

ALTERNATIVE VIEWPOINTS

Rhabdomyolysis Caused by a Potential Sitagliptin-Lovastatin Interaction – What about the Diltiazem?

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Key Words: Diltiazem, Lovastatin, Sitagliptin, Rhabdomyolysis
(*Pharmacotherapy* 2009;29(6):176e)

DiGregorio and Pasikhova speculate on an interaction between sitagliptin and lovastatin causing rhabdomyolysis,¹ but we were surprised that they dismiss the contribution of diltiazem to this event because the last dose adjustment was 10 months earlier. Prescribing information advises restricting lovastatin dosage to 40 mg daily when used in combination with diltiazem, but an interaction study showed diltiazem increased systemic exposure to lovastatin by a mean additional 250% (range 51–906%).² In this case, the combination may be equivalent on average to a dose of lovastatin 140 mg, a potentially toxic dose, especially in an older female patient with diabetes and treated hypothyroidism.³ Interactions with diltiazem appear to persist with chronic dosing as illustrated by an interaction with simvastatin⁴ and by the common practice of giving diltiazem along with cyclosporine to reduce the long term dose requirement and cost.

Although muscle damage usually occurs within one month of starting a high dose of statin or an interacting drug combination, the onset can occur at any time, possibly in relation to triggering factors such as excessive physical exertion,⁵ inadequate treatment of hypothyroidism or a minor deterioration in renal

or hepatic clearance of the drug, which could be related to the addition of a new drug or progression of underlying diseases. In subjects at risk of myopathy with simvastatin 80 mg, because of the genetic variant of the hepatic uptake transporter OATP1B1, myopathy did not occur until after at least 6 months treatment in over 50% of cases.⁶ Sitagliptin did not show significant interaction with simvastatin,⁷ which has similar drug interactions to lovastatin. It is possible that the addition of sitagliptin finally tipped the balance in this patient on a potentially toxic combination of lovastatin and diltiazem, but other factors, including deterioration in glycemic, lipid or thyroid control, should also be considered.

References

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Authors' Reply

The authors declined the opportunity to reply.

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Dr. Tomlinson has received research funding to perform clinical studies from AstraZeneca, Bayer, Boehringer Ingelheim, Daiichi Sankyo, Kowa, Merck, Merck Sharp and Dohme, Novartis, Otsuka, Pfizer, Roche, Sanofi-Aventis and Servier and has acted as a consultant or speaker on occasions for AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, Kowa, Merck, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Aventis, Schering-Plough, and Servier.

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