Background:
Postoperative respiratory depression is a potentially life threatening, albeit preventable, complication of opioids. Inter-individual variability in adverse effect responses to opioids is a significant problem. Earlier, we demonstrated that Caucasian children experience a higher incidence of opioid-related adverse effects as compared to African-American children (1). Roles of genetic risk factors in these adverse effects are not well studied in children.

Fatty acid amide hydrolase (FAAH) is an important enzyme in the endocannabinoid pathway responsible for anandamide catabolism and is hypothesized to influence variability in response to pain and opioids. The aim of this study is to evaluate the influence of genetic variants of FAAH on perioperative opioid-related adverse effects in children.

Methods:
We conducted a prospective, genotype-blinded observational study evaluating the effect of genetic variants of FAAH on opioid-related adverse effects following tonsillectomy in children. A sample of 275 healthy children between 6 and 16 years of age were included. All participants received standard perioperative care with a standard anesthetic and an intraoperative dose of morphine. Opioid-related safety outcomes included incidences of respiratory depression and postoperative nausea and vomiting (PONV) leading to prolonged stay in the post anesthesia recovery unit (PACU). Reductions in ventilatory response to carbon dioxide (hypercapnic ventilatory response), the most sensitive and objective indicator of opioid induced respiratory depression (2), were also compared between genetic variants.

Results:
• Allelic frequencies of specific FAAH polymorphisms were significantly different between the African-American (n=44) and Caucasian (n=219) patients.
• Specific FAAH SNP, rs2295632, had a significant association with opioid-induced respiratory depression (CC: 9.5%, AA: 15.4% and CA: 29.9%, p=0.034), PONV (CC: 10.3%, AA: 38.5% and CA: 18.2%, p<0.0001) and prolonged PACU stay (p=0.026).
• Postoperative minute ventilation and respiratory response to carbon dioxide were significantly lower compared to preoperative baseline values with minute ventilation reductions differing between FAAH genotypes (p=0.007)

Conclusion:
• Similar doses of perioperative morphine in a homogenous pediatric population undergoing tonsillectomy resulted in different incidences and severity of opioid-induced respiratory depression, PONV, prolonged PACU stay due to opioid-related adverse effects and hypercapnic ventilatory responses.
• When managing children’s pain, clinicians need to anticipate potentially higher incidences of opioid-induced respiratory depression and PONV in children with certain genetic variants of FAAH.

References: