

## Academic Detailing of Meperidine at a Teaching Hospital

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**Abstract** — Meperidine (Demerol) is an opiate analgesic that is not considered first-line therapy for most pain management indications because of concerns about its safety and efficacy. Inpatient data from a 417-bed community teaching hospital revealed high use of meperidine in oral, IM, and IV forms. A multifaceted academic detailing approach was employed to change prescribing behavior and decrease meperidine use. This approach included conducting two concurrent Medication Use Evaluations; Grand Rounds presentations for pharmacy staff, nurses, and medical residents; solicitation of opinion leaders; pocket and table-top cards; newsletter articles; and provision of pharmaceutical care. Comparing the number of meperidine doses dispensed per adjusted patient day before and after the intervention, use was reduced by 0.0966 doses per patient ( $P < 0.05$ ; 95% CI, 0.0955 to 0.0977). The number of patients receiving meperidine was reduced by 2.43% ( $P < 0.05$ ; 95% CI, 1.97 to 2.88). This translates into a relative reduction of 29.5% in patients receiving meperidine and a relative reduction of 31% in meperidine doses dispensed per patient after academic detailing initiatives vs before. Eighty-five percent of standard orders were changed to improve therapy; these changes included converting meperidine to morphine or hydromorphone, decreasing cumulative acetaminophen daily dosages, using controlled-release and immediate-release opioids for pain management when oral therapy was tolerated, and combining modalities with different mechanisms of action for synergy and to decrease potential adverse effects from larger dosages of single entities. Academic detailing of meperidine resulted in short-term changes in prescribing patterns and decreased meperidine use at this institution. Long-term implications for pain management have not yet been assessed.

**Key Words** — Demerol, medication use evaluation, meperidine, pain management

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Clinical Practice Guidelines published by the Agency for Health Care Quality and Research<sup>1</sup> and the American Pain Society<sup>2</sup> outline strategies for proper pain assessment and treatment in various health care settings. According to the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), pain is the fifth vital sign<sup>3</sup> and must be assessed, documented, and treated appropriately for all inpatients and outpatients.

To ensure that our institution, a community teaching hospital, was providing adequate pain management, a Pain Management Committee was formed. Data were collected via computer query to investigate various therapeutics issues related to pain management.

Before the project, inpatient data indicated high use of meperidine in oral, IM, and IV forms at our institution. Most of these orders were the result of habitual prescribing behavior. Additionally, multiple standing orders for meperidine for various pain management indications enabled physicians to continue this prescribing behavior.<sup>4–7</sup> These standing orders were the result of older studies that touted the utility of meperidine vs other opioids.<sup>8–10</sup>

Current JCAHO standards<sup>3</sup> for pain assessment and documentation were presented to all health care practitioners. To assess compliance with these new standards, a concurrent Medication Use Evaluation (MUE) was conducted. Results of the concurrent MUE demonstrated noncompliance with the current JCAHO standards and the clinical practice guidelines for acute

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Table 1

## Results of Preintervention and Postintervention MUEs

MUE	Before	After	P-value
Number of Patients	30	30	NS
Age: Median (95% CI)	47 (30–64)	52 (35–69)	NS
Gender: male/female	11/19	8/22	NS
Selected Indications			
Pancreatitis (%)	10	33	< 0.05
S/P Surgery > 24 Hours (%)	13	10	NS
Chronic Pain (%)	7	3	NS
Duration > 48 hours (%)	57	40	NS
Duration: Median (days)	3	2	NS
Doses Received: Median	5	5	NS
Contraindications (%)	7	7	NS
Precautions (%)	47	30	0.008
ADRs (%)	53	23	0.001

NS = not significant at the 95% Confidence Interval (CI) level

pain management.<sup>1</sup>

The American Pain Society has established guidelines for meperidine (Demerol) use in acute and chronic pain management.<sup>2</sup> These guidelines recommend that the “use of meperidine should be reserved for very brief courses in patients who have demonstrated an allergy or intolerance to other opioids such as morphine or hydromorphone.”<sup>1</sup> Despite these recommendations, meperidine remained one of the most commonly prescribed first-line medications for the relief of acute pain at our institution.

Meperidine is a synthetic opioid compound in the phenylpiperidine class that produces analgesia by acting predominantly as a m-receptor agonist.<sup>11</sup> Meperidine is similar to other opioids in terms of analgesia, tolerance, and dependence; but it differs with regard to potency, pharmacokinetics, and drug interactions.<sup>1–7</sup>

Meperidine has several disadvantages that should limit its use.<sup>4–7</sup> It has been associated with inadequate pain control due to subtherapeutic dosages

and it has the potential for adverse effects.<sup>1–2</sup> The drug's short duration of action (2 to 3 hours) is less than the typical standard dosing interval (3 to 4 hours). Thus it may not provide adequate pain relief for the duration of the dosing interval. Meperidine is an irritant at the site of injection when given subcutaneously. Therefore, painful IM injections or IV administration are the only two acceptable parenteral routes of administration.

