The Institute for Safe Medication Practices Canada (ISMP Canada) is an independent Canadian nonprofit agency established for the collection and analysis of medication error reports and the development of recommendations for the enhancement of patient safety.

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Meperidine (Demerol®): Issues in Medication Safety

This bulletin addresses concerns raised by healthcare professionals regarding the place of meperidine (Demerol®) in Canadian hospitals. This brief review was prompted by medication error reports, including mix-ups between meperidine and other opioids as discussed in a previous bulletin,[1] as well as the desirability for hospitals to standardize formulary options. ISMP Canada recently received two reports of adverse events involving meperidine that resulted in morbidity and mortality:

> The first case involved a patient who had been taking meperidine 200 mg orally every 4 hours for acute pain. On admission to hospital the same dose was continued intramuscularly. When converting from the oral to the parenteral route, doses should be reduced accordingly (the bioavailability of oral meperidine is 40-60%.[2]) Shortly after admission the patient developed disorientation and confusion, which was initially attributed to the presenting medical condition. Meperidine 200 mg IM q4h continued to be given for approximately 48 hours. On the third day the patient experienced a grand mal seizure and was transferred to the Intensive Care Unit. The accumulation of the active meperidine metabolite, normeperidine, was suspected as the cause of the seizure. Within 48 hours of discontinuing meperidine, the confusion and disorientation resolved. The patient subsequently recovered without further incident.
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> In the second case, meperidine 50-75 mg IM q4h prn was ordered for an elderly individual with known hepatic impairment. The patient received the drug every 4 hours for 72 hours and was found without vital signs two hours after the last administered meperidine dose. Resuscitation attempts were unsuccessful. A follow-up investigation determined that the patient had a toxic meperidine level (and a high normeperidine level), likely contributing to the patient's death.

These incidents highlight the challenges of understanding the pharmacodynamics, dose conversions and monitoring requirements of opioids, not only meperidine. ISMP Canada has suggested general opioid safeguards in a previous bulletin.[1] This bulletin will focus on information that suggests restricting the use of meperidine to enhance medication safety.

Over the last decade, there has been progressive movement away from using meperidine in pain management in the United States.[3] The Joint Commission on Accreditation of Health Care Organizations (JCAHO) published pain management guidelines that discourage the use of meperidine.[4] These guidelines were based on a two-year collaboration with the University of Wisconsin-Madison, as well as on previous guidelines, including those by the Agency for Health Care Policy and Research (AHCPR) and the American Pain Society (APS).[4,5,6,7] Numerous U.S. organizations now view the usage of meperidine as an inverse indicator of quality of care.[4]

Meperidine has been widely used for over half a century for the management of acute pain.[5] There are relatively few applications for which meperidine would currently be considered a first line opioid, yet it continues to be ordered and administered in cases where scientific evidence for better alternatives exists. The potentially severe adverse reactions that can occur with the use of meperidine may be under recognized. The drug is metabolized via two hepatic pathways; the most clinically significant of these produces the active metabolite normeperidine. Normeperidine has half the analgesic potency of its parent compound but has 2-3 times the neurotoxic potential. Normeperidine is a potent central nervous system stimulant and signs of toxicity can include irritability, tremors, muscle twitching, disorientation, agitation, hallucinations, hypertension and grand mal seizures. The half-life of normeperidine ranges from 14-48 hours, and is even longer in patients with renal dysfunction. Repeated administration of meperidine can lead to an accumulation of normeperidine and predisposes patients to neurotoxicity.[3,8]

Considerations when reviewing the formulary status of meperidine may include:

- Meperidine is poorly tolerated in the elderly and is the opioid most often associated with delirium in the geriatric surgical population.[9]
- Meperidine is reported to have a duration of action of between 2 and 3 hours, therefore, the commonly prescribed q4h dosing may result in poor pain relief.[5] On the other hand, administration with a shorter dosing interval may predispose patients to toxicity.
- There is no specific benefit to meperidine compared to other opioids at equi-analgesic doses in pain management associated with biliary colic or pancreatitis.[3]
- Patients using PCA meperidine are at a particularly high risk of experiencing adverse drug reactions due to cumulative doses and duration of treatment.[10]
- Due to meperidine's euphoria and mood altering effects, it is a poor choice where drug-seeking behaviour is a potential issue.[3]
- The potential for neurotoxicity and anticholinergic effects make meperidine an inferior choice to other opioids in a number of conditions, including Sickle Cell Disease.[5]

- Fatal drug interactions have been reported between meperidine and monoamine oxidase inhibitors (MAOIs).[2,3]

ISMP Canada recommends healthcare facilities evaluate their use of meperidine and consider recommendations outlined by the AHCPR, APS and JCAHO,[4,5,6,7] to improve the safety of meperidine such as:

1. Remove oral meperidine from the formulary.
2. Review and revise pre-printed order sets to discourage use of meperidine.
3. Restrict the use of parenteral meperidine to:
   a. The prevention and treatment of drug-induced or blood product-induced rigors (e.g., amphotericin B, platelets)
   b. Treatment of postoperative shivering
   c. Short term pain management in individuals with normal renal, hepatic and CNS function **where alternative opioids are contraindicated** (e.g. drug allergy), and
      i. Do not exceed 600 mg/24 hours,
      ii. Limit the duration of use to 48 hours.
4. Avoid the use of meperidine in elderly patients since adverse effects are associated with increasing age.
5. Consider an automatic review of meperidine orders by a pharmacist to verify that the daily dose and duration of therapy comply with recommended guidelines.
6. Have information about meperidine restrictions, maximum dosing, treatment duration and signs of toxicity readily available at the point of care.
7. Implement an Acute Pain Service to promote best practices.

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ISMP Canada is a national voluntary medication incident and 'near miss' reporting program founded for the purpose of sharing the learning experiences from medication errors. Implementation of preventative strategies and system safeguards to decrease the risk for error-induced injury and thereby promote medication safety in healthcare is our collaborative goal.

To report a medication error to ISMP Canada: (i) visit our website www.ismp-canada.org or (ii) email us at info@ismp-canada.org or (iii) phone us at 416-480-4099. ISMP Canada guarantees confidentiality and security of information received. ISMP Canada respects the wishes of the reporter as to the level of detail to be included in our publications.

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