Meperidine, a synthetic opioid analgesic, has traditionally been among the most widely prescribed parenteral analgesics in hospitals. The routine use of meperidine has been accepted in managing both acute and chronic pain.\(^1,2\) It is frequently used in brief surgical procedures and to manage postoperative shivering and rigors associated with the administration of blood products and drugs (for example, amphotericin).\(^1,2\)

Despite its extensive use, meperidine has no more effectiveness than other opioid analgesics such as morphine and fentanyl when used for pain management. In addition, meperidine has the disadvantages of low oral bioavailability and a short duration of action.\(^3-6\) In fact, its lack of potency and short duration of action are disadvantages that result in suboptimal pain management in many cases.

Of greater concern is the fact that meperidine is metabolized by the liver to an active metabolite, normeperidine.\(^7-10\) Normeperidine is a very weak opioid analgesic and is also a central nervous system (CNS) irritant that may cause dysphoria, irritability, and seizures at higher concentrations. The primary route of elimination of normeperidine is via urinary excretion. Although meperidine’s half-life is only 3–4 hours, the half-life of normeperidine is 14–21 hours in patients with normal renal function, which can be extended to 35 or more hours in patients with renal dysfunction. The likelihood of CNS effects of normeperidine is increased in patients who are elderly, those with impaired renal function, and those receiving high doses or prolonged therapy.\(^11-13\)

Unfortunately, the negative CNS effects of normeperidine are not reversed by naloxone. In addition, meperidine inhibits serotonin CNS reuptake, particularly in the brainstem.\(^14\) Unlike other opioids, meperidine has the potential to cause serotonin syndrome, a drug-related complication that can occur when a combination of two drugs capable of increasing serotonin are administered together. In its most severe form, fatalities have been reported. A common example would be a patient who has been taking a monamine oxidase inhibitor and subsequently receives meperidine.

The less-than-optimal risk-to-benefit profile of meperidine has led to recommendations to minimize its use. The Agency for Health Care Policy and Research (AHCPR), now known as the Agency for Healthcare Research and Quality (AHRQ), developed guidelines for the management of acute pain.\(^15\) These guidelines recommend that meperidine be reserved only for brief courses of treatment in otherwise healthy patients who have had allergic reactions to other opioid analgesics (for example, morphine, hydromorphone). In addition, the American Pain Society has recommended restricting meperidine use to no more than 48 hours, with doses not to exceed 600 mg in a 24-hour period.\(^16,17\) A MEDLINE search conducted in September 2001 recovered only two articles (from the same institution) describing a quality improvement (QI) effort to reduce meperidine use within a hospital.\(^18,19\) In those reports, meperidine use was substantially reduced, but only after a period of 12–18 months.
In the University of Michigan Health System, the acute pain service initially restricted meperidine patient-controlled analgesia to patients with normal renal function who could not tolerate other opioid analgesics. Subsequently, the acute pain service and the pharmacy and therapeutics committee endorsed the American Pain Society guidelines, thereby reserving meperidine use for the following indications:

- Short-term (≤ 24 hours) pain control at adult doses of ≤ 600 mg/day
- Management of infusion-related reactions (rigors) or postoperative shivering

Furthermore, the acute pain service required its approval for administration of meperidine as patient-controlled analgesia. Given the significant and varied uses of meperidine, changing prescribing practice was anticipated to be a major challenge. This article describes an interdisciplinary, multiphase process used to change the widespread prescribing practices of meperidine.

Methods

Baseline Evaluation Study

A study conducted in September 2001 to evaluate meperidine use in the institution for the previous three months demonstrated that the drug was widely prescribed, frequently for extended duration and at potentially high doses (that is, ≥ 600 mg/day). Given meperidine's frequent use, a multidisciplinary (nursing, pharmacy, physicians, acute pain service) meperidine task force was convened to develop plans for staff education and implementation of the meperidine restriction policy.

