Drug interaction between sevelamer and cyclosporin

Sir,

Sevelamer hydrochloride is a calcium-free polymer licensed recently as a phosphate binder in haemodialysis (HD) patients. Its use is associated with a slower progression of coronary and aortic calcifications than the use of calcium-based binders in such patients [1]. Sevelamer not only binds phosphate but also bile acids, thereby reducing LDL cholesterol levels [2]. Whether this effect on the enterohepatic cycle may lead to clinically relevant drug interactions is unknown.

We report a definite interaction between sevelamer and cyclosporin A (CsA) in a liver transplant (TP) recipient on maintenance HD.

A 70-year-old female on thrice weekly HD for 3 years for a chronic glomerulopathy (not biopsied) was started on sevelamer for persistent hyperphosphataemia (7.1 mg/dl).


Her daily drug treatment included: cyclosporin (Neoral®) 60 mg, propranolol 40 mg, doxepin 25 mg, clonazepam 0.25 mg, zolpidem 10 mg, omeprazole 10 mg, insulin and calcium carbonate. Physical examination showed a body mass index of 17 and a non-tender liver palpable 3 cm below the right costal margin.

Upon start of sevelamer (3 x 806 mg/day), CsA trough level, previously stable, decreased markedly, prompting an increase of CsA dosage to 85 mg (arrow in Figure 1).

Complaints of digestive intolerance prompted subsequent sevelamer withdrawal. The CsA level then increased soon, to decrease again consistently upon resumption of sevelamer (Figure 1).

Our case provides evidence for an impact of sevelamer intake on CsA level, confirmed by rechallenge. The mechanism of this interaction likely involves the reduction of CsA absorption through an effect on the enterohepatic cycle of bile acids. The absorption by the gut of CsA (including the Neoral® formulation) is indeed bile dependent [3]. Alternative explanations appear unlikely as sevelamer is not absorbed by the gastrointestinal tract and thus is devoid of any ‘systemic’ effect [1].

The observed interaction is relevant for the growing cohort of renal TP recipients entering ESRD under CsA, but also for the 5–10% of liver and heart TP recipients with ESRD [4,5]. This interaction may have been favoured by the cirrhotic state of our patient.

Whether sevelamer may interact with other lipophilic drugs such as tacrolimus, that shares many drug interactions with CsA, will require further investigation.

Conflict of interest statement. None declared.

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Fig. 1. Impact of sevelamer intake on CsA trough level.