

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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Adverse effects of cholinesterase inhibitors

The cholinesterase inhibitors (CIs) include donepezil (Aricept[®]); galantamine (Reminyl[®]) and rivastigmine (Exelon[®]), and are currently the main pharmacological agents used in the management of mild to moderate cognitive symptoms associated with Alzheimer's disease. They have only limited efficacy, and are associated with considerable risk of adverse effects. A Cochrane systematic review estimated that the number needed to harm (NNH) is 10; that is, of 10 patients treated with a CI for six months, one patient will cease therapy due to adverse effects. This E-Bulletin summarises the more common adverse effects, along with some less common but potentially serious adverse effects, associated with CIs.

Gastrointestinal: Nausea (incidence of 11–44%), vomiting (7–30%), diarrhoea (8–13%) and weight loss (7–11%) are common, particularly during the first few weeks of treatment or after a dose increase. These effects can be minimised by slow upward dose titration and taking the drug with food.

CNS: Headache, insomnia, vivid dreams, depression, drowsiness, fatigue and tremor are common. Insomnia appears to be more common with donepezil (especially if dosed at night) compared with galantamine and rivastigmine. Seizures, agitation, hallucinations and confusion have been reported rarely.

Cardiovascular: Dizziness is common (10% incidence). Importantly dizziness may be a clinical manifestation of changes in blood pressure and heart rhythm, and may manifest as syncope and falls. CIs are associated with a decrease in heart rate; and bradycardia, bundle branch block, atrioventricular block, syncope and arrhythmia have all been reported. A recently published observational study highlighted these concerns in its findings of increased rates of syncope, bradycardia, pacemaker insertion, and hip fracture associated with CI use in patients with dementia. It is important to check pulse rate before initiating a CI and then at least monthly during dose titration, then every six months thereafter. CIs should be avoided in patients with heart block, and particular caution is required in patients with sick sinus syndrome and in patients receiving other medications that can reduce heart rate (e.g. beta-blockers and digoxin).

Urinary tract: New onset or worsening of existing urinary incontinence is common with CIs. Depending on individual patient circumstances, this may necessitate a dose reduction or cessation of the CI. Ideally, the use of an anticholinergic agent (e.g. oxybutynin, solifenacin, tolterodine, darifenacin, propantheline) to manage urinary incontinence in patients with dementia treated with a CI should be avoided due to the risk of delirium, cognitive decline, and other troublesome adverse effects, such as dry mouth and constipation.

Other adverse effects: Sweating and muscle cramps are common. Other reported adverse effects include new or worsened extrapyramidal effects, hepatic adverse effects (rare); pancreatitis (rare), increased salivation, rhinitis, asthenia and blurred vision.

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