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LETTER TO THE EDITOR

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Kidney graft dysfunction after drug interaction between miocamycin and cyclosporin

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Sir: Miocamycin, a new 16-member macrolide [3] recently introduced into the Belgian pharmacopeia, is prescribed for respiratory and urogenital tract infections. While several macrolide antibiotics have been reported to increase cyclosporin A (CyA) blood levels by inhibiting hepatic cytochrome P 450 enzymes (erythromycin [6], josamycin [7], midecamycin [2], and clarithromycin [1, 8]), others do not (spiramycin [4]) or only rarely so (azithromycin [5]). We report here on an interaction between CyA and miocamycin (Merced, Minarini).

A 25-year-old woman received a cadaveric kidney graft for renal dysplasia in July 1994. Plasma creatinine (P creat, μmol/l) reached a nadir of 171 and remained stable at about 180 μmol/l thereafter. Maintenance immunosuppression consisted of azathioprine (50 mg/day), prednisone (5 mg/day), and CyA (100 mg b.i.d.). The CyA dose was unchanged during the last 14 months and blood CyA trough levels were around 100–120 ng/ml during that period. In October 1997, the patient received miocamycin (600 mg b.i.d.) for rhinopharyngitis. Four days later, CyA blood levels had increased from 97 to 203 ng/ml, and P creat from 182 to 217 μmol/l. As shown in Fig. 1, discontinuation of the miocamycin therapy resulted in a progressive decrease in CyA blood levels and in the resolution of CyA-induced nephrotoxicity.

This case appears to be the first report of an interaction between miocamycin and CyA leading to increased CyA concentrations. We thus believe that miocamycin should be added to the list of drugs likely to increase CyA blood levels.

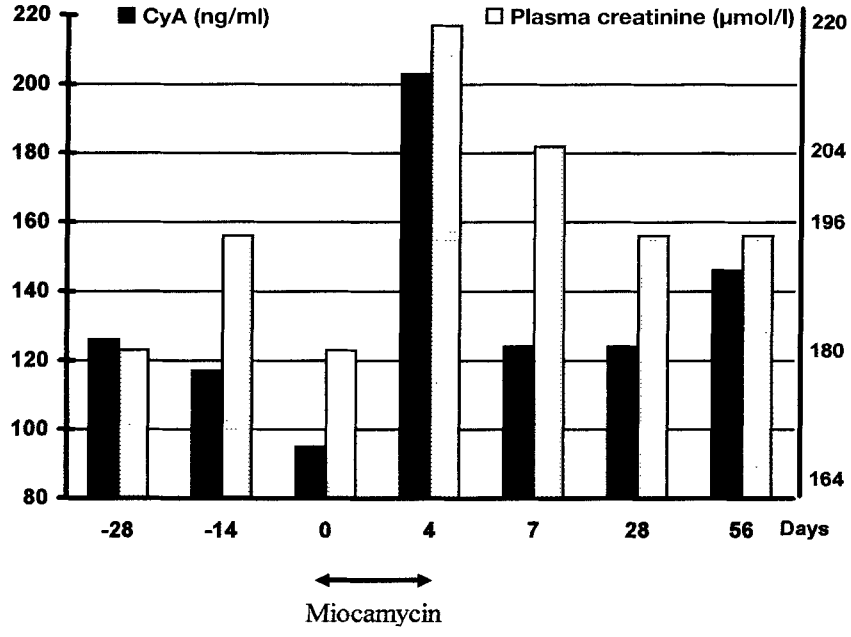

Fig. 1 Effect of miocamycin on trough CyA blood levels and plasma creatinine

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LETTER TO THE EDITOR

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Expansion of donor pool: lack of function predictors

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Sir: The review article by Dafoe and Alfrey [1] focuses on the current debate over the use of marginal kidneys (especially older kidneys) for expansion of the donor pool. Whilst we applaud this first review on dual kidney transplants, it raises the issue of assessing kidneys prior to retrieval. Kidneys harvested from such marginal donors, if transplanted together, offer the potential of increasing the donor pool by using organs that would normally be discarded. However, if kidneys are incorrectly labelled as being marginal when, in fact, they have more potential, then the dual renal transplant program would reduce the donor pool.

According to the authors, the identification of donor kidneys ideal for dual kidney transplantation is based on donor serum creatinine clearance. This approach relies totally on the use of serum creatinine as a marker of glomerular filtration rate (GFR). Transplant centers have evolved individual policies and scoring systems for dual kidney transplantation. In addition to including donor creatinine, they also consider donor age, percent of glomerulosclerosis, and kidney weight [Prof. N. Senninger, Munster, Germany, personal communication].

The daily variation in creatinine excretion, even in normal subjects, makes the measuring of endogenous creatinine clearance unreliable [3]. Even a 24-h urine collection for creatinine clearance is notoriously unreliable, as its reproducibility is rather low; therefore, this parameter of kidney function can only be used as a screening tool [3]. This is attributed to the unpredictable patterns of change in the rate of tubular transport of creatinine [5]. Repeated measurements of serum creatinine clearance have been shown to be unreliable, as the variation in serial creatinine clearance is high and potentially misleading [5]. The change in GFR suggests progression of disease whilst creatinine clearance does not necessarily follow this [6]. In addition, many donors with raised intracranial pressure have diabetes insipidus. This causes their creatinine to be abnormally low, affecting the creatinine clearance.

The Cockfort and Gault formula used by the authors reduces the variability of serum creatinine estimates of glomerular filtration [7]. However, this formula does not take into account the differences in creatinine production between individuals of the same age and sex or the variation in an individual over time [2].

The use of this criterion for the selection of dual kidney donors will not be feasible for non-heart-beating donors (NHBD), who constitute a major group of marginal donors. This source has, in recent years, increased the donor pool, providing 40% more kidneys in some centers, as reported by the Maastricht group [4]. Consequently, serum creatinine clearance can, at best, function as an indicator of donor GFR in stable, marginal donors who have not suffered from large fluid shifts.

We feel that, at present, there is no reliable indicator of donor kidney function that can be used to accurately predict whether or not a dual or single graft is more appropriate. This issue needs further evaluation before the dual transplant program using marginal donors can be allowed to flourish freely.

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