A. Background
Problems associated with meperidine use have resulted in inadequate pain control and adverse effects for many patients through the years. First-line opioids such as morphine, hydromorphone or oxycodone should be used in preference to meperidine, which should be utilized only as outlined below. Meperidine, in spite of its FDA labeled indication, is not suitable for chronic pain.

Through the years, the use of meperidine has often been accompanied by problems that have decreased the quality of patient care. Meperidine is a synthetic opioid, an analog of fentanyl, sufentanil and alfentanil with analgesic properties similar to morphine. It is not as potent as morphine and has a shorter duration of action, so that larger doses should be given more frequently. Studies have shown repeatedly that this is often not the case in clinical situations, where patients may have to endure recurrent pain unnecessarily. It is not well absorbed orally. Because the oral equianalgesic equivalent is three times the parenteral dose, patients often hesitate to take a therapeutic dose (at least three 50-mg tablets) even if it is prescribed.

Meperidine is transformed into a neurotoxic metabolite, normeperidine, that can accumulate after repeated administration even in mild renal insufficiency, so that in spite of its FDA-labeled indication, it is unsuitable for chronic use. Adverse effects of normeperidine include tremor, myoclonus and seizures.

Meperidine has interacted unpredictably with MAO inhibitors, producing case reports of a symptom cluster that includes agitation, fever and seizures progressing in some instances to coma, apnea and death. One case of a possible interaction with selegiline, an MAO type-B inhibitor, has also been reported. The narcotic analgesic of choice for patients taking an MAOI is morphine.

In spite of widespread use to abort migraine headache, especially in emergency care settings, meperidine is seldom the drug of choice for this indication. The primary reason for this is that, in spite of the language often used to describe therapy, the headache is not aborted in most cases, but the patient does obtain temporary pain relief. Meperidine may only offer two hours of analgesia. A longer acting agent is preferable. Please consult the Guidelines on Abortive Therapy for Migraine Headache.

When all these disadvantages are considered in comparison to other opioid analgesic choices, meperidine is clearly not a first-line agent. Guidelines have been developed for its use that reflect the consensus that first-line opioids such as morphine, hydromorphone or oxycodone should be used in preference to meperidine, which should be utilized only as outlined below. Meperidine does have unique therapeutic niches that are included in the appropriate indication section.

B. Appropriate Indications for Use
1.0 Management of acute episodes of moderate to severe pain if the patient has a history of one or more of the following problems:
   1.1 Unmanageable adverse reactions to other first-line opioids.
   1.2 Treatment failure to other first-line opioids given in adequate doses.

2.0 Prevention or treatment of drug-induced or blood product-induced rigors (e.g., amphotericin B, muromonab, platelets), and treatment of post-anesthesia shivering.

3.0 Conscious sedation used as a single injection prior to adult procedures requiring pre-procedure analgesia, where rapid onset and short duration may improve patient care.
4.0 Research protocols specifying the use of meperidine.

5.0 Neuraxial analgesia for acute pain management, administered by the anesthesiology service.

C. Dose, Route and Duration of Therapy

1.0 Meperidine should not be used for longer than 48 hours or at doses greater than 600 mg/24 hours in patients with normal renal function.

2.0 Adult parenteral doses may range from 50 to 150 mg SC every 3 hours as needed. The slow IV push route may also be used, at a starting dose of 25 mg, increasing in 25 mg increments to a maximum of 100 mg, every 2 to 3 hours as needed, within the limitations noted in point 1.0 above. Intramuscular (IM) absorption is erratic and IM injections are painful.

3.0 For the prevention of rigors, 12.5 to 50 mg should be administered via slow IV push. For treatment of rigors or post-anesthesia shivering, 12.5 to 50 mg should be given by slow IV push every 15 to 20 minutes until symptoms are controlled.

4.0 For pre-procedural sedation, single doses of 50 to 100 mg IM 30 minutes prior to procedures or 12.5 to 50 mg IV may be given, preferably incrementally, 5 to 10 minutes prior to procedures. Note: Intravenous administration or administration of intramuscular doses greater than 50 mg require heightened sedation monitoring (see UWHC Conscious Sedation Guidelines).

5.0 Meperidine is seldom indicated for analgesia in children. The analgesic dose is 1 to 1.5 mg/kg SC or slow IV push every 3 hours as needed. For the prevention or treatment of rigors, a single dose of 0.5 mg/kg may be administered via slow IV push.

6.0 The oral dosage form SHOULD NOT BE USED (Due to high first pass metabolism and increased concentration of normeperidine.)

D. Contraindications

- Hypersensitivity to meperidine.
- Patients who are receiving monoamine oxidase (MAO) inhibitors or those who have received MAO inhibitors in the past 14 days.
- Patients with renal insufficiency (creatinine clearance less than 50 ml/min).
- Patients with untreated hypothyroidism, Addison's disease, benign prostatic hypertrophy, or urethral stricture.

E. Inappropriate Indications

1.0 Meperidine has not been shown to have any specific benefit in patients with biliary colic.

2.0 Meperidine has not been shown to have any unique benefit in the treatment of pain due to acute pancreatitis.

3.0 Routine use of meperidine prior to the first dose of amphotericin is inappropriate. If a patient does develop rigors, prophylactic use prior to subsequent doses is warranted.
F. Precautions

1.0 Meperidine should be discontinued when the following central nervous system effects occur:

- Anxiety
- Fluctuations in awareness levels
- Hallucinations
- Agitation
- Illusions
- Disorientation
- Restlessness
- Bizarre feelings (feeling frightened)
- Seizures
- Diaphoresis
- Shakiness
- Myoclonic jerks
- Nervousness
- Tremors
- Confusion

1.1 In cases of meperidine neurotoxicity, naloxone should not be used. Naloxone does not reverse the effects of normeperidine, and may actually precipitate seizure activity as the sedative effects of meperidine are reversed allowing the full effect of normeperidine to act on the central nervous system. Naloxone is effective in reversing episodes of apnea induced by meperidine.

1.2 The following management guidelines have been recommended: (1) Discontinue meperidine completely; (2) Add an alternative opiate agonist (morphine or hydromorphone); and (3) Use diazepam, phenytoin or other anticonvulsants for seizure control (Kaiko RF, et al. *Ann Neurol* 1983;13:180-5.).

2.0 In all cases, meperidine should be given with caution. The initial dose should be reduced in all patients with decreased renal or hepatic function, and in the elderly.

3.0 Meperidine should be used with extreme caution in patients with pre-existing convulsive disorders, and in patients receiving drugs that are known to predispose patients to seizures (e.g., imipenem).

4.0 Meperidine should be used with caution in patients with atrial flutter or other supraventricular tachycardias.

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