

# RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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## Nightmares and sleep disturbance with statins

Sleep disturbances and abnormal dreams are not uncommon, current nightmares being reported by approximately 5% of the population. Several etiologies have been suggested, including medications (refer E-Bulletin 25-7).

There have been a number of reports in the literature of sleep disturbance or nightmares related to the use of HMG-CoA reductase inhibitors (statins), most commonly with the more lipophilic agents. In one report, a 72 year old woman taking atorvastatin experienced nightmares 5 days after initiation of the drug. These disappeared on cessation and recurred on rechallenge, correlating to a “definite causality” according to the Naranjo probability scale (refer E-Bulletin 20-11). Nightmares resolved on discontinuation of treatment. In another report a 55 year old man reported restless nights and nightmares 3 months after simvastatin and metoprolol were initiated. No improvement was observed when the dose of metoprolol was decreased, however, some improvement was noted with simvastatin was replaced with pravastatin and nightmares resolved with metoprolol was replaced by atenolol. More recently, fluvastatin has been associated with nightmares in a 79 year old man. He had previously experienced nightmares during treatment on simvastatin. After cessation of the statin the patient was treated with ezetimibe without complaint

Lipophilic statins (simvastatin, atorvastatin) cross the blood-brain barrier more readily and are absorbed into the brain to a greater degree than hydrophilic statins (pravastatin, fluvastatin, rosuvastatin) and this may account for the observed effect. However, the relevance of lipophilicity of statins is not clear as sleep monitoring during treatment comparing simvastatin, lovastatin and pravastatin have shown no significant differences between these agents. The potential adverse effect could also be a result of pharmacokinetic (CYP3A4) or pharmacodynamic interaction. Beta blockers have also been shown to cause nightmares and concurrent use of both agents may enhance this effect. Statins have also been found to affect tryptophan metabolism therefore the appearance of nightmares may relate to disturbances in CNS serotonin availability.

To date the Advisory Committee on the Safety of Medicines (ACSOM) has received 99 reports of possible nightmares or sleep disorders associated with the use of statin drugs, but in many of these HMG-CoA reductase inhibitors were not the sole suspected agent and a number of other drugs could be implicated. In approximately 10% of cases a beta blocker was being administered concurrently.

Nightmares or sleep disturbances appear to be a rare class effect of statins. Some studies question the relevance of lipophilicity, however chemical characteristics of the drug may be important in individual patients and substitution with more hydrophilic agents or dose reduction may be an option to consider.

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