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# Association of sleep disordered breathing symptoms with early postoperative analgesic requirement in pediatric ambulatory surgical patients

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ABSTRACT

*Introduction:* Sleep disordered breathing (SDB) symptoms are associated with increased rates of opioid-induced respiratory depression as well as enhanced nociception. Consequently, practitioners often withhold or administer lower intraoperative doses of opioids out of concern for postoperative respiratory depression. Therefore, SDB may be a critical determinant of analgesic requirement in the post-anesthesia care unit (PACU). We investigated whether preoperative SDB classification was independently associated with need for PACU analgesic intervention in a cross-sectional sample of 985 children who underwent elective, painful ambulatory surgical procedures.

*Methods:* Using prospectively collected data, children aged 4–17yr were grouped into two categories based on whether or not they had symptoms of SDB. Perioperative variables were compared between the exposed and control groups using Chi-squared test for categorical or *t*-test for continuous variables. Logistic regression analysis was used to assess the association between SDB and the odds of requiring PACU IV opioids.

*Results:* Children with preoperative SDB symptoms (N = 325) compared with the reference group of children who did not have these symptoms had higher rates of PACU analgesic intervention (47.1% vs. 37.4%; $p = 0.004$) and higher mean arousal pain scores ($3.7 \pm 3.5$ vs.$1.9 \pm 2.9$; $p < 0.001$). In our primary multivariable logistic regression model adjusted for a number of variables, preoperative SDB symptoms was associated with a two-fold increased odds of receiving PACU intravenous opioid (OR = 2.01, 95%CI, 1.29–3.12; $p = 0.002$).

*Conclusion:* These results suggest that preoperative SDB symptoms in children undergoing ambulatory surgery, exerts a significant influence on PACU pain behavior and analgesic requirement. Mechanisms underlying this enhanced pain experience deserve further elucidation.



## 1. Introduction

About 3.3 million children undergo ambulatory surgery every year in the United States [1]. Unfortunately, postoperative pain remains a major cause of morbidity after these procedures with an estimated incidence as high as 80%, particularly following ENT procedures [2].

Opioids have long been the cornerstone of perioperative pain therapy, but their use is often associated with significant side effects [3,4]. Indeed, use of opioids for treating acute and chronic pain has increased dramatically in the last two decades [5]. One of the enduring dilemmas in the care of ambulatory pediatric surgical patients is the high prevalence of obstructive sleep disordered breathing (SDB) [6] which is known to be associated with increased rates of opioid-induced respiratory depression [7,8].

Compounding this therapeutic dilemma is the observation that obstructive SDB may be associated with enhanced nociception because of chronic systemic inflammation [9,10]. Thus, on the one hand these patients may have overall heightened pain sensitivity while on the other they have hypoxia-induced amplified sensitivity to the respiratory depressant effects of opioids [8]. This has resulted

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in a pervasive culture of opiophobia in the care of children with SDB. To this end, practitioners often withhold or administer lower intraoperative doses of opioids out of concern for delayed recovery from general anesthesia and opioid-related respiratory depression [8]. An unintended consequence of this practice is that patients undergoing ambulatory surgical procedures are at increased risk of postoperative pain requiring treatment upon recovery from anesthesia in the post-anesthesia care unit (PACU).

Several potential predictors of early postoperative pain following ambulatory surgical procedures have been identified [11–13]. However, patient-specific predictors of clinically important PACU pain following ambulatory surgery in children have not been comprehensively determined. Exploring simple self-report measures such as symptoms of SDB (habitual snoring, witnessed apnea and history of OSA) that could help identify children who are likely to require analgesic intervention upon recovering from anesthesia in the PACU could prove critical to the provision of "personalized analgesia". Therefore, the broad objective of this study was to identify preoperative phenotypic characteristics (such as habitual snoring, witnessed apnea and history of OSA) and to explore their association with early postoperative analgesic requirement (any, opioid and non-opioid). We tested the primary hypothesis that preoperative SDB is independently associated with early PACU analgesic requirement. We also tested the secondary hypothesis that preoperative SDB is associated with higher early mean postoperative pain scores in our subjects.

## 2. Methods

### 2.1. Study design

The present report is a component of a larger on-going study to determine the incidence and risk factors for postoperative pain requiring treatment in the PACU among children aged 4–17years undergoing elective, ambulatory surgical procedures at the Mott Children's Hospital (Ann Arbor, MI). The Institutional Review Board of the University of Michigan approved this prospective, observational, cross-sectional study (*HUM00077285).* Present analyses included patients recruited from January 24, 2015 to May 31, 2016 who underwent painful ambulatory surgical procedures.

