The American Journal of Surgery (2016) 211, 565-570

The American Journal of Surgery®

Midwest Surgical Association

Hydromorphone vs fentanyl for epidural analgesia and anesthesia

Melissa N. Nguyen, Pharm.D., B.C.P.S.[a], Lisa Hall Zimmerman, Pharm.D., B.C.P.S., B.C.N.S.P., B.C.C.C.P., F.C.C.M.[a,*], Kathy Meloche, B.S.N., R.N.-B.C.[b], Heather S. Dolman, M.D., F.A.C.S.[c], Alfred E. Baylor, M.D., F.A.C.S.[c], Samir Fuleihan, M.D.[d], Robert F. Wilson, M.D., F.A.C.S., M.C.C.M.[c], James G. Tyburski, M.D., F.A.C.S.[c]

[a]Department of Pharmacy Services, Detroit Receiving Hospital, 4201 St. Antoine Blvd, UHC-1B, Detroit, MI 48201, USA; [b]Department of Anesthesia, Harper University Hospital/Hutzel Women's Hospital, Detroit, MI, USA; [c]Department of Surgery, Wayne State University/Detroit Receiving Hospital, Detroit, MI, USA; [d]Department of Anesthesiology, Detroit Medical Center, Harper University Hospital, Detroit, MI, USA

KEYWORDS:
Analgesia;
Epidural;
Anesthesia;
Hydromorphone;
Fentanyl

Abstract

BACKGROUND: Epidural analgesia/anesthesia is used during surgery because it dramatically relieves pain and attenuates the stress response. Because limited data exist regarding the relative merits of hydromorphone (HM) and fentanyl (FENT), the objective was to determine which was more safe and effective.

METHODS: Prospective case-matched, observational study evaluated elective surgery patients: 30 HM and 60 FENT. Variables were measured perioperatively.

RESULTS: Of the 90 patients, mean age was 52 years; simplified acute physiology score was 26 ± 10; and American Society of Anesthesiologists score was 2.4 HM vs 2.7 FENT, $P = .03$. HM patients were more apt to be excessively sedated (16% HM vs 1% FENT, $P = .007$) and have poor mental unresponsiveness (6% HM vs 0% FENT, $P = .04$). The incidence of hypotension was not different, 76% HM vs 80% FENT, not significant.

CONCLUSIONS: In a closely case-matched population, FENT caused less excessive sedation and unresponsiveness. FENT patients had better intraoperative urine output and tended to have less repeated episodes of hypotension.

There were no relevant financial relationships or any sources of support in the form of grants, equipment, or drugs.

The authors declare no conflicts of interest.

The study was performed at Detroit Receiving Hospital, Harper University Hospital, Detroit, Michigan

* Corresponding author. Tel.: +1-586-943-5994; fax: +1-313-745-2965.
E-mail address: lisahallzimmerman@gmail.com

Manuscript received July 12, 2015; revised manuscript December 9, 2015

Acute pain generally occurs because of tissue damage or inflammation. Inadequate postoperative pain relief has been identified as an important predictor of long-term morbidity and mortality.[1–4] In an effort to improve postoperative pain management, in 2001 The Joint Commission implemented standards for pain management that made it a medical priority and stated that all patients have the right to pain assessment and treatment.[5] In addition, numerous

0002-9610/$ - see front matter © 2016 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.amjsurg.2015.12.003

organizations have published guidelines to help improve pain management.[6,7]

The pain of major surgery induces a stress response that leads to pathophysiologic changes in all major organs as well as alterations in hemodynamics, metabolism, immunology, and hemostasis.[8] Previous studies and meta-analyses have shown epidural analgesia and anesthesia (EAA) to be advantageous to parenteral opioids for pain management in the perioperative period.[2,9] We could not find any studies comparing the efficacy and safety of the 2 most commonly used opioids in epidurals, hydromorphone (HM) and fentanyl (FENT). Consequently, we chose to evaluate these 2 opioids in the setting of perioperative EAA. The primary objective was to determine which was safer and more effective, FENT or HM.

