Droperidol: cardiovascular toxicity and deaths

Reason for posting: Health Canada has warned that the injectable form of droperidol, commonly used as a neuroleptic and antiemetic, has been associated with 8 deaths in Canada.[1] The drug is also commonly used intramuscularly to treat migraine headache[2] and to sedate combative patients[3] including children and adolescents.[4] Worldwide, more than 60 cases of QT prolongation, serious cardiac arrhythmias (e.g., torsades de pointes [TdP]) and sudden death have been reported in association with injectable droperidol.[1] One international manufacturer, Janssen-Cilag, announced in March 2001 its discontinuation of droperidol production after chronic oral use of the drug by psychiatric patients was found to be associated with fatal cardiac arrhythmias. In December 2001 the US Food and Drug Administration announced that the warning labels for droperidol would be strengthened to recognize that cases of TdP were occurring even at doses of the drug below those recommended.[5] Health Canada is assessing whether further regulatory action regarding droperidol is required in Canada.[1]

The drug: Droperidol is approved for use in Canada as a neuroleptic drug and is an effective antiemetic for postoperative nausea[6] and nausea associated with Meniere's disease.[7] It is available in Canada only in injectable forms. Droperidol is a butyrophenone and acts in part as a dopamine antagonist.[6] It also inhibits α-adrenergic receptors, which leads to peripheral vasodilation (and possible hypotension). It acts within minutes of injection and has a half-life of 2.2–10 hours depending on its route of administration.[4,8] As a neuroleptic it has known adverse effects including sedation, extrapyramidal symptoms (restlessness, akathisia, dystonia and oculogyric crises) and neuroleptic malignant syndrome.[6,7] Droperidol is to be avoided in patients with liver or renal disease, Parkinson's disease or epilepsy.[7] Cardiovascular effects of the drug may be due to delayed myocardial repolarization, with QT prolongation and increased risk of TdP.[5] QT prolongation was apparently not mentioned in any of the reports of death in Canada, and other medications were concurrently being administered.[1]

What to do: Patients should be screened for a history of or risk factors for long QT syndrome. Patients predisposed to QT prolongation and TdP include those with electrolyte disturbances (low serum potassium or magnesium levels), bradycardia, cardiac conduction disturbances, congestive heart failure, cardiac hypertrophy, a history of alcohol abuse or recurrent blackouts, or a family history of sudden death. QT prolongation may also be more common in people 65 years and older and in those concomitantly using benzodiazepines, volatile anesthetics, intravenous opiates, antiarrhythmics (quinidine, sotalol or amiodarone), antipsychotics (thioridazine), some tricyclic antidepressants (amitriptyline), antibiotics (erythromycin, ketoconazole, moxifloxacin or pentamidine), antihistamines (astemizole or terfenadine), antiemetics (dolasetron), arsenic (for leukemia treatment) or migraine therapies (naratriptan). Droperidol should not be given to people whose baseline 12-lead electrocardiogram (ECG) reveals a QTc interval greater than 440 ms for males and 450 ms for females. Injectable droperidol should be used only in a hospital setting, where vital signs and ECG monitoring is available. The US manufacturer recommends 2–3 hours of cardiac monitoring after administration;[9] however, the appropriate duration of monitoring is unclear (arrhythmias and QT prolongation have occurred up to 24 hours after the drug's administration), and it is unclear whether continuous monitoring will detect or prevent serious QT prolongation, arrhythmia and death.[1]

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