### 2.2. Study population and data source

Patients were enrolled on randomly selected weekdays during the preoperative interview. All patients scheduled for outpatient surgery on selected days were approached for possible inclusion in the study. Perioperative caregivers (anesthesiologists and nurses) did not know subject recruitment days in advance nor were they aware of the study's hypotheses. Consistent with routine clinical care, all perioperative interventions were at the discretion of the anesthesia care givers. Trained research assistants (RAs) collected baseline clinical and anthropometric data on study enrollees. Patients with chronic pain disorders or those on preoperative analgesia were excluded from the study. Patients were also excluded if they did not speak English or were unable to self-report their pain after surgery (significant cognitive impairment). For the purposes of the present analyses, we only included painful surgical procedures identified by the intraoperative administration of intravenous analgesia (opioid or non-opioid), use of local anesthetic infiltration or nerve block.

### 2.3. Outcome measures

Our primary outcome measure was the administration of PACU IV opioid analgesia. As a sub-aim, we also examined overall PACU analgesia use (any, opioid – intravenous or oral, and non-opioid) by SDB group. We considered PACU analgesia consumption as the primary outcome, rather than patient reported pain intensity, because PACU analgesic administration is associated with a more accurate and consistent nursing documentation. If a child was sleeping during the first 15min of PACU admission, the nurses recorded a pain score of zero. This is consistent with routine clinical practice and has been previously reported [13]. Furthermore, the primary objective of this report was PACU rescue analgesic requirement, hence cross-sectional (first or arousal and the highest recorded pain scores) were noted for all patients.

PACU analgesic administration was recorded as categorical (yes/no) as well as by type (opioid or non-opioid). Total dose of PACU analgesic used for each patient was also recorded. PACU opioids were converted to morphine equivalents per kilogram body weight. Typically, the PACU nurses administer analgesics prescribed by anesthesia caregivers for clinically significant postoperative pain (numeric pain score $\geq$4).

Our secondary outcome measures included pain intensity upon recovery from anesthesia as well as PACU length of stay, defined as the time in minutes from PACU admission to PACU discharge. During the pre-operative assessment, study patients were provided with the following information regarding PACU pain monitoring: "when you get to the wake up room after your operation, you will be asked to rate your pain by choosing a face or a number that best show how you are hurting. You should choose the face or provide the number that best describes how you are feeling." The RAs noted the numeric pain scores recorded upon recovery from anesthesia or within 15min of PACU admission (first arousal pain score) as well as the highest PACU pain score for each patient.

### 2.4. Potential confounding variables

These were selected on the basis of statistical significance and clinical and/or biological plausibility. Variables previously shown to be associated with postoperative pain such as age, race and surgical specialty () were automatically included as exploratory variables.

Primary exposure variable was SDB symptoms defined as the presence of one or more of the following: habitual snoring (HS), witnessed apnea and history of OSA. HS was investigated with the question: "Does your child snore very loudly on at least 3 or more nights per week?" Based on this criterion, study subjects were classified into habitual snorers and non-habitual snorers [14]. For witnessed apnea, parents were asked "have you ever seen your child stop breathing when he/she was asleep?" (No or yes). Finally, parents or caregivers were asked the direct question "has your child ever been formally diagnosed with obstructive sleep apnea (OSA)?" Subjects who were habitual snorers or gave a positive history of witnessed apnea or OSA were then classified as having SDB and patients without these two symptoms as controls.

The following variables were also recorded: age (yr.), sex, surgical specialty, height (cm), weight (Kg), body mass index (BMI in $kg/m^2$), as well as type and duration of surgery and anesthesia. Type of intraoperative opioid used was noted as was the use of intraoperative multimodal analgesia. Multimodal analgesia was defined as the administration of two or more different classes of analgesics (e.g. opioids + intravenous acetaminophen or non-steroidal analgesia). Intraoperative opioids were converted to morphine equivalents per kilogram body weight. Morphine equivalents were calculated using equivalents formulae [15].

### 2.5. Statistical analysis

Data analyses were performed with PASW Statistics v.22.0 program for Windows (SPSS Inc. Chicago, IL). Basic descriptive