Educational Program

An educational program, implemented from September through December 2001, was selected as the first of a planned two-step intervention. The meperidine task force published recommendations on the appropriate use of meperidine and the equianalgesic doses for alternative opioid analgesics. In addition, e-mail communications were sent, requesting that department chairs and service chiefs discuss this issue with their faculties and house officers. Similar communications were shared with nursing and pharmacy staffs. After the educational intervention was implemented, a follow-up meperidine use evaluation was conducted to measure the educational intervention's impact. Meperidine utilization data from June–August 2002 were compared with those of the same period in 2001—before the educational intervention.

Operational Changes in and Restrictions on Meperidine Use

As a second intervention, operational changes and restrictions were imposed to further minimize the use of meperidine. The following activities were conducted:

- Additional communications were disseminated regarding the rationale for restricting meperidine use.
- Dosage sizes for injectable meperidine > 25 mg were removed from most automated dispensing cabinets on the patient care units. The 100-mg syringes were removed from all areas except for a select few, where procedures that involved single doses of meperidine were common.
- The quantity of meperidine syringes stored in the cabinets was reduced.
- Notes regarding the restrictions on meperidine use and the equianalgesic doses for other opioid analgesics were posted on the automated dispensing cabinets to remind nurses of the restrictions on meperidine use.
- Pharmacists and nurses were instructed to contact physicians and change any orders for meperidine that were for > 600 mg/day or beyond two doses, unless approved by the acute pain service.

After these operational changes and restrictions were implemented, another three-month data collection was conducted from September 16 to December 15, 2002. An additional three-month data collection occurred three to six months after these changes and restrictions were implemented to determine if improvements were sustained. Data were also collected in July–September 2003 to monitor the initiative's progress.

Results

The results from the two interventions are provided in Table 1 (page 279). The initial educational intervention resulted in a significant reduction in meperidine administration, especially in orders with the highest potential to cause toxicity. The mean number of meperidine orders per day that could potentially exceed a daily maximum of 600 mg was reduced by more than 63% (p < .05). In addition, ongoing as-needed (PRN) orders for meperidine were reduced by nearly 75% (p < .05).
There was an important relationship between the reduction of PRN orders and orders with a potential daily maximum dose of ≥ 600 mg. Many of the orders with the potential for high daily doses were a result of PRN orders that, if all possible doses were administered, would have resulted in a total daily dose of ≥ 600 mg or greater. By reducing the number of ongoing and PRN orders, the number of high daily dose orders was similarly reduced.

Data collected after the implementation of the operational changes and restrictions revealed that there were further reductions, although not statistically significant, in the mean orders per day with a potential daily dose exceeding 600 mg and in the number of ongoing PRN orders. Overall meperidine use—mean number of orders per day—was significantly reduced in the restriction intervention compared to both the baseline and the educational intervention periods (p < .05).

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The combined educational and restriction interventions resulted in a > 75% reduction in the number of meperidine orders per day (p < .05), the number of ongoing PRN orders per day (p < .05), and the number of orders per day with a potential daily dose of ≥ 600 mg (p < .05). Finally, these changes in meperidine utilization were sustained, as demonstrated by the data collected 3–6 months following the implementation of the operational changes and restrictions, as well as in the second follow-up observation period—one year after the educational intervention and 9–12 months after the restriction and operational interventions.

Discussion

Meperidine has been associated with a number of patient safety concerns, primarily in patients with renal insufficiency, the elderly, and patients receiving high daily doses or treatment for prolonged periods of time. These concerns prompted The University of Michigan Health System to address meperidine administration as a patient safety initiative. Yet in spite of meperidine’s intrinsic problems, many physicians remain comfortable with prescribing it.20 As Donald Berwick has recently observed, “an enormous amount of . . . scientific knowledge remains unused. Too often, American health care . . . fails to deliver the best care it could.”21(p. 1969)

