Drugs Potentiating Cyclosporin Nephrotoxicity

M.	Michel	Jadoul
Y.	Yves	Pirson
C.v.Y.	Charles van Ypersele	de Strihou

Department of Nephrology, Cliniques Universitaires **St-Luc**, University of Louvain Medical School, Brussels, Belgium

Michel Jadoul, University of Louvain Medical School, Department of Nephrology, Cliniques Universitaires **St-Luc**, B-1200 Brussels (Belgium)

Dear Sir,

In their comprehensive editorial on the nephrological aspects of liver transplantation, Delaney and Nasir [1] mention the deleterious effect of several drugs potentiating cyclosporin (CS) nephrotoxicity. Unfortunately, their table listing the incriminated drugs includes several drugs without clinically significant interaction with CS. As these drugs may be of benefit to CS-treated patients, we provide here some additional information. Contrary to the claim of Delaney and Nasir [1] neither H₂ blockers nor oral trimethoprim increase CS nephrotoxicity. As recently shown by us and others, the serum creatinine concentration is not affected by ranitidine administration to CS-treated patients [2, 3]. The increase in serum creatinine observed under cimetidine treatment merely reflects an impaired tubular secretion of creatinine, whereas glomerular filtration rate, determined by inulin clearance, remains unchanged [3]. The same phenomenon has been demonstrated for oral trimethoprim in this journal [4]. There is thus no reason to withhold either H₂ blockers or trimethoprim whenever they are indicated.

The assertion that ciprofloxacin enhances CS toxicity is based on a single case report better interpreted as an example of acute interstitial nephritis unrelated to CS therapy. Indeed, in this observation CS whole blood levels failed to rise under ciprofloxacin [5]. Several larger studies have clearly demonstrated that neither ciprofloxacin nor other fluoroquinolones such as norfloxacin and ofloxacin interact with CS [6–8]. These antibiotics may thus be confidently prescribed to CS-treated patients.

Finally, we would like to complete the information concerning calcium channel blockers. Besides diltiazem [9] and verapamil [10], nicardipine also increases CS levels [11, 12]. Fortunately, other calcium channel blockers like nifedipine, nitrendipine and isradipine do not significantly interact with CS, [13,14, unpubl. observations] and may thus be safely prescribed.

Delaney and Nasir [1] quite rightly point out the importance of being aware of possible drug interactions potentiating CS nephrotoxicity. The simultaneous use of CS and investigational or newly released drugs should prompt close monitoring of CS levels and glomerular filtration rate (rather than only serum creatinine), particularly if this drug is also extensively metabolized by the liver.

References

Delaney V, Nasir M: Liver transplantation: A challenge to nephrologists. *Nephron* 1990;55:353–360.

Jadoul M; Hené RJ: Ranitidine and the cyclosporine-treated recipient. *Transplantation* 1989;48:359.

Pachon J, Lorber MI, Bia MJ: Effects of H₂-receptor antagonists on renal function in cyclosporine-treated renal transplant patients. *Transplantation* 1989;47:254–259.

Berg KJ, Gjellerstad A, Nordby G, Rootwelt K, Djøseland O, Fauchald P, Mehl A, Narverud J, Talseth T: Renal effects of trimethoprim in ciclosporin- and azathioprine-treated kidney-allografted patients. *Nephron* 1989;53:218–222.

Avent CK, Krinsky D, Kirklin JK, Bourge RC, Figg WD: Synergistic nephrotoxicity due to ciprofloxacin and cyclosporine. *Am J Med* 1988;85:452–453.

Krüger HU, Proksch B, Göbel M, Ehninger G: No severe drug interaction of the 4-quinolone derivative ciprofloxacin with ciclosporin. *Abstr 15th EBMT Meet and Meet on 'Computational and statistical research in bone marrow transplantation'*, Badgstein, 1989, p91.

Jadoul M, Pirson Y, van Ypersele de Strihou C: Norfloxacin and cyclosporine – A safe combination. *Transplantation* 1989; 47: 747–748.
384

Jadoul/Pirson/van Ypersele de Strihou

Vogt P, Schorn T, Frei U: Ofloxacin in the treatment of urinary tract infection in renal transplant recipients. *Infection* 1988; 16:175.

Pochet JM, Pirson Y: Cyclosporin-diltiazem interaction. *Lancet* 1986;i:979.

Lindholm A, Henricsson S: Verapamil inhibits cyclosporin metabolism. *Lancet* 1987 ;i: 1262–1263.

Bourbigot B, Guiserix J, Airiau J, Bressollette L, Morin JF, Clodes J: Nicardipine increases cyclosporin blood levels. *Lancet* 1986 ;i: 1447.

Cantarovich M, Hiesse C, Lockiec F, Charpentier B, Fries D: Confirmation of the interaction between cyclosporine and the calcium channel blocker nicardipine in renal transplant patients. *Clin Nephrol* 1987;28:190–193.

Propper DJ, Whiting PH, Power DA, Edward N, Catto GRD: The effect of nifedipine on graft function in renal allograft

recipients treated with cyclosporin A. *Clin Nephrol* 1989; 32: 62–67. 14 Copur MS, Tasdemir I, Turgan C, Yasavul Ü, Caglar S: Effects of nitrendipine on blood pressure and blood ciclosporin A level in patients with posttransplant hypertension. *Nephron* 1989; 52:227–230.