Conflict of interest statement. None declared.

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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].

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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 ± 660 to 3230 ± 612 ng/h/ml, C_{max} decreased from 955 ± 193 to 855 ± 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.

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