Effect of ketoconazole plus low-dose prednisone on progression of chronic renal failure.

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Patients with any of four different types of chronic renal failure (CRF) (glomerular disease, interstitial nephritis, diabetic nephropathy, or polycystic disease) were observed using sequential determinations of glomerular filtration rate (GFR). Those whose GFR showed progression were either given ketoconazole 200 to 600 mg/d (to suppress cortisol production) plus prednisone 2.5 mg/d (to prevent anterior pituitary escape) and observed with the use of more GFRs, or were observed while four additional GFRs were determined before starting these drugs; some patients were subsequently withdrawn from these drugs and were observed using more GFRs. The effect of these drugs on rate of progression was estimated by a linear spline technique, using observations before, during, and (when available) after treatment. In 20 patients, sufficient data were obtained to estimate the magnitude of this effect. In seven patients with chronic glomerular disease, progressing at -0.62 +/- 0.12 mL/min/mo, progression slowed by 66% +/- 12% (P < 0.01). In five patients with interstitial nephritis of various etiologies, progressing at -1.19 +/- 0.34 mL/min/mo, progression slowed by 55% +/- 27% (P < 0.05). In five diabetic patients progressing at -1.22 +/- 0.14 mL/min/mo, progression slowed by an average of 77% +/- 14% (P < 0.01). In contrast, in four patients with polycystic kidney disease, progression accelerated by 99% +/- 63%. Mean urinary steroid excretion decreased significantly; plasma corticotropin did not increase. Neither proteinuria nor serum lipid levels changed. Urinary nitrate excretion decreased significantly, but serum nitrate did not change. Blood pressure decreased slightly (4.3 mm Hg). Three patients developed transiently elevated serum transaminase levels; two others withdrew because of side effects. We conclude that in chronic glomerular disease, diabetic nephropathy, and interstitial
nephritis, this combination of drugs is as safe as ketoconazole in the absence of renal disease and shows promise of slowing progression. In polycystic kidney disease, it is apparently ineffective or harmful.

Publication Types:

- Clinical Trial
- Controlled Clinical Trial

PMID: 9100038 [PubMed - indexed for MEDLINE]