

PART XXXVIII

WORKSHOP ON TOXIC ACUTE RENAL FAILURE

TOXIC ACUTE RENAL FAILURE

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The first part of the workshop was devoted to aminoglycoside nephrotoxicity. Dr Giuliano et al of Antwerp [1] presented results on the early renal cortical uptake of various aminosides (gentamicin, tobramycin, netilmicin, amikacin), administered to conscious rats, either by continuous i.v. infusion or by repeated injections. Intermittent administration led to higher cortical uptake of gentamicin but did not modify tobramycin cortical accumulation. The renal cortical uptake of gentamicin and netilmicin was saturable at clinically relevant serum concentrations whereas that of tobramycin and amikacin was not. Tobramycin and amikacin uptake was dependent on serum concentrations. The authors also administered gentamicin to humans, either thrice daily for a four-day period at a dose of $4.5\text{mg}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$, or intravenously for one day at the same daily dose. Renal cortical uptake of gentamicin was similar with both regimens. In contrast, uptake of amikacin was higher after four-day than after one-day treatment.

Mioli et al from Ancona [2] reviewed their clinical experience with aminoglycoside nephrotoxicity. They emphasized that toxicity was highest in elderly patients. Two points were further discussed by the audience (Dr Kokot, Cracovia, Poland; Dr Brunner, Basel, Switzerland; Dr Iaina, Ashkelon and Dr Bernheim, Kfar Saba, Israel): whether increased enzymuria is an adequate index of nephrotoxicity and how to assess routinely renal function in elderly patients. Dr Kleinknecht from Montreuil [3] underlined from a prospective survey that toxic acute renal failure represented approximately 18 per cent of all cases of acute renal failure, and antibiotics average 35 per cent of the causes of drug-induced acute renal failure.

The second part of the workshop dealt with calcium antagonists in acute renal failure. Dr Neumayer et al from Berlin [4] presented evidence that diltiazem administered in conscious dogs prior to and after renal ischaemic insult improved GFR by approximately 50 per cent. In contrast, Papadimitriou et al from Athens [5] showed that verapamil did not improve (and rather aggravated) netilmicin-induced acute renal failure superimposed on renal ischaemia. Dr Lameire from

Gent indicated that in the norepinephrine model in the rat, renal blood flow was less severely depressed in verapamil-treated than in control rats. The protective effect may therefore be ascribed to a lesser degree of ischaemia. In addition, verapamil did not exert protection when administered after reflow. In the following discussion, Dr Neumayer pointed out that in a preliminary study, diltiazem pre-treatment improved kidney function in transplanted patients.

Lastly, Dr Ponti et al from Lecco reported two cases of dichloropropane acute renal failure, accompanied by haemolytic anemia, thrombocytopenia and abnormalities suggestive of disseminated intravascular coagulation. Inhalation or sniffing of this compound, which is widely found in commercial solvents, may be responsible for acute renal failure. D'Amico et al from Milan performed a prospective and randomized study comparing an ionic (diatrizoate) and a non-ionic (iopamidole) radiological contrast medium for intravenous pyelography in patients with chronic renal failure. Urinary excretion of brush-border enzymes (gamma-glutamyl-transferase and alanine-aminopeptidase) increased more after diatrizoate administration whereas N-acetyl- β -glucosaminidase excretion was not enhanced. D'Amico et al suggested that non-ionic compounds were less toxic. This conclusion was discussed, particularly by Dr Brunner who again pointed out that increased enzymuria was not necessarily predictive of increased renal toxicity.

Papers presented

- 1 Giuliano RA, Verpooten GA, De Broe ME. *Kidney cortical accumulation kinetics of Gentamicin, Netilmicin, Amikacin and Tobramycin in infused conscious rats*
- 2 Mioli V, Perilli A, Lombardo V, Micucci G, Bibiano L, Castelli P, Bordoni E, Palumbo P, Boggi R. *Aminoglycoside nephrotoxicity: a 480 case personal review*
- 3 Kleinknecht D, Landais P, Goldfarb B. *Drug associated acute renal failure a prospective multicentre report*
- 4 Neumayer HH, Wagner K, Rafelt M, Achenbach V, Distler A, Molzahn M. *Do calcium antagonists improve the course of post-ischaemic acute renal failure in conscious dogs?*
- 5 Papadimitriou M, Tsobanelis T, Alexopoulos E, Kalpakoglou S, Kelesi A, Leontsini M, Metaxas P. *The effect of Verapamil on a combined ischaemic and aminoglycoside model of acute renal failure in dogs*