Methods

This was a human investigations committee-approved, prospective, observational study of patients who had an epidural catheter placed for perioperative analgesia and anesthesia at an academic medical center. Elective nontrauma surgery patients age 18 years or older who received EAA perioperatively were included for evaluation. Obstetric patients, patients with only a nerve block, and surgical cases with inadequate numbers of patients to case match were excluded.

Patients were case matched according to the surgical procedure and divided in a 1:2 ratio, HM vs FENT, which was decided *a priori*. For example, 1 gastric bypass HM patient was matched to 2 gastric bypass FENT patients. Most of the patients received FENT epidurals for surgical procedures. Hence, the intent was to control for sparse data problems which might exist between the 2 opioids which could allow the data to favor FENT based on outcomes.

All patients received concomitant epidural bupivacaine with concentrations of .0625% and .075% with no difference between the groups. The adequacy of pain control was compared to the typically described dosage ranges for epidural HM .15 to .3 mg/hr and FENT .5 to 1.0 mcg/kg/hr.[8] Weight-based dosing (mcg/kg/hr) exists for FENT based in the pharmacokinetic properties of this synthetic opioid. FENT is highly lipophilic crossing the blood brain barrier easily. Weight-based dosing is used to prevent under or overdosing which can lead to ineffectiveness or over sedation, respectively. HM is a more hydrophilic opioid and dosed in mg/hr based on the efficacy data.

Baseline characteristics and severity of illness scores were collected. The rates and severity of decreases in blood pressure and other epidural-related complications possibly related to the EAA were evaluated. Blood pressure was evaluated before placement of the epidural, then every 15 minutes after the initiation of the epidural during the operative theater and in the postanesthesia care unit. Then, blood pressure was evaluated hourly for 2 hours, then every 2 hours for 16 hours, and then every 4 hours until the epidural therapy was discontinued. The Anesthesia Pain Service managed the epidural dosing throughout and also determined when to discontinue the epidural catheter.

A significant decrease in blood pressure was defined as a decline in systolic blood pressure 20 -mm Hg or more from the baseline.[9] A reduction in blood pressure was anticipated after induction of general anesthesia. Hence, analysis of blood pressure variations occurred after hemodynamic stabilization after general anesthesia induction. Repeated episodes of decreases in blood pressure or hypotension were defined as occurrences 2 or more events. To be deemed as repeated episodes, the initial hypotensive event had to recover to normal blood pressure and maintained recovery for at least 6 hours.

The level of pain was evaluated both at rest and during activity by the visual analoge scale (VAS) score. Pain with activity was assessed during the time the patient was standing out of bed or ambulating. Inadequate pain control was defined as a VAS score of 5 or more, plus the need for medication interventions. These interventions included increasing the epidural infusion rate or providing intravenous opioids, specifically morphine. An epidural failure was defined as the need for intravenous opioids or increase in the epidural infusion rate.

Complications evaluated included hypotension, pruritus, extremity paresthesias, excessive sedation (Modified Ramsey Sedation Score [MRSS] $\geq$ 4), nausea/vomiting, chest pain, and unresponsiveness (MRSS = 6).[10]

Statistical analyses were performed using the Statistical Package for the Social Sciences, version 21.0. Descriptive statistics, Chi-square, Fisher's exact, Mann-Whitney *U*, and *t* tests were used as appropriate. Multiple regression analyses were performed to determine whether there were any variables that had a positive correlation to decreases in blood pressure or increases in epidural dose requirements. A power analysis was performed *a priori* and found that at least 28 patients would be needed for the primary objective. Statistical significance was determined by a *P* value less than .05.

Results

Of the 409 patients evaluated for inclusion, only 90 elective, nontrauma surgery patients met inclusion criteria and case matching. The primary reasons for exclusion were due to patients receiving an epidural for obstetrical reasons and limited numbers of patients receiving HM to case match based on the surgical procedure. The most frequent surgeries performed were total abdominal hysterectomy (36%), exploratory laparotomy with resection (34%), gastric bypass (13%), and genitourinary procedures (9%).

Baseline characteristics were similar between the groups regarding age, sex, race, and simplified acute physiology score (Table 1). The epidural catheter was placed at a thoracic site in 53% of the patients and at a lumbar site in 47%. Initiation of the epidural catheter was primarily