Letter to the Editor

Nephron 41: 207–208 (1985)

0028-2766/85/0412-0207$2.75/0

Effect of Rifampicin on Cyclosporin A Blood Levels in a Renal Transplant Recipient

Michael J.D. Cassidy, Roal Van Zyl-Smit, Michael D. Pascoe, Charles R. Swanepoel, Jack E. Jacobson

Departments of Medicine and Surgery, University of Cape Town, Medical School and Groote Schuur Hospital, Cape Town, South Africa

Dear Sir,

Rifampicin is a powerful enzyme inducer acting on the cytochrome P 450 enzyme system in the liver and thus may affect the metabolism of a number of drugs [1]. The interaction of rifampicin with glucocorticoids is well recognised and the adverse effect of this combination of drugs on renal allograft function has previously been reported [2]. It has been recommended that renal transplant recipients have their dose of prednisolone increased, by a factor of at least 2, should they be treated concurrently with rifampicin [3]. We report on a renal transplant recipient who developed low whole blood levels of cyclosporin whilst being treated with rifampicin for tuberculosis. A 57-year-old man with Balkan nehropathy and end-stage renal failure received a cadaveric renal allograft in March 1984. He had a past history of pulmonary tuberculosis and a grossly abnormal chest radiograph. At the time of surgery he received 250 mg of methylprednisolone intravenously, and immunosuppression was achieved thereafter with methylprednisolone, 24 mg/day by mouth and cyclosporin A, 4 ml twice daily (13 mg/kg/day) diluted in orange juice. In addition, antituberculous therapy consisting of isoniazid, 300 mg, pyrazinamide 1,500 mg, and rifampicin, 450 mg, daily was commenced. There was immediate graft function following transplantation, the serum creatinine falling to 334 μmol/l (3.8 mg/dl) by day 2 and 165 μmol/l (1.9 mg/dl) by day 20 after transplantation. Whole blood cyclosporin levels (Sandoz Radioimmunoassay) fell progressively and remained low despite an increased dose of cyclosporin. Blood samples were drawn for the trough levels 1 h prior to the administration of the morning dose of cyclosporin and the peak levels were obtained at 4 h following the dose. On the withdrawal of rifampicin, blood levels of cyclosporin rose dramatically (fig. 1). Renal function has remained satisfactory and cyclosporin blood levels have remained within the therapeutic range, on a smaller dose of this drug.

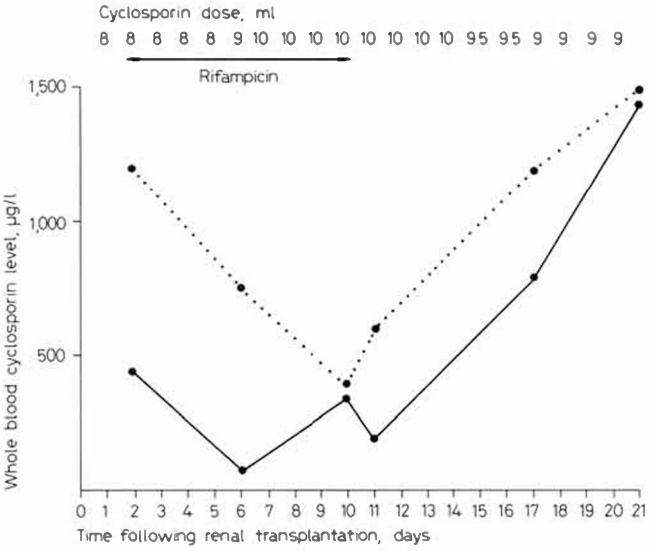

Fig. 1. Whole blood cyclosporin levels (Sandoz Radioimmunoassay) trough (——) and peak (....) plotted against time in days following transplantation. The relationship to the daily dose of cyclosporin and concurrent treatment with rifampicin is illustrated.

Cyclosporin A is an effective immunosuppressive agent selectively inhibiting T-cell function. It is widely used either alone, as the sole immunosuppressive agent, or in combination with corticosteroids in renal allograft recipients. Within the bloodstream, approximately half of the cyclosporin is taken up by erythrocytes; of the total present in plasma, 5% is free in plasma water, 25% is bound to lipoprotein and 5% is bound to other proteins [4]. The drug is rapidly metabolised, the major route of excretion appears to be in the bile, and enterohepatic recirculation of cyclosporin is probable [5]. In our patient, the concurrent use of rifampicin appeared to increase the rate of elimination of cyclosporin from the blood. We would suggest that renal transplant recipients

receiving cyclosporin A, who require treatment with rifampicin, should have cyclosporin blood levels closely monitored as the dose of cyclosporin may have to be modified.

References

1 Meyer, H.; Hoigne, R.: Drugs used in tuberculosis and leprosy; in Dukes, Meyler's side effects of drugs, p. 530 (Excerpta Medica, Amsterdam 1980).
2 Buffington, G.A.; Dominguez, J.H.; Piering, W.F.; Hebert, L.A.; Kauffman, H.M.; Lemann, J.: Interaction of rifampicin and glucocorticoids. Adverse effect on renal allograft function. J. Am. med. Ass. *236:* 1958–1960 (1976).
3 Ogg, C.S.: Problems with the immunosuppressed patient. Prescrib. J. *23:* 113–118 (1983).
4 Beveridge, T.: Pharmacokinetics and metabolism of cyclosporin A.; in White, Cyclosporin A. Proc. Int. Symp. Cambridge, pp. 35–44 (Elsevier Biomedical Press, Amsterdam 1982).
5 Kahan, B.D.; Ried, M.; Newburger, J.: Pharmacokinetics of cyclosporine in human renal transplantation. Transplant. Proc. *15:* 446–449 (1983).

Dr. M.J.D. Cassidy,
Departments of Medicine and Surgery,
University of Cape Town,
Medical School and Groote Schuur Hospital,
Cape Town (South Africa)