Interaction between Clonidine and Cyclosporine A

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Reference

Luke J, Luke DR, Williams LA, LeMaistre CF, Yau JC: Prevention of cyclosporine-induced nephrotoxicity with transdermal clonidine. *Clin Pharmacol* 1990;9:49-53.

Dear Sir,

We have recently observed an important interaction between clonidine and cyclosporine A (CsA) which has not previously been described.

A 3-year-old boy underwent a cadaver donor renal transplant for end-stage renal failure secondary to non-diarrhoea-associated haemolytic-uraemic syndrome. The immunosuppression consisted of prednisone, azathioprine and CsA. Postoperatively, considerable difficulty was experienced in controlling his blood pressure. A combination of propranolol, hydralazine, frusemide and nifedipine was inadequate. Minoxidil was added. Although this controlled his blood pressure adequately, the unpleasant cosmetic effects of minoxidil, especially in combination with steroids and cyclosporine, were considered unacceptable, therefore clonidine was substituted. Whole-blood CsA levels (determined by RIA) increased dramatically, despite a reduction in the CsA dose, reaching a peak of 927 µg/l (therapeutic range 150-300; fig. 1). Since it was concluded that clonidine may have interfered with the metabolism of CsA, it was withdrawn. The CsA level fell rapidly. Blood pressure control was eventually established with the addition of an angiotensin-converting enzyme inhibitor.

Approximately 60% of a dose of clonidine is excreted unchanged in the urine, and inhibition of the hepatic CsA metabolism was completely unexpected. Luke et al. [1] 1,000

Postoperative day

Fig. 1. Effect of CsA and clonidine dose: change in CsA levels. □ = CsA level (µg/l); ▨: CsA dose (mg/day); Δ = clonidine (µg/day).

found higher trough CsA levels in bone marrow transplant recipients given clonidine to protect them from the nephrotoxic effects of CsA. These levels remained significantly higher even when corrected for the dose administered [1]. We conclude that clonidine must be

partially metabolised via the cytochrome P-450 pathway and urge those treating patients on CsA with clonidine to exercise extreme caution.