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Opioid-related adverse effects in children undergoing surgery:
unequal burden on girls

Background: Unpredictable inter-individual variability in response to opioids results in inadequate analgesia and opioid-related adverse effects; a portion of this variability is race-related. Although multiple, yet inconsistent studies exist regarding opioid modulation and its relation to gender among the adult populace, the effect of the child’s sex on opioid response has not been well studied.

Methods: In this prospective observational study, 275 children between 6 and 15 years of age undergoing outpatient tonsillectomy were recruited. All participants received standard perioperative care with a standard intraoperative dose of morphine. Opioid-related analgesia and safety outcomes included incidences of respiratory depression, postoperative nausea and vomiting (PONV), pruritus and incidence of prolonged stay in the post anesthesia recovery unit (PACU) due to opioid related adverse effects. Continuous variables were compared using t-test or Wilcoxon rank-sum test, categorical variables using Fisher’s exact test, and the relationship between morphine dose and outcomes by sex using Spearman correlation coefficients.

Results: Given the small sample size available for non-white patients, this study focused on 219 white male and female children. Univariate analysis showed significant effects of morphine on girls, but not on boys for PONV (p=0.001), overall major opioid adverse effects (p=0.032), prolonged PACU stay due to PONV (p=0.010), and prolonged PACU stay due to major opioid adverse effects (p=0.011) (Figure 1). The incidence of major adverse effects was more in white girls than boys as the total perioperative morphine dose increased.

Conclusions: This study demonstrates that a child’s sex influences morphine’s adverse effects. White girls have an unequal burden with higher incidences of PONV, respiratory depression and prolonged PACU stay following tonsillectomy as total morphine doses are increased. When managing pain in children, clinicians need to anticipate potentially higher PONV and adverse effects in young white girls for similar doses of morphine than white boys.