Courting hyperlipidemia

Hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase activity peaks at night[1] or while the patient is fasting, with corresponding increases in hepatic cholesterol synthesis. Short-acting HMG-CoA reductase inhibitors (statins) must therefore be taken within a few hours of going to sleep. In contrast, atorvastatin[2] has a longer duration of action and can therefore be taken at any time of the day. In the following case a trivial change in timing of the patient's medication nullified the therapeutic effect.

In May 1997, a 70-year-old woman was given a prescription for simvastatin 20 mg daily, to be taken at bedtime. Her lipids were within the target range for the period March 1998 to April 2000 (Fig. 1), and she tolerated the medication well, with no side effects. Five months later, in September 2000, her lipids had risen to levels similar to those before she started the medication, and it appeared that she might have stopped her drug therapy. On questioning, she claimed that she had been taking simvastatin daily for the past 2 years. I then asked if there had been any changes in her routine over the previous 6 months that might have led to the changes in her lipid levels. She noted that about 5 months previously (late spring 2000) she had started dating someone, and they had been going out regularly for dinner and dancing. She claimed that she was watching her diet even though she was eating out more frequently. However, because she was coming home late at night, she sometimes forgot to take her medication before going to bed. To avoid missing doses, she had started taking the drug in the morning with breakfast.

This information solved the mystery. I discussed the timing of action of simvastatin with the patient and stressed the importance of taking the medication at night. She resumed evening dosing in October 2000, and by March 2001 her lipid levels had returned to within the target range.

This case illustrates the importance of proper timing of the daily dose for some medications and demonstrates that a seemingly trivial change in timing can affect the therapeutic outcome.[3]

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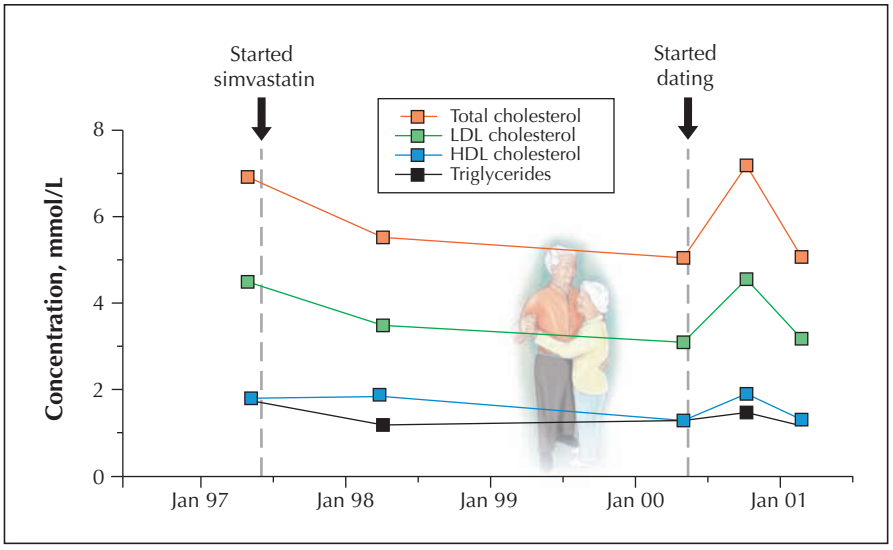

Fig. 1: Lipid values for a 70-year-old woman who started taking simvastatin 20 mg daily in May 1997. She started dating about a month after lipid levels were measured in April 2000 and subsequently started taking her simvastatin in the morning rather than before bed. In October 2000, she resumed taking the drug in the evening. HDL = high-density lipoprotein, LDL = low-density lipoprotein.

References
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2. Cilla DD, Gibson DM, Whitfield LR, Sedman AJ. Pharmacodynamic effects of atorvastatin after administration to normocholesterolaemic patients in the morning and evening. *J Clin Pharmacol* 1996;36:604-9.
3. Wallace A, Chinn D, Rubin G. Taking simvastatin in the morning compared with in the evening: randomised controlled trial. *BMJ* 2003; 327:788.

Competing interests: None declared.

Whence the Readers' Advisory Panel?

I think your Readers' Advisory Panel[1] is a wonderful idea and congratulate you on the same. However, given the addresses of the panel members, it