whether pyridoxamine would add to the benefit of angiotensin-converting enzyme inhibition (ACEi) by enalapril. In first set of experiments mice were treated with ACEi (benazepril) and an angiotensin II receptor blocker (valsartan) combination for 16 weeks after the onset of diabetes. In second group, mice with established DN were treated with pyridoxamine for 8 weeks. In a third set, mice with established DN were treated with pyridoxamine and enalapril combination for 16 weeks. Benazepril and valsartan combination partially prevented the development and progression of DN. Pyridoxamine treatment, as single therapy, decreased the progression of albuminuria and glomerular lesions. The combination of pyridoxamine with enalapril reduced both mortality and the progression of DN. In conclusion, (1) C57 BL6 db/db mice are a model of progressive type II DN; (2) The combination of pyridoxamine with enalapril decreased progression of type 2 DN and overall mortality. Thus, pyridoxamine could be a valuable adjunct to the current treatment of established type II DN.

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