Case Report

Acute on chronic renal failure induced by simvastatin

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Introduction

Hyperlipidaemia may contribute to the increased cardiovascular risk in patients with renal failure [1] and has also been implicated in the progression of renal failure [2]. Despite this there has been a reluctance to use lipid-lowering drugs in patients with renal failure because of their poor tolerability and the increased risk of toxicity, particularly rhabdomyolysis [3]. The statins (3-hydroxy-3 methylglutaryl coenzyme A reductase inhibitors), however, are effective, well tolerated, relatively safe and, in view of the recent evidence of their beneficial effects in hyperlipidaemic patients with normal renal function [4, 5], they may be increasingly used in patients with renal failure. Statins can cause rhabdomyolysis with resultant acute renal failure, and the incidence of this is increased by concomitant therapy with cyclosporin [6], fibric acid derivatives [7], nicotinic acid [8], and erythromycin [9]. Caution is advised when prescribing the statins in patients with renal impairment, although the reasons for this recommendation are not given in the data sheets. We report a patient who developed acute on chronic renal failure without evidence of rhabdomyolysis, on two occasions following treatment with simvastatin.

Case report

A 60-year-old man with chronic renal failure due to membranous glomerulonephritis who had stable renal function, with a serum creatinine of 360–420 μmol/l, a creatinine clearance of 18 ml/min, and proteinuria of 20 g/day was under long-term nephrological review. He had a history of ischaemic heart disease requiring coronary artery bypass grafting, diet-controlled diabetes mellitus, and hypertension treated with lisinopril and atenolol. In addition he was being treated with frusemide, ferox sulphate, isosorbide mononitrate, and erythropoietin.

Simvastatin 20 mg daily was introduced by his general practitioner for hypercholesterolaemia and when he was seen in the clinic 5 weeks later, although he was symptomatically unchanged, the serum creatinine was noted to have risen from 382 μmol/l to 571 μmol/l (Figure 1) and the creatinine kinase (CK) was mildly elevated at 364 U/l (reference range <150 U/l). Simvastatin was discontinued, and 1 week and 1 month later the serum creatinine was respectively 455 μmol/l and 410 μmol/l.

The patient was then admitted to another hospital with an extensive left temporal intracerebral haematoma, confirmed by computerised tomography. On admission intravenous fluids were commenced and simvastatin was reintroduced. The hemiparesis failed to recover but his clinical course was otherwise unremarkable with no hypotension, dehydration, or intercurrent infection. Nifedipine was commenced a week following admission as his blood pressure was 180/100 mmHg but no other changes in drug therapy were made. Renal function deteriorated, the serum creatinine rising from 398 μmol/l following admission to 727 μmol/l after 13 days and 1125 μmol/l after 29 days.

At this stage the patient was transferred for assessment and found to be oliguric but well hydrated and normotensive with no signs of sepsis. Simvastatin was discontinued and he was managed conservatively with intravenous fluids, frusemide and dopamine. The CK was 218 U/l and his liver function tests were normal. Dialysis was never required, his renal function recovered and after 4 weeks the serum creatinine returned to and remained at its previous levels.

Discussion

Although acute renal failure due to rhabdomyolysis has been described as a rare complication of statins this is the first report where acute on chronic renal failure in the absence of rhabdomyolysis has occurred. On two occasions the deterioration in renal function in this patient was temporally related to the introduc-

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Simvastatin-induced renal failure

Fig. 1. Plot of serum creatinine and mean arterial blood pressure against time, with bars representing the period of simvastatin therapy, and showing the deterioration of renal function whilst receiving simvastatin and the recovery when simvastatin was withdrawn.

...tion of simvastatin and both episodes resolved following the withdrawal of the drug, suggesting that it was the causative agent. No other factors could be identified to explain this reversible decline in renal function, and in particular there was no evidence of hypotension, fluid depletion, or sepsis and no exposure to nephrotoxic drugs. Clinical experience with statins in patients with renal failure is limited but is likely to increase. We have no explanation for the mechanism of statin-induced deterioration of renal function but this case illustrates the need for vigilance in such patients, and in particular the importance of monitoring renal function closely.

References


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Editor’s note

Please see also Biesenbach et al., Nephrol Dial Transplant 1996; 11: 2059–2060.