Unpredictable inter-individual variations in responses to perioperative opioids result in inadequate analgesia and excessive opioid related adverse effects. Race of children is associated with an unequal burden of surgical pain and opioid adverse effects: African-American children experience disproportionally more postoperative pain and Caucasian children experience higher incidences of opioid related adverse effects with similar doses of opioids (1). Effects of sex of a child on opioid responses have not been well studied. The aim of this large prospective study is to determine the effects of sex on perioperative opioid-related adverse effects in children.

In this prospective observational study, 275 children between 6 and 16 years of age undergoing outpatient tonsillectomy were recruited. All participants received standard perioperative care with a standard intraoperative dose of morphine. Opioid-related safety outcomes included incidences of respiratory depression, excessive sedation and postoperative nausea and vomiting (PONV) and incidence of prolonged stay in the post anesthesia recovery unit (PACU) due to opioid related adverse effects. Total perioperative (intraoperative and postoperative) morphine was correlated with probability of opioid related adverse effects in girls versus boys.

Due to relatively smaller sample sizes of non-Caucasian children (44 African-Americans and 12 other races), we focused only on 219 Caucasian children (114 girls and 105 boys). Though mean age and weight were comparable, Caucasian girls had higher incidence of Obstructive Sleep Apnea (OSA) (50% vs. 36%, p = 0.04).

Caucasian girls had a significantly higher PONV (p = 0.01) and prolonged PACU stays due to opioid adverse effects (p = 0.002) than Caucasian boys.

The probability of PONV (p = 0.0005) and prolonged PACU stay due to opioid adverse effects (p = 0.0113) increased as total dose of morphine increased in Caucasian girls than Caucasian boys (Figure 1).

Though incidence of PONV and opioid adverse effects were greater in younger pre-pubertal Caucasian girls (<9 years) than older Caucasian girls (≥9 years), the differences were not statistically significant.

Caucasian girls have unequal burden of high incidences of PONV and prolonged PACU stays due to opioid related adverse effects than Caucasian boys. Though adult women have higher incidences of PONV probably due to effects of estrogen, we did not observe such hormonal effect when we compared pre-pubertal to post-pubertal Caucasian girls.

When managing children’s pain, clinicians need to anticipate potentially higher PONV and adverse effects in young Caucasian girls for similar doses of morphine than Caucasian boys.