Organic Cationic Drugs and Renal Creatinine Secretion

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Sir,

Regarding the article 'Inhibition of renal creatinine secretion by cimetidine in humans' by Burgess et al. -Renal Physiol., Basel 5: 27–30 (1982) -, this is not the first cationic drug to show substantial inhibition of tubular secretion of creatinine in humans as stated in the article. In 1975, Berglund et al. [1] showed elevated serum creatinine concentrations, approximately 25%, after 5 days of trimethoprim, 160 mg twice daily. The average increase of 2 mg/dl creatinine was reversible. ¹³¹I-iothalamate clearances were unchanged even though clearances of creatinine decreased significantly. From the results, Berglund and his co-authors hypothesized that trimethoprim competitively inhibits the tubular secretion of creatinine through the organic cation (base) secretory mechanism.

Creatinine is filtered, reabsorbed, and secreted by kidneys [2] and seems to be secreted by both organic anion and organic cation transport in some species [3, 4]. Using in vitro techniques, Lee et al. [5] showed that trimethoprim inhibits active uptake of ¹⁴C-TEA (organic cation), not its efflux, and that the inhibition is competitive. Thus, the ability of trimethoprim to compete for organic cation transport was established. These results are consistent with the hypothesis of Berglund et al. [1] concerning the inhibition of renal creatinine secretion via competition for transport.

Therefore, both trimethoprim and cimetidine, two drugs used heavily in clinical practice, may elevate serum creatinine concentrations without causing renal malfunction. Accordingly, other cationic drugs might be expected to cause similar findings. The knowledge that organic cations can elevate serum creatinine with-

out influencing the glomerular filtration rate is important to clinicians, for continuance of a successful therapeutic regimen may depend on it.

References

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