BRIEF REPORT

A Retrospective Assessment of the Incidence of Respiratory Depression After Neuraxial Morphine Administration for Postcesarean Delivery Analgesia

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Respiratory depression can occur after neuraxial morphine administration. In the obstetric population, there are little data on respiratory depression after neuraxial morphine administration in women undergoing cesarean delivery. In this single-center, retrospective study in 5036 obstetric patients (mean body mass index = 34 kg/m^2) who underwent cesarean delivery and received neuraxial morphine, we did not identify any instances of respiratory depression requiring naloxone administration or rapid response team involvement. Therefore, the upper 95% confidence limit for respiratory depression in our study is 0.07% (1 event per 1429 cases). (Anesth Analg 2013;117:1368–70)

Neuraxial morphine is commonly used for analgesia after cesarean delivery; however, both early- and delayed-onset respiratory depression are possible complications of its administration.[1] In the obstetric population, data on respiratory depression in this setting are sparse with an incidence of 0% to 0.9% reported in the literature.[2–6] Although some believe that improved pain control outweighs the risk of respiratory depression, others withhold or limit the use of neuraxial morphine because of the potential risk, particularly in patients with high body mass index (BMI) or obstructive sleep apnea.[7] Respiratory depression can have dire consequences; a recent American Society of Anesthesiologists closed claims analysis reported a 78% incidence of death or permanent brain damage among 86 cases of respiratory depression.[8]

At Duke University Medical Center, neuraxial morphine is used routinely in all women undergoing cesarean delivery. We therefore performed this study to identify instances of respiratory depression in women who received neuraxial morphine for postcesarean delivery analgesia as identified by the need for naloxone for the treatment of respiratory depression or by rapid response team (RRT) involvement for the same purpose.

METHODS

After IRB approval, data were compiled from the perioperative database of women who underwent cesarean delivery and received neuraxial morphine from December 1, 2006, to December 31, 2011. These data were correlated with the Adverse Drug Event Surveillance (ADE-S) System and the RRT databases to identify instances of naloxone administration or the need for the RRT to manage respiratory depression in an obstetric patient who received neuraxial morphine for postcesarean delivery analgesia. The study period was chosen based on the time of initiation and availability of the ADE-S system at our institution. The computerized ADE-S system is an internally developed application that evaluates inpatient medications, laboratory and patient demographic information against a set of clinical rules to alert for the occurence of ADE-S. The system delivers an electronic, daily report that details all triggers fired; the events are then evaluated for causality and severity to ensure they are true instances of harm.[9] For the naloxone trigger, the system identified all instances of naloxone administration in patients who had surgery in the previous 9 days. Naloxone administration was identified by documentation on the anesthetic record for intraoperative use or by being withdrawn from the Pyxis Medstation ® system for postoperative administration. Administration of naloxone was confirmed by a clinical pharmacist the following day.

All women undergoing cesarean delivery under neuraxial anesthesia in our institution receive neuraxial morphine, except if they have a morphine allergy. Our protocol for monitoring parturients who received neuraxial morphine consists of hourly monitoring for 2 hours followed by monitoring every 2 hours for 24 hours of the following: vital signs, oxygen saturation, respiratory rate, pain score, and sedation score. We also have nursing standing orders for naloxone administration for respiratory rate <8/min or Richmond Agitation Sedation Scale (RASS) ≤−3, together with immediate notification of medical staff, and an order to notify medical staff for oxygen saturation <90% or RASS <−2. Postoperative analgesia is provided with regularly scheduled nonsteroidal anti-inflammatory drugs and acetaminophen 325 mg/oxycodone 5 mg 1 to 2 tablets as needed every 3 to 4 hours. Breakthrough pain is managed by the obstetricians in consultation with the anesthesiologists in the first 24 postoperative hours.

The route of morphine administration (spinal versus epidural), morphine dose, patient height, weight, BMI,

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age, and the nature of event that required naloxone or RRT involvement were recorded for all postcesarean patients who received neuraxial morphine. Descriptive statistics are reported. The exact 95% confidence interval for the incidence of respiratory depression was calculated using the Clopper-Pearson method (SAS software, version 9).

RESULTS

Five thousand thirty-six women fulfilled the inclusion criteria and were included in the analysis. One thousand eighty patients received epidural morphine and 3554 spinal morphine. Morphine 3 and 0.15 mg were the most commonly used epidural and spinal doses (92.9% and 90.4%, respectively). Spinal doses ranged from 0.05 to 0.25 mg, and epidural doses from 1 to 5 mg. Two patients received epidural morphine after intrathecal morphine due to inadequate spinal anesthesia: one patient received 0.15 mg spinal and 1 mg epidural, and the other patient received 0.15 mg spinal and 1.5 mg epidural.

