Letters and Replies

Advance Access publication 23 March 2010

Rhabdomyolysis and acute kidney injury secondary to concomitant use of fluvastatin and rapamycin in a renal transplant recipient

Sir,

We recently read a paper published by Hurst et al. who investigated incidence, predictors and associated outcomes of rhabdomyolysis (RM) in renal transplant recipients [1]. RM is rarely reported in this population, with most of the cases occurring in patients treated with calcineurin inhibitors in combination with statins. In a retrospective cohort of 20,366 renal transplant recipients, the incidence rate of RM was 1.4 per 1000 person-years. Factors associated with RM after renal transplantation were black race and cyclosporine [1]. Sirolimus may cause RM in liver transplant patients when used concomitantly with simvastatin [2].

Our patient developed severe RM and acute kidney injury requiring dialysis after treatment with sirolimus and fluvastatin. A 66-year-old female patient received allograft from a deceased donor in December 2006. She was treated with cyclosporine A, mycophenolate mofetil and steroids. Two years later, she was operated for meningioma and switched from cyclosporine to sirolimus. She had stable graft function with serum creatinine within the normal range. Dyslipidaemia demanded introduction of fluvastatin 80 mg/day. Two weeks later, she was admitted to hospital febrile and with severe diarrhoea. Serum creatinine was 751 μmol/l, blood urea nitrogen (BUN) was 29.2 mmol/l and creatine kinase (CK) was 15,138 IU/l. She was oliguric and required dialysis for 2 days. Evaluation demonstrated Escherichia coli sepsis. Treatment with ceftriaxone and symptomatic therapy resulted in normalization of renal function and overall clinical status. Fluvastatin was immediately omitted.

Sirolimus was not associated with RM on bivariate and multivariate analysis in the study published by Hurst et al. [1]. It is well known that sirolimus causes dyslipidaemia, but its interaction with statins remains unknown [3]. Our case demonstrates for the first time that a combination of sirolimus and fluvastatin may cause severe RM. It is possible that the associated sepsis contributed to the development of RM by altering cytochrome P450 enzyme metabolism [4]. Finally, strong association of myopathy with the rs4363657 single-nucleotide polymorphism (SNP) located within SLCO1B1 on chromosome 12 was demonstrated [5]. Identification of patients with these genetic variants may help to avoid serious side effects of statin treatment.

Conflict of interest statement. None declared.

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We read with great interest the letter responding to our recently published article [1]. The authors describe a 66-year-old female renal transplant recipient who developed post-transplant dyslipidaemia after cyclosporine was switched to sirolimus, which was treated with fluvastatin. Two weeks later, she presented with sepsis and severe rhabdomyolysis requiring dialysis. The authors conclude that the rhabdomyolysis was possibly related to a drug–drug interaction between sirolimus and fluvastatin.

Sirolimus is known to cause dyslipidaemia post-transplant, which may result in the addition or increased dosing of lipid-lowering therapy. In a trial using a sirolimus maintenance immunosuppressive regimen, resulting dyslipidaemia required statin and fibrate drug use in 80% and 25% of patients, respectively, compared with a baseline frequency of use of 15% and 3% [2]. Sirolimus and fluvastatin are both metabolized in part via the cytochrome P450 3A4 (cyp3A4) pathway, although fluvastatin relies on this pathway to less of an extent than other statins, and is thought to be relatively safe when used in combination with cyclosporine in renal transplant recipients [3].


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