Meperidine is metabolized to a toxic metabolite, normeperidine (6-N-desmethyimeperidine) that has numerous adverse effects. Normeperidine is a cerebral irritant. Potentially toxic effects of this active metabolite include dysphoria, agitation, irritability, nervousness, tremors, and decreased seizure threshold.<sup>1–7</sup> This active metabolite accumulates in the central nervous systems of patients with normal renal function receiving prolonged multiple doses and is significantly increased in patients with impaired renal function.<sup>12–14</sup> Oral meperidine has been shown to generate greater

amounts of normeperidine than equianalgesic IV dosages. These toxic effects are usually more prominent after 48 hours of meperidine treatment due to the long half-life of normeperidine (18 to 30 hours).

Naloxone, an opiate antagonist commonly used to treat opiate overdose, has been shown to be ineffective in reversing the toxic effects of normeperidine in documented cases of normeperidine toxicity.<sup>12–15</sup> Adequate treatment of toxicity includes discontinuation of meperidine, use of an alternative opioid, use of an anticonvulsant for seizure control, and dialysis.<sup>12</sup>

Clinical Practice Guidelines suggest that appropriate indications for meperidine include relief of moderate to severe pain in patients who experience treatment failure or cannot tolerate other opioid analgesics such as morphine, hydromorphone, or oxycodone.<sup>1,2</sup> To prevent normeperidine accumulation, the duration of meperidine therapy should not exceed 48 hours. Other appropriate meperidine indications include preoperative sedation, as an adjunct to anesthesia, moderate sedation, and treatment of amphotericin B-associated chills and rigors.

Meperidine is frequently prescribed without regard to contraindications or precautions.<sup>4–7</sup> Before beginning therapy, renal and hepatic function should be evaluated and dosages adjusted accordingly. Other parameters that should be monitored at baseline and during therapy include vital signs<sup>10</sup> and mental status.<sup>12</sup> Obstetrics,<sup>24–28</sup> sickle cell disease pain,<sup>29</sup> and diseases such as pancreatitis<sup>16–23</sup> are considered questionable indications for meperidine therapy.

Similar to other opioid analgesics, common adverse effects of meperidine include respiratory depression and CNS depression (eg, fatigue, drowsiness, and dizziness). Constipation is the most common adverse GI effect, but nausea and vomiting often occur.

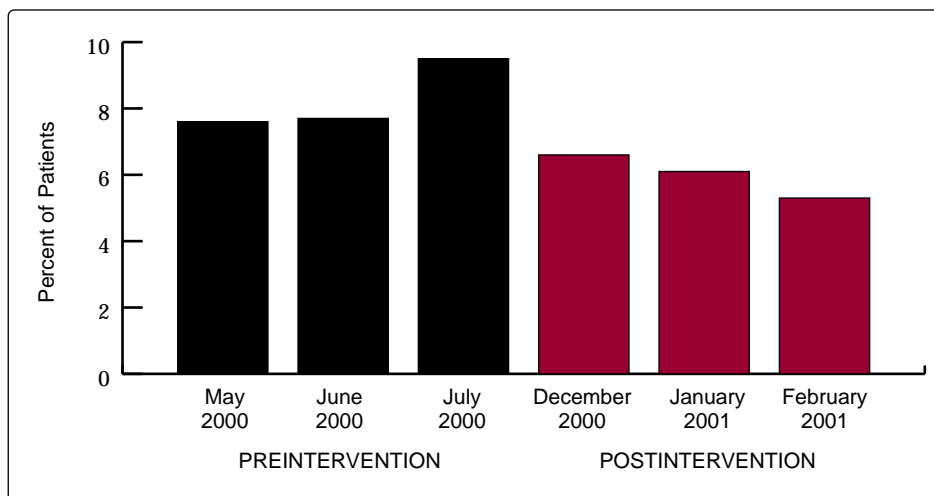


Figure 1. Percentage of patients receiving meperidine per month

Other frequently observed adverse effects are hypotension and pruritus.

Meperidine interacts additively with other drugs (eg, MAOIs), sometimes leading to severe cardiovascular and/or neurologic adverse reactions. This interaction is believed to be caused by an accumulation of serotonin; therefore, other drugs that may potentiate the effects of serotonin such as serotonin re-uptake inhibitors (SSRIs), sibutramine (Meridia),<sup>31</sup> clomipramine, and serotonin receptor agonists (eg, sumatriptan) should be used cautiously with meperidine.

