Incidence and Demographics of Post-Operative Naloxone Administration: A 13-Year Experience at a Major Tertiary Teaching Institution

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**Background:** Perioperative use of opioids is associated with the risk of opioid-induced respiratory depression. Naloxone is a competitive opioid antagonist typically administered to reverse opioid-induced respiratory depression. Postoperative administration of naloxone may be considered a proxy for significant postoperative opioid-induced respiratory depression and data regarding its use may be utilized as a quality measure. Few large studies have been done to characterize the population and define an incidence of naloxone recipients in the postoperative inpatient setting.

**Objectives:** We aimed to characterize the demographics of patients receiving postoperative naloxone, as well as the incidence of administration in the first 72 post-operative hours at a large urban academic medical center in the United States.

**Study Design:** This is a retrospective cohort study.

**Setting:** Major urban tertiary teaching institution.

**Methods:** The robust electronic record database of The Department of Anesthesiology at The Icahn School of Medicine at Mount Sinai, as well as the institution’s data warehouse were instrumental in allowing almost 450,000 surgical cases performed between 2001 and 2014 to be screened for naloxone administration within the first 72 postoperative hours. Organ harvests, outside of OR intubations, cancelled cases, and patients age less than or equal to 18 were excluded from the total case count.

**Results:** Naloxone was administered 433 times in a total of 442,699 postoperative cases. This yielded an incidence of 0.1%. Additionally, the demographics of the group receiving naloxone were described. The mean age was 60, mean body mass index (BMI) was 27, 60% were women, and the mean American Society of Anesthesiologists (ASA) status was 3. Average time to naloxone administration was 21 hours (standard deviation 7) after surgery. Thirteen percent of the cases were emergent. Breakdown of anesthetic technique revealed that 81% of the cases were performed under general anesthesia, 7% with monitored anesthesia care (MAC), and 12% under neuraxial anesthesia. This study lays the groundwork for further elucidating risk factors for postoperative administration of naloxone.

**Limitations:** This is a retrospective study.

**Conclusion:** The overall incidence of postoperative naloxone administration over a 13 year period in approximately 450,000 patients was 0.1%. Demographics of this group were older, ASA 3 women, qualifying as overweight, but not obese, undergoing elective surgery with a general anesthetic technique. Average time to administration was 21 hours postoperatively.

**Key words:** Post-operative, naloxone, respiratory depression, incidence
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Perioperative use of opioids is associated with the risk of opioid-induced respiratory depression. Naloxone is a competitive opioid antagonist typically administered to reverse opioid-induced respiratory depression. Postoperative administration of naloxone may be considered a proxy for significant postoperative opioid-induced respiratory depression and data regarding its use may be utilized as a quality measure. Few large studies have been done to characterize the population and define the incidence of naloxone administration in the postoperative inpatient setting.

Methods

Institutional IRB approval was obtained for the study under the Master Retrospective Review protocol. Our anesthetic database from 2001 to 2014 was queried to identify the administration of naloxone in the perioperative period, including up to 72 hours in the postoperative period outside of the care of anesthesiologists in the post anesthesia care unit. Exclusion criteria included emergent intubations, cancelled cases, organ harvests, and pediatric patients (< 18 years). The sample included patients receiving perioperative epidural and intrathecal morphine, such as those on the obstetric service. Any dose or regimen (e.g., single bolus vs. infusion) of naloxone was included. Data regarding the morphine equivalent daily dosing (MEDD) of patients receiving naloxone was not available. The database did not include data regarding any side effects of naloxone administration. Cases for which data was incompletely or inaccurately entered or where interpolation of values was not possible were excluded from analysis.

Results

Four hundred thirty-three cases were identified in the adult population who received naloxone within 72 hours of operative time, yielding an incidence of 0.1% of all cases. The mean age was 60, mean body mass index (BMI) was 27, 60% were women, and the mean American Society of Anesthesiologists (ASA) status was 3. Average time to naloxone administration was 21 (standard deviation 7) hours after surgery. Thirteen percent of the cases were emergent. Breakdown of anesthetic technique revealed that 81% of the cases were performed under general anesthesia, 7% with monitored anesthesia care (MAC), and 12% under neuraxial anesthesia. Demographics are summarized in Table I.

Discussion

The incidence of naloxone administration in postoperative patients has been previously described, albeit in much smaller cohorts. A trial of women receiving intrathecal morphine for cesarean delivery put the incidence of postoperative respiratory depression requiring naloxone administration at 0.07% (1). A recent study (approximately 10,000 patients) aimed at delineating the incidence of postoperative naloxone administration in the general adult postoperative cohort was performed in 2003 at the University of Wisconsin (2). This trial examined all operative cases requiring inpatient admission performed at that institution in 2003. The incidence of naloxone administration was found to be 0.53%, however 25% were later found to have a new diagnosis that contributed to sedation. Other older studies put the incidence of postoperative naloxone administration in patients who received epidural/intrathecal opioids at 0.19 to 3% and at 0.23% to 2.7% for those receiving parenteral opioids (2).

The population of individuals receiving naloxone in the perioperative period tended to be older ASA 3 women qualifying as overweight, but not obese,

Table I. Demographics of postoperative naloxone administration.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Mean or Percent</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60</td>
<td>16</td>
</tr>
<tr>
<td>Gender</td>
<td>60% female</td>
<td>-</td>
</tr>
<tr>
<td>ASA status</td>
<td>3</td>
<td>N/A</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>27</td>
<td>7</td>
</tr>
<tr>
<td>Latency to naloxone (hours)</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>Emergent cases</td>
<td>12%</td>
<td>-</td>
</tr>
<tr>
<td>General anesthesia</td>
<td>81%</td>
<td>-</td>
</tr>
<tr>
<td>Monitored anesthesia care (MAC)</td>
<td>7%</td>
<td>-</td>
</tr>
<tr>
<td>Neuraxial anesthesia</td>
<td>12%</td>
<td>-</td>
</tr>
</tbody>
</table>
undergoing elective surgery with a general anesthetic technique. These findings are consistent with available literature on risk factors for opioid administration, which include advanced age, as well as significant co-morbid cardiac, pulmonary, and/or renal disease, for which the ASA status of 3 or greater serves as a de facto proxy (2-5).

It is important to underline that these are not risk factors for naloxone administration, simply demographic descriptors of the population receiving naloxone. Further research, involving the development of a case-control regression model, would be needed to elicit risk factors for administration of naloxone from this dataset. However, this study is useful in that it defines the demographic group, as well as postoperative time interval, in which interventions aimed at reducing postoperative naloxone administration, and potentially postoperative respiratory depression, may be focused.

**Conclusions**

The overall incidence of postoperative naloxone administration over a 13 year period in approximately 450,000 postoperative patients was 0.1%. Demographics of this group were older, ASA 3 women, qualifying as overweight, but not obese, undergoing elective surgery with a general anesthetic technique. Most cases of postoperative naloxone administration occurred within the first 24 hours.

**References**
