Drug Interaction between Midecamycin and Cyclosporin

P.	Paul	Finiez ^a
J.-M.	Jean-Michel	Mondon ^b
C.	Christian	Chuet ^a
J.	José	Guiserix ^a

Departments of ^aNephrology and ^bFunctional Reeducation and Rehabilitation, CHG Saint-Pierre-Le Tampon, Réunion Islands, France

Dr. Paul Finiez, Department of Nephrology, CHG Saint-Pierre-Le Tampon, BP350, F-97448 Saint-Pierre Cedex, Réunion Islands (France)

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Fig. 1. Creatinine (Cr) and serum CsA versus CsA dose regimen (-■-).

josamycin has already been described [4], but such a problem has never been pointed out, to our knowledge, with midecamycin. It is of paramount importance to determine CsA blood levels 3 days after the introduction of any medication whose interaction

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Dear Sir,

We report an interaction between ciclosporin A (CsA) and midecamycin, a macro-lide antibiotic, in a 53-year-old woman kidney-transplanted 8 months previously following initial polycystic kidney disease. An immunosuppressive drug regimen, predni-sone (10 mg), azathioprine (75 mg) and CsA (120 mg twice) daily, kept her well. Patient characteristics were: 170/80 mm Hg arterial pressure, 47 kg weight, 133 μmol creatininemia, whole blood HPLC ciclosporine-mia being 95 ng/ml (therapeutic range: 100-200 ng/ml). A diagnosed amygdalitis led us to add a midecamycin (800 mg twice a day) prescription, because the absence of known interaction of this molecule with CsA and an allergy to betalactamins. Three days later, she complained about edema, tremor and gingival pain. Her characteristics had changed to: 200/100 mm Hg, 49 kg, 150 μmol/l, 380 ng/ml (fig. 1). Midecamycin was maintained at the same dosage, but CsA reduced to 50 mg twice a day. Five days later symptoms had resolved, and CsA blood level has dropped to 150 ng/ml. Following discontinuation of midecamycin, CsA was increased to the previous dosage, i.e. 120 mg twice a day, with CsA blood level remaining stable within therapeutic range.

Since the liver cytochrome P450 III, one of the largest ways of metabolism, also metabolizes CsA, pharmacokinetic interactions (induction or inhibition) frequently occur [1]. Most macrolides, except spiramycin [2], are reported to increase CsA blood level. Two other macrolides, josamycin and midecamycin, have been demonstrated, both in vitro and in vivo, not to form a complex with cytochrome P450 [3]. Consequently they may be prescribed safely with molecules using the same pathway. However, an interaction with

r 250

200

150

100

50

Cr CsA Cr CsA Cr CsA Day 0 Day 3 Day 8

with CsA is unknown, whatever the pharmacology or class of the molecule. As previously reported for calcium inhibitors [5], different molecules from a same pharmacologic class can have different effects on CsA metabolism.

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