Meperidine interacts additively with other drugs that cause respiratory and/or CNS depression. These drugs/drug classes include barbiturates, benzodiazepines, general anesthetics, some H<sub>1</sub>-blockers, phenothiazines, tricyclic antidepressants, tramadol, or other opiate agonists. Concurrent use of meperidine with antiarrhythmics or other drugs with anticholinergic properties can lead to severe constipation.

Another significant interaction occurs between meperidine and inducers of the cytochrome P-450 enzymes (phenytoin, carbamazepine, etc.), resulting in an increase in the metabolism of meperidine to normeperidine.

Cimetidine, an H<sub>2</sub> antagonist, inhibits the metabolism of meperidine, resulting in increased sedation and respiratory depression.<sup>1-2,4-7,11,33</sup>

All things considered, meperidine should not be considered a first-line agent for pain management. Recent recommendations indicate that opioids such as morphine, hydromorphone, or oxycodone should be used before meperidine.

#### PRIMARY OUTCOME MEASURES

The number of patients receiving meperidine prior to the study (during May, June, and July 2000) were compared with the number of patients receiving meperidine after the study (during December 2000 and January and February 2001), using the z-test for proportions (see Figure 1). Alpha was set at the 0.05 level and beta at the 0.2 level.

In addition, the number of meperidine doses dispensed after the intervention period was compared with the number of doses dispensed before the intervention period. This data was analyzed using the student's t-test (see Figure 2). All data were normalized with regard to changes in hospital census and excluded the pediatric population.

#### METHODS

Two concurrent MUEs (see Table 1) were conducted, before and after academic detailing initiatives. The specific initiatives for policy changes and education that have been effective in changing physician-prescribing patterns at similar institutions were conducted and are described below.<sup>4-7,34-36</sup> The computer database was queried to quantify the number of doses of meperidine dispensed and the number of patients prescribed meperidine. These values served as surrogate markers to illustrate changing physician prescribing patterns.

#### Phase 1: Initial Baseline Data Collection

Computer-generated reports for May, June, and July 2000 were analyzed to quantify the number of patients prescribed meperidine and the number of doses of meperidine dispensed over that time period. This data was normalized with regard to the varying hospital census and excluded the pediatric population.

A concurrent MUE for meperidine was conducted in September 2000. Baseline data from this MUE was used to identify physicians for academic detailing initiatives. In addition, the MUE illustrates the percentages of appropriate vs inappropriate indications for meperidine, dosages used, number of doses prescribed, drug interactions, and adverse drug reactions (ADRs) (see Table 1).

#### Phase 2: Educational Interventions

Grand Rounds presentations on pain management were provided for the medical residents, pharmacists, and nurses; the use of meperidine was discouraged. Pocket-size equipotent analgesic cards and pain pathways were provided to the medical residents

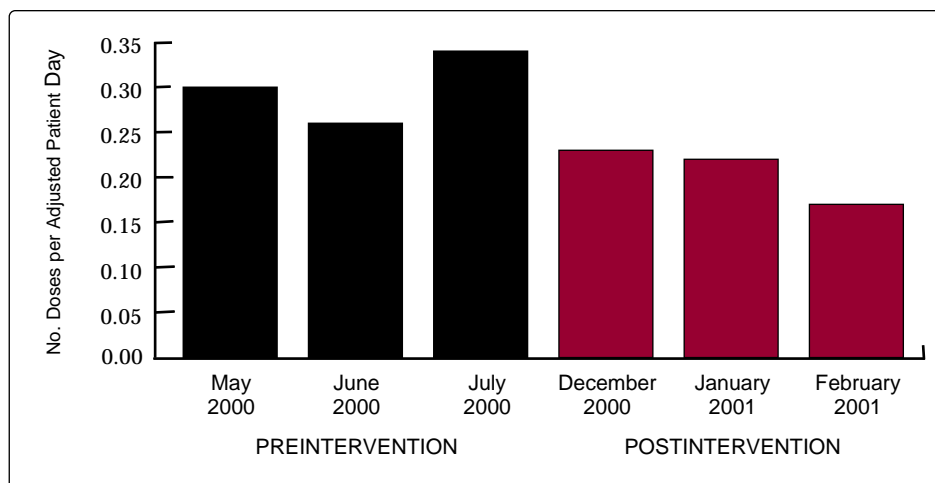


Figure 2. Meperidine doses per adjusted patient day

and pharmacists as reference aids. Visual analogue scales for use in pain assessment were provided to all nurses and attached to bedside medication administration records. An article on meperidine was published in the Pharmacy Bulletin. In addition, table-top cards emphasizing the reasons for discouraging meperidine use were designed. These cards were displayed in the physician's private dining room for the duration of the intervention and postintervention periods. Finally, physicians that agreed with these initiatives served as opinion leaders in conversations with other physicians and on clinical rounds.