One of the key QI principles is that best practices need to be disseminated into daily work as a matter of course through the use of system changes. Davis et al. found that medical education activities are conducted in the belief

| Table 1. Changes in Meperidine Use Following Interventions, June 2001–September 2003* |
|------------------|------------------|------------------|------------------|------------------|------------------|
| Mean no. orders/day (±S.D.) | 9.4 (4.1) | 4.1 (2.3)† | 2.3 (1.5)† ‡ | 1.9 (1.2)† | 2.3 (1.4)† |
| % change from baseline | — | -56.4% | -75.5% | -79.8% | -75.5% |
| Mean no. orders/day limited to 1–2 doses (±S.D.) | 3.5 (2.6) | 1.5 (1.4)† | 1.0 (0.9)† | 0.7 (0.6)† | 0.7 (0.7)† |
| % change from baseline | — | -57.1% | -71.4% | -80.0% | -80.0% |
| Mean no. orders/day written as ongoing or PRN (±S.D.) | 4.3 (2.2) | 1.1 (1.3)† | 0.9 (1.0)† | 1.2 (1.2)† | 0.9 (1.1)† |
| % change from baseline | — | -74.4% | -79.1% | -72.1% | -79.1% |
| Mean no. orders/day with potential daily dose ≥ 600 mg (±S.D.) | 1.9 (1.6) | 0.7 (1.0)† | 0.4 (0.7)† | 0.5 (0.6)† | 0.4 (0.6)† |
| % change from baseline | — | -63.2% | -78.9% | -73.7% | -78.9% |

* S.D., standard deviation; PRN, as needed.
† One-way analysis of variance (ANOVA); p < .05 compared to baseline.
‡ One-way ANOVA; p < .05 compared to educational intervention period.
that gains in knowledge lead physicians to improve how they practice and thus improve patient outcomes. 22 Yet many studies have demonstrated a lack of effect of current practice guidelines on physicians’ performance or sizable gaps between real and ideal performance. 23 Bero et al., who conducted a systematic review of evidence of the effectiveness of different strategies to promote the implementation of research findings, found that passive dissemination of information alone is generally ineffective: “It seems necessary to use specific strategies to encourage implementation of recommendations and to ensure changes in practice.” 23(p. 465)

Given meperidine’s long-standing and widespread use in our institution—an academic medical center—changing physician behavior represented a formidable task. Our data suggest that the multifaceted educational intervention, selected initially to inform prescribers about the significant side effect profile of meperidine and to reduce the overall utilization, particularly use of high doses or for prolonged durations, significantly reduced meperidine prescribing.

Despite the initial educational intervention’s success, in view of the literature, 21–23 persistent concerns remained regarding the long-term effectiveness of an educational intervention alone. A decision was made to reinforce the educational intervention to reduce the frequency of high-dose or long-duration meperidine regimens even further. Specific restrictions helped to solidify the effect of the educational intervention and further reduced meperidine utilization.

The results presented here differ somewhat from those reported previously by Gordon et al., 18 who also described a QI team’s use of a multifaceted approach entailing widespread education and operational changes. They did not see a substantial reduction in meperidine use until one year after the introduction of formulary guidelines and operational changes. It is unclear why the response to their QI initiatives was delayed. Also, they did not specifically report on the impact of their efforts on prescriptions with the potential to result in daily meperidine administration of ≥ 600 mg. Therefore, this is the second report of the success of a multifaceted approach in reducing meperidine use in a teaching institution. The differences in the time course of response to the QI efforts remain difficult to explain.

This experience demonstrates the effectiveness of a phased multimodal approach to changing long-standing prescribing behavior, yielding improvements in patient safety. Because the use of meperidine was so strongly ingrained in the institution, we believe that moving directly to a restriction policy would likely have caused significant dissatisfaction among the staff and potentially would have disrupted patient care. The initial educational phase permitted a greater understanding of the safety issues while offering a variety of alternatives to prescribers. The operational change and restriction intervention that followed helped to preserve these gains and resulted in less disruption in care because much of the behavioral change occurred voluntarily through education.

We present this multidisciplinary and multiphased approach for consideration for other situations requiring changing long-standing practices. For example, we are currently using this approach to address the use of unapproved, high-risk abbreviations in written communications. We believe that a similar combination of education followed by operational restrictions will prove successful and will result in improved patient safety.

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