Acute Rhabdomyolysis and Hemoglobin Reduction after Bezafibrate Overdose in Hyperlipidemic Patients on Hemodialysis

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Dear Sir,

Many patients with chronic renal failure (CRF) develop hyperlipidemia. Frequently, to correct this abnormality some form of pharmacological intervention is necessary. In clinical trials bezafibrate was administered to hyperlipidemic patients with CRF [1] or in regular dialytic treatment (RDT) [2]. Severe adverse reactions were reported infrequently but in some patients suffering from CRF [3] bezafibrate therapy induced rhabdomyolysis. We present 2 cases of bezafibrate overdose complicated with rhabdomyolysis and acute hemoglobin reduction in patients on RDT.

Case 1: A 63-year-old man on RDT for 5 months owing to diabetic nephropathy was treated with bezafibrate at the dosage of 400 mg every second day. Four weeks later he experienced diffuse muscle weakness and nocturnal cramps. Laboratory studies showed a slight increase in serum creatine phosphokinase (CPK) and lactic dehydrogenase (LDH) with a small reduction in Hb concentration (from 8.1 to 7.4 g/dl). Because of the persistence of hypertriglyceridemia, we recommended that the patient continue the bezafibrate therapy with a more appropriate dosage (i.e. 200 mg every third day). The erroneous understanding of our prescription made the patient carry on with the same dosage of the drug. After a further 4 weeks he experienced aching of his muscles, which gradually worsened, leading to generalized weakness and severe fatigue in walking. The most significant laboratory data are shown in figure 1. There was also a light increase of serum and urine concentrations of myoglobin without reduction of daily diuresis. The drug

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Fig. 1. Effects of short-term administration of bezafibrate overdose in a uremic patient on RDT (case 1). The asterisk points out the values after blood transfusion. The arrow shows the time of the drug discontinuation.

discontinuation and blood transfusion supplements favored the regression of clinical symptomatology.

Case 2: A 64-year-old man on RDT for 26 months owing to nephrosclerosis was treated with bezafibrate at the dosage of

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200 mg daily to correct severe type IV hyperlipidemia. Eight weeks after the beginning of bezafibrate administration the patient was admitted to hospital because of severe diffuse muscle and abdominal pain. The patient was anuric; laboratory data were as follows: hemoglobin 8.9 g/dl, CPK 1444 U/l, LDH 445 U/l. Serum myoglobin was weakly elevated. Twelve hours after admission the serum muscle enzyme concentrations increased (CPK 8,200 U/l, LDH 858 U/l, respectively) while the hemoglobin decreased to 7.3 g/dl. Drug treatment was stopped and the patient was confined to bed. Two weeks later, CPK and LDH returned to normal values but the hemoglobin was further reduced (6.7 g/dl).

Severe reversible myopathy associated with bezafibrate therapy has been reported in some patients with CRF [3] but, on the contrary, small reductions in hemoglobin were demonstrated only in patients without CRF and treated with bezafibrate for a long time at the recommended dosage [4]. Our results confirm that the administration of bezafibrate in hemodialysis patients can induce rhabdo-myolysis but also show that this drug may favor a marked reduction of the hemoglobin (fig. 1).

The mechanisms by which bezafibrate causes these clinical adverse events are not clear.

However, it is certain that bezafibrate side effects are more frequent if its dosage is not carefully adjusted to avoid drug accumulation. Because pharmacokinetic studies suggest that a suitable dosage in patients on renal dialysis is 200 mg every third day [5], it is a well-founded supposition that the rhabdo-myolysis and acute anemia, probably due to hemolytic damage, observed in our patients were the consequence of the toxic action of this lipid-regulating agent.

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