### Phase 3: Policy Changes Within the Institution

All current physician standing orders were reviewed to replace meperidine with alternative opiates as appropriate. Standard orders were corrected for other therapeutic issues such as cumulative daily acetaminophen doses and combination therapy for synergy in pain control as appropriate. All meperidine patient-controlled analgesia (PCA) syringes were removed from the automated dispensing units.

A 48-hour meperidine stop order policy was proposed to the Pharmacy and Therapeutics Committee and

incorporated into a guideline for meperidine use. The guideline consists of appropriate, questionable, and unclear indications for meperidine use and was approved by the Pharmacy and Therapeutics Committee and the Medical Executive Committee. It was published in the Pharmacy Bulletin and displayed in the Patient Care areas and in the physicians' dining room. Development of a standard order sheet for assessment and initiation of drug therapy for pain management was completed and implemented. Pharmacist's interventions included participation in daily rounds, daily medication administration record review, and personal contact with physicians.

### Phase 4: Collection of Outcome Data and Evaluation

At the end of the postintervention study period, computer-generated reports listing the number of patients receiving meperidine and the number of doses dispensed were tallied, normalized for the changing hospital census, and compared to the preintervention period. Meperidine doses dispensed after the intervention were compared to meperidine doses dispensed before the intervention. In addition, the number of patients prescribed

meperidine after the intervention was compared to the number of patients that were prescribed meperidine before the intervention.

### RESULTS

Analysis of MUEs conducted before and after academic detailing initiatives revealed trends in prescribing patterns for various pain management indications (see Table 1). MUE criteria include indications, dosages, efficacy, and safety outcomes. Efficacy was measured by the decrease on the 10-point pain scale, and safety was assessed

by counting adverse events reported by patients, nursing personnel, and routine ADR screening tools.

A statistically significant decrease in the number of documented ADRs and precautions were noted after academic detailing initiatives. A decrease in the number of patients receiving meperidine for durations greater than 48 hours was observed; however, this decrease was not statistically significant. This may be due to a lack of power to detect a difference in this endpoint because of the small sample size ( $n = 30$ , Table 1). The number of meperidine doses received was reduced by 2.43% ( $P < 0.05$ : 95% CI, 1.97 to 2.88), a relative reduction of 29.5% in patients receiving meperidine after academic detailing initiatives (see Figure 1). The number of doses dispensed per adjusted patient day was reduced by 0.0966 doses per patient ( $P < 0.05$ : 95% CI, 0.0955 to 0.0977), a relative reduction of 31% in meperidine doses dispensed per patient (see Figure 2).

Furthermore, 85% of standard orders were changed to correct therapeutic issues. Some of these changes included converting meperidine to morphine or hydromorphone, decreasing cumulative acetaminophen daily dosages, using controlled-release and

immediate-release opioids for pain management in oral therapy, and combining drug therapy modalities with different mechanisms of action for synergy (to decrease potential adverse effects associated with larger dosages of single drugs).

Similar studies using educational interventions as tools to change physician prescribing behavior suggest that policy education alone is ineffective in changing physician prescribing patterns.<sup>4-7,34-36</sup> This study demonstrated changes in prescribing patterns with minimal policy changes and multiple educational interventions. However, how long these physician prescribing pattern changes will stay in effect remains to be seen.

The statistically significant decrease in meperidine use seen in this study is not overwhelming. However, the decreasing meperidine usage trends are a step in the right direction.

### FUTURE DIRECTIONS

#### Pain Assessment and Documentation

Pain assessment and documentation forms that mirror the JCAHO standards for pain assessment and documentation were implemented by nursing and inserviced by pharmacy to nurses, physicians, and pharmacists.

The benefit of these tools for improved pain management has yet to be assessed. However, regularly scheduled pain assessments based on a standardized scale and patient input should improve pain management, if care plans are being adjusted accordingly. Education of patients about pain management and their right to receive effective pain relief will have a positive effect on pain assessment. Future research will involve troubleshooting the pain assessment forms, analyzing their utility and efficacy, and determining any nursing problems associated with their use.

A pharmacy shadow chart form has been developed. This consultation

form will aid clinical pharmacists in making pain management recommendations to physicians, documenting interventions, and following patients over time to assess pain control. This chart will also promote clinical pharmacists' active participation in pain management and the promotion of clinical pharmacy throughout our institution.

Several policy changes are in various stages of completion. A 48-hour stop order policy for meperidine was discussed with the Pain Management Subcommittee but was not accepted. An automatic substitution policy enabling pharmacists to substitute equianalgesic doses of formulary opiates for meperidine is also an option in the future.

In summary, academic detailing of meperidine resulted in short-term changes in prescribing patterns and decreased meperidine use at this institution. Assessment of long-term changes in prescribing patterns and additional drug-policy changes are currently underway.

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