

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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Benzodiazepines and opioids

Opioids are used in the management of chronic pain and in maintenance programs as substitutes for illicit opioids. Depression, substance use and benzodiazepine use are all risks for adverse events from opioids. Patients that take opioid medications are frequently co-prescribed benzodiazepines. Studies of patients in methadone maintenance programs have revealed 50-70% take benzodiazepines. Within this population of patients it has been estimated that 18% to 50% have benzodiazepine dependence or abuse.

Clinical indications for benzodiazepines include anxiety, agitation and sleep problems that may occur at times during withdrawal syndromes from reducing or ceasing alcohol or opioids. Studies have reported that some patients experience intoxicating effects from taking benzodiazepines with methadone. Long term use of benzodiazepines may create dependence which leads to continued use. Patients are then vulnerable to misinterpreting withdrawal symptoms, such as increased anxiety or sleep disturbance, from cessation of benzodiazepines to be justification for continued use of the benzodiazepine.

A significant issue is that only one third of patients identified with benzodiazepine abuse or dependence believe benzodiazepines to be a problematic drug. Potential harm associated with benzodiazepines in combination with medications such as opioids seems to be poorly understood by users of both medications. In opioid-dependent polydrug users it has been reported that benzodiazepines are perceived as “less risky” as compared to illicit drugs.

Of concern is the potential contribution of benzodiazepine use to opioid-related deaths where it is common for multiple drugs are involved. Research suggests that prevalence of benzodiazepine use in methadone-related deaths have varied from low to high. For example, levels of use in Texas have been reported at 10%, in the UK at 20%, and up to 80% in Australian studies of methadone related deaths.

It has been reported recently that risk of methadone fatality may be linked to the presence of CYP2B6*6 allele, (which is a characteristic observed amongst slow metabolisers of methadone) and that a significant correlation was found with post-mortem benzodiazepine concentration and the μ -opioid receptor gene, *OPRM1* A118G allele GA, in methadone related, but not morphine, related deaths. Consequently in some patients taking methadone, benzodiazepines may contribute to drug toxicity by a mechanism yet to be fully understood.

Health professionals managing patients who are concurrently treated with both opioids and benzodiazepines need to review these patients regularly, assessing for therapeutic benefits, adverse effects, aberrant behaviour and any psychological disorders.

This E-Bulletin is based on work by Dr Brian Simmons, DATIS, RGH

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