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Letter to the Editor

Severe myopathy induced by the co-administration of simvastatin and itraconazole

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Treatment with statins has been associated with myopathy ranging from myalgia to severe life-threatening rhabdomyolysis [1]. Only a minority of patients develops myopathy in response to lipid-lowering agents [1]. The co-administration of itraconazole with statins has, on rare occasions, been associated with myopathy; in most of these cases, another drug, such as cyclosporine or gemfibrozil, may have contributed to the myopathy [2]. We present a case of severe myopathy resulting from the co-administration of itraconazole and simvastatin alone.

A 67-year-old woman had been taking simvastatin 40 mg daily for 2 years. She was otherwise healthy and had not been on any other medication. Two weeks prior to her present admission, she consulted a dermatologist for onychomycosis of the toenails and she was prescribed itraconazole 100 mg twice daily for 5 days. Two days after termination of itraconazole, the patient started suffering from weakness and generalized severe myalgia.

She denied having done any strenuous exercise, intramuscular drug injection, or recent trauma.

Physical examination was remarkable for severe muscle tenderness, particularly of the proximal muscles of the upper and lower limbs. In addition, we detected weakness on abduction of the arms and on flexion of the thighs. No erythema was detected.

Laboratory tests revealed alanine aminotransferase 783 IU/L, aspartate aminotransferase 1365 IU/L, lactate dehydrogenase 4669 IU/L, alkaline phosphatase 57 IU/L, and creatine phosphokinase 45348 IU/L. These tests had been normal 1 month earlier. Urine was positive for myoglobin. Blood cell count, electrolytes, calcium, phosphorus, and renal and thyroid function tests were normal.

The patient was treated with fluids and bicarbonate infusion with diuretics. After 5 days, she was discharged. Her levels of creatine phosphokinase and transaminases, and her symptoms had improved dramatically.

Our patient was stable on chronic treatment with simvastatin until the addition of itraconazole for 5 days caused severe myopathy.

HMG-CoA reductase inhibitors are primarily metabolized by the cytochrome *P*450 [2]. Of the several isoenzymes of the cytochrome *P*450, simvastatin is metabolized by CYP3A4 [2]. Drugs like itraconazole, which inhibit CYP3A4, increase the plasma concentration of simvastatin and significantly increase the risk of myopathy in these patients [1].

The increasing awareness of the public of minor fungal infections like tinea pedis and onychomycosis inevitably increase the prescription of antifungal drugs. Doctors should be aware of the interaction between itraconazole and statins, even when short-term therapy is prescribed with itraconazole, as it may lead to severe adverse effects like that which occurred in our patient. We recommend temporarily discontinuing statin therapy when itraconazole is prescribed for a short period. When longer treatment with itraconazole is required, either reducing the statin dosage or changing to another statin that is not metabolized by CYP3A4 should be considered.

References

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