

*Conflict of interest statement.* None declared.

Division of Nephrology – Jean-Pierre Wauters  
Hypertension Dominik Uehlinger  
University Hospital Hans-Peter Marti  
Bern  
Switzerland  
Email: jean-pierre.wauters@insel.ch

1. Guillen-Anaya MA, Jadoul M. Drug interaction between sevelamer and cyclosporin. *Nephrol Dial Transplant* 2004; 19: 515
2. Trull AK, Tan KKC, Tan L *et al.* Absorption of cyclosporin from conventional and new micro-emulsion oral formulations in liver transplant recipients with external bile diversion. *Br J Clin Pharmacol* 1995; 39: 627–631
3. Jensen RA, Lal SM, Diaz-Arias A *et al.* Does cholestyramine interfere with cyclosporine absorption? Prospective study in renal transplant patients. *ASAIO J* 1995; 41: 704–706
4. Product Information Brochure USA and Summary of Product Characteristics of the EMEA.

doi:10.1093/ndt/gfh298

## Reply

Sir,  
We thank Jean-Pierre Wauters and colleagues for their helpful comments. The lower level of cyclosporin A (CsA) under sevelamer may indeed be due to a direct binding of CsA by sevelamer, rather than to an indirect impact of sevelamer on bile acids. Thus, the recommendation of a delay between the intake of sevelamer and that of drugs such as CsA is fully warranted. We disagree, however, on the claim that calcium-based binding is fully specific for phosphate. Indeed, the co-administration of either calcium acetate or sevelamer with ciprofloxacin recently has been shown to reduce the oral bioavailability of the latter drug by some 50% [1].

*Conflict of interest statement.* None declared.

Miguel-Angel Guillen-Anaya  
Michel Jadoul

1. Kays MB *et al.* Effects of sevelamer hydrochloride and calcium acetate on the oral bioavailability of ciprofloxacin. *Am J Kidney Dis* 2003; 42: 1253–1259

doi:10.1093/ndt/gfh298

## Sevelamer and pharmacokinetics of cyclosporin A after kidney transplantation

Sir,  
In their interesting article, Pieper *et al.* analysed prospectively the effect of sevelamer on the pharmacokinetics of cyclosporin (CsA) and mycophenolate mofetil (MMF) in kidney transplanted patients [1]. They provide the reassuring message that, in contrast to MMF, CsA kinetics are not significantly modified by the intake of sevelamer. These results are in sharp contrast to the observation and potential mechanisms that we reported recently [2,3].

The short duration (4 days) and limited statistical power (10 adults and eight children) of the study of Pieper *et al.* make such a strong message rather questionable [4]. Indeed, only 4 days after starting sevelamer, none of the CsA parameters (measured by Cedia and FPIA assays) was completely stable: the area under the curve (AUC) decreased from  $3547 \pm 660$  to  $3230 \pm 612$  ng/h/ml,  $C_{\max}$  decreased from  $955 \pm 193$  to  $855 \pm 272$  ng/ml and  $T_{\max}$  increased from 1.3 to 1.5 h. In addition, when measured with polyclonal antibodies, the CsA levels decreased significantly and, among its primary metabolites determined by HPLC, the AUC and  $C_{\max}$  of AM1—which also has an immunosuppressive action [5]—decreased significantly by 30 and 25%, respectively.

Despite these observations, the authors conclude that ‘sevelamer intake for several days does not significantly influence CsA kinetics’. Based on their data, this conclusion appears at least premature, especially if the risk of transplant rejection due to insufficient immunosuppression is considered [6]. Great caution in the use of sevelamer in transplanted patients is still warranted until a careful long-term, large size study on the potential interaction of sevelamer with CsA solves the question.

*Conflict of interest statement.* None declared.

<sup>1</sup>Division of  
Nephrology-Hypertension  
University Hospital  
Bern

Dominik Uehlinger<sup>1</sup>  
Hans-Peter Marti<sup>2</sup>  
Michel Jadoul<sup>3</sup>  
Jean-Pierre Wauters<sup>1</sup>

<sup>2</sup>Division of Nephrology  
University Hospital  
Zurich  
Switzerland

<sup>3</sup>Division of Nephrology  
Cliniques Universitaires Saint-Luc  
Brussels  
Belgium

Email: jean-pierre.wauters@insel.ch

1. Pieper AK, Buhle F, Bauer S *et al.* The effect of sevelamer on the pharmacokinetics of cyclosporin A and mycophenolate mofetil after renal transplantation. *Nephrol Dial Transplant* 2004; 19: 2630–2633
2. Guillen-Anaya MA, Jadoul M. Drug interaction between sevelamer and cyclosporin. *Nephrol Dial Transplant* 2004; 19: 515
3. Wauters JP, Uehlinger D, Marti HP. Drug interaction between sevelamer and cyclosporin. *Nephrol Dial Transplant* 2004; 19: 1939–1940
4. Felipe CR, Silva HT, Pinheiro Machado PG, Garcia R, da Silva Moreira SR, Medina Pestana JO. Time-dependent changes in cyclosporine exposure: implications for achieving target concentrations. *Transplant Int* 2003; 16: 494–503
5. Copeland KR, Yatscoff RW, McKenna RM. Immunosuppressive activity of cyclosporine metabolites compared and characterized by mass spectrometry and nuclear magnetic resonance. *Clin Chem* 1990; 36: 225–229
6. Waiser J, Slowinski T, Brinker-Paschke A *et al.* Impact of the variability of cyclosporin A trough levels on long-term renal allograft function. *Nephrol Dial Transplant* 2002; 17: 1310–1317

doi:10.1093/ndt/gfh700