PROTECTIVE EFFECTS OF DIURETICS IN GENTAMICIN NEPHROTOXICITY

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We have studied the effects of three diuretics – frusemide (F), bumetanide (B) and piretanide (P) – on the nephrotoxic effects of gentamicin (G).

Male MF₁ mice (42–56 days old) were injected intraperitoneally by the dosage schedule shown. Urinary N-acetyl-β-D-glucosaminidase (NAG) excretion was measured 0–6 and 18–24 hours following each injection. From animals in each group (N=10), killed at either 7 or 10 days, kidneys were removed for measurement of tissue NAG and electron microscopy (see diagram).

G caused a graded increase in urinary NAG with a peak on the seventh day; values returned to normal before the end of treatment. The combination of diuretic with G prevented the increase in the 18–24 hour samples. Renal NAG levels were increased above controls in all treatment groups (p < 0.001); controls 75.3 ± 2.6, G 189.5 ± 49.3, G + F 145 ± 28.4, G + B 152 ± 35.8, G + P 134 ± 13.7μmol 4 MU released/hour/g wet weight. Electron microscopy showed sublethal proximal tubular damage, with prominent cytosegregosomes and myeloid figures, in all treatment groups, most striking with G alone.

Conclusions

1. The concomitant administration of these high ceiling diuretics with a toxic dose of gentamicin reduces the nephrotoxicity of this antibiotic.

2. Although urinary NAG levels are sensitive indicators of cellular damage in experimental nephrotoxicity, random NAG estimations must be interpreted with caution.

(for diagram see next page)