Valacyclovir is a prodrug which increases oral acyclovir bioavailability 3–5-fold. When high dosages (6–8 g/day) are used, oral intake of valacyclovir achieves plasma concentrations (area under the curve: AUC) comparable with those of intravenous (i.v.) acyclovir 10 mg/kg three times daily [3]. It is well known that i.v. acyclovir can cause crystal formation in renal tubules that can lead to acute renal failure [4–5]. About one third of patients experienced a transient increase in the serum creatinine level during i.v. acyclovir therapy [4]. This acyclovir-induced nephrotoxicity is potentiated by cyclosporin [6]. The appearance of acyclovir crystalluria is considered to be a warning sign which precedes the rise of the serum creatinine level [7].

We investigated the frequency of crystalluria and the renal drug safety in kidney transplant recipients treated with cyclosporin in whom oral valacyclovir was used for the prevention of CMV disease. Six patients were enrolled in the study. All were CMV-seronegative patients transplanted with a graft from a CMV-seropositive donor. The immuno-suppressive regimen was quadruple and sequential consisting of antithymocyte globulin for 6–8 days, associated with mycophenolate mofetil and corticosteroids. Cyclosporin A was introduced 2 days before the antithymocyte globulin was discontinued.

Valacyclovir was started on the 3–7 day after transplantation at the dosage of 6 g/day if the creatinine clearance exceeded 50 ml/min or 4.5 g/day if the clearance was between 25 and 50 ml, and continued for 3 months. Because all patients had good renal function they were treated with 6 g of valacyclovir after 2 weeks of transplantation. Serum creatinine concentrations did not increase during treatment. Granulocytes were analysed weekly for CMV antigen. During the first 3 months of valacyclovir treatment, the granulocyte test became positive in only one of the six patients, and this patient remained asymptomatic.

A search for urinary crystals was performed on fresh urine samples two times per week during the first month and once per week over the next 2 months using polarization microscopy. Acyclovir crystalluria was never detected in the six patients at any time during the 3 months of treatment.

We conclude that valacyclovir is effective and safe in the prevention of CMV disease in renal allograft recipients. The pharmacokinetic properties of this drug which has an AUC similar to that of i.v. acyclovir without a serum peak could account for the absence of crystalluria and deterioration of renal function. However, our preliminary findings, especially the absence of crystalluria, need to be confirmed in a larger series of patients.

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