Patients' demographics are summarized in Table 1. Sixty-three percent of the patients were obese (BMI ≥30 kg/m^2). Data from the ADE-S showed no instances of naloxone administration for the reversal of respiratory depression, and there were 2 naloxone infusions recorded for the treatment of pruritus. There was 1 RRT recorded for an obstetric patient 55 hours after cesarean delivery for severe preeclampsia; the patient had received 0.15 mg spinal morphine. The patient became hypotensive with low oxygen saturation (91%–93%) after receiving an increased dose of nifedipine XL (60 mg increased from 30 mg). The patient's condition had stabilized once the RRT arrived, and no further management or naloxone was needed. Therefore, the upper 95% confidence limit for respiratory depression in our study is 0.07% (1 event per 1429 cases).

DISCUSSION

In this single-center, retrospective study, we did not identify any instances of respiratory depression requiring naloxone administration or RRT involvement in 5036 obstetric patients (mean BMI = 34 kg/m^2) after cesarean delivery with neuraxial morphine. Because the incidence of respiratory depression is low in the obstetric population, we could have failed by chance to find any cases. However, our study is the largest study performed to date giving us a precise estimate of the true population incidence.

Table 1. Patient Demographics

Age, y	29.3 ± 6.5
Weight, kg	87.9 ± 23.0
BMI, kg/m^2	33.7 ± 8.0 [Median (range) = 32.2 (17.1–79.4)]
Underweight (<18.5)	1 (<1)
Normal weight (18.5–24.9)	427 (8.5)
Overweight (25–29.9)	1427 (28.4)
Obesity class I (30–34.9)	1424 (28.3)
Obesity class II (35–39.9)	859 (17.1)
Obesity class III (≥40)	886 (17.6)
ASA PS	
I	102 (2)
II	3838 (76.2)
III	1086 (21.6)
IV	10 (0.2)

Data are mean ± SD or number (%).
BMI = body mass index; ASA PS =American Society of Anesthesiologists Physical Status.

Multiple definitions for respiratory depression have been used in the literature, including low respiratory rate, hypercarbia, low oxygen saturation, sedation, depressed ventilatory response to hypoxia or hypercarbia, and naloxone treatment.[10] Respiratory depression was defined as a respiratory rate <10/min in all previous studies in obstetric patients,[2–6] and 1 study also included patients who had an oxygen saturation ≤85%.[3] In that study involving 856 parturients who received 0.2 mg intrathecal morphine, respiratory depression, defined by a respiratory rate <10/min or oxygen saturation ≤85%, occurred in 8 patients, all of whom were obese. Six of those patients received naloxone.

Parturients might be at a lower risk of respiratory depression due to younger age, less comorbidity, and lower neuraxial morphine doses used.[11] However, with the increased prevalence of obesity, the incidence of sleep apnea is also likely increasing, with a potential increase in the risk of respiratory depression. Sixty-three percent of patients in our study were obese; therefore, we likely included patients considered at high risk for respiratory depression. Despite this, we did not identify any instances of clinically significant respiratory depression requiring naloxone administration. The nature and timing of the 1 RRT recorded suggest that it was likely not attributable to neuraxial morphine.[1]

This study has several limitations. Our methodology does not identify episodes of minor hypoventilation or desaturation that did not require the interventions recorded in our study and that could meet other definitions of respiratory depression used in previous studies. Also since monitoring is intermittent, it is possible that episodes of hypoventilation or desaturation could have occurred when parturients were undisturbed and not monitored. However, our ability to capture all cases of naloxone administration and all RRT calls to obstetric patients excludes any clinically significant respiratory depression. Information about other risk factors for respiratory depression such as sleep apnea was not available to us. A range of morphine doses was included in this study, and since the risk of respiratory depression is dose-dependent, patients who received lower doses may have been at lower risk. However, the doses were fairly standardized with 90% and 93% of patients receiving the same spinal or epidural morphine doses, respectively. The strengths of our study include the fact that it is the largest study in the literature to date in this patient population and includes 63% obese parturients, whereas none of the previous studies reported the BMI of the entire study population.

In conclusion, we found no instances of respiratory depression in 5036 parturients who received neuraxial morphine for postcesarean analgesia despite a frequent incidence of obesity.

DISCLOSURES

Name: Theresa R. Crowgey, BS.
Contribution: This author helped conduct the study, analyze the data, and prepare the manuscript.
Attestation: Theresa Crowgey approved the final manuscript and attests to the integrity of the original data and the analysis reported in this manuscript.

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Attestation: Ashraf Habib approved the final manuscript and attests to the integrity of the original data and the analysis reported in this manuscript and is the archival author.
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