Levofloxacin and rhabdomyolysis in a renal transplant patient

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Rhabdomyolysis can lead to fatal hyperkalaemia, acute renal failure and compartment syndromes in renal transplant patients. The most common cause for rhabdomyolysis in these patients is a drug interaction between statins and ciclosporin A [1]. Statins are known to be myotoxic [2], and their serum levels can be elevated with the concomitant use of ciclosporin A, as the metabolism of both drugs is dependent on the 3A4 coenzyme of the cytochrome P450 system. Some argue that the safest statins for transplanted patients are those whose elimination is independent of the P450 system, e.g. pravastatin.

Flouroquinolones have become widely used antibiotics. In this report, levofloxacin led to rhabdomyolysis in a renal transplant patient. Although scattered reports are beginning to appear showing that these agents can induce rhabdomyolysis [3–5], this is the first such description of a possible levofloxacin–induced rhabdomyolysis in a renal transplant recipient.

A 68-year-old man was admitted with a 3-day history of fever and cough. Past medical history included a first, cadaveric-donor, renal transplant in 1980. In 1994, the patient received a second, cadaveric-donor, renal transplant. Dual immunosuppression was maintained with prednisone and ciclosporin A. Renal function was stable, with a glomerular filtration rate (GFR) (MDRD) \(\sim 30\) cc/min/1.73 m\(^2\). Ischaemic heart disease required coronary artery bypass grafts in 1993, and recurrent gouty arthritis was treated with colchicine. Other daily medication included simvastatin (40 mg).

Admission chest X-ray revealed consolidation of the middle lobe of the right lung. Intravenous ceftriaxone and roxithromycin were commenced. After 3 days, the patient was afebrile; oral levofloxacin, 250 mg/day, was commenced and all other antibiotic therapy ceased.

After 10 days of levofloxacin therapy, the patient returned to the hospital with worsening myalgia and difficulty in walking. Proximal leg muscle groups were tender. Serum CPK level was 4800 IU/ml and myoglobinuria was present. Levofloxacin, simvastatin and colchicine were stopped. Intravenous hydration was maintained for 5 days. Serum CPK levels peaked at 6200 IU/ml before starting to drop. Muscle pain and tenderness disappeared after \(\sim 14\) days. Today, the patient has resumed all previous medication and repeat CPK levels are normal.

The diagnosis of rhabdomyolysis in this patient is clear cut and the most probable ‘cause-effect’ relationship involves levofloxacin therapy. Chronologically, rhabdomyolysis developed only after levofloxacin had been added to this patient’s existing medication, and after the pneumonia had begun to improve. Furthermore, after cessation of levofloxacin, rhabdomyolysis cleared completely, despite the renewal of all other potential myotoxic medications.

In 1999, Baril \textit{et al.} [3] described a patient who received ofloxacin. Marked proximal muscle weakness developed quickly. Peak CPK levels reached 24 000 U/L. After stopping the quinolone, the rhabdomyolysis cleared. In 2001, Guis \textit{et al.} [4] observed acute and severe muscle disease in a patient given norfloxacin. Again, cessation of the offending agent led to full muscle recovery. Of major interest is the communication by Petitjeans \textit{et al.} [5] in 2003. Their elderly patient received levofloxacin for \(\sim 1\) week before presenting with rhabdomyolysis and dialysis-dependent renal failure. The authors then reviewed the database at the WHO Collaborating Center for International Drug Monitoring for information regarding levofloxacin and rhabdomyolysis. Since 1998, 27 ‘suspect cases’ have been reported, with four fatalities [5].

Levofloxacin has predominant renal elimination. As such, dose reductions are necessary in patients with significant renal dysfunction [6]. Metabolism does not involve the P450 system and Doose \textit{et al.} [7], after studying 12 healthy subjects, concluded that ‘a clinically important
pharmacokinetic interaction between levofloxacin and cyclosporine A (CyA) is unlikely’. However, CyA is a potent inhibitor of P-glycoprotein—a drug transporter which reduces cellular concentrations of certain drugs [8]. In this way, CyA may actually prolong tissue levofloxacin concentrations, especially if levofloxacin dosage is inappropriately high. Quinolones are known to cause tendon rupture. Add to this the communiqué of Petitjeans et al. [5] and it seems prudent to monitor musculoskeletal activity in patients taking this drug, especially if they are already on medication which is possibly myotoxic.

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References


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