[YIA1-4] Pediatric Postoperative Pain and Genome-wide Association Study (GWAS): Novel Fatty Acid Amide Hydrolase Genetic Variants Predict Postoperative Opioid-Induced Respiratory Depression, PONV and Length of Hospital Stay

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Introduction: 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 clinical and economic problem. Roles of genetic risk factors in postoperative opioid-induced respiratory depression and other opioid adverse effects are not well studied. The aim of this study is to evaluate the influence of all important genetic variants of fatty acid amide hydrolase (FAAH) (an important enzyme in endocannabinoid pathway responsible for anandamide catabolism) from a genome-wide array on perioperative opioid related adverse effects in children.

Methods: Prospective genotype blinded observational study evaluating effect of genetic variants of fatty acid amide hydrolase on opioid related adverse effects following tonsillectomy in children. A sample of 269 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 clinical respiratory depression and postoperative nausea and vomiting (PONV) leading to prolonged stay in post anesthesia recovery unit (PACU). Illumina Human Omni5GWAS array with 70 FAAH SNPs was used for genotyping and population stratification by ancestry.

Results: Self-reported race correlated well with genetic ancestry of origin in 269 African-American and Caucasian children studied (Figure 1a). Allelic frequencies of specific FAAH polymorphisms were significantly different between white and black children. Specific FAAH SNP, rs2295632 had significant associations with PONV and opioid-induced respiratory depression in white and black children. (Figures 1b and 1c).

Conclusions: This is the first and large prospective GWAS in children associating with specific genetic variants with respiratory depression and PONV. Similar doses of perioperative morphine in a homogenous pediatric population undergoing tonsillectomy resulted in different incidences and severity of opioid-induced respiratory depression, PONV and prolonged PACU stay due to opioid related adverse effects. When managing children’s pain, clinicians need to anticipate potentially higher incidences of opioid-induced respiratory depression and PONV in children with certain FAAH genetic variants

Figure 1a. Self-reported race & Genetic Ancestry Correlate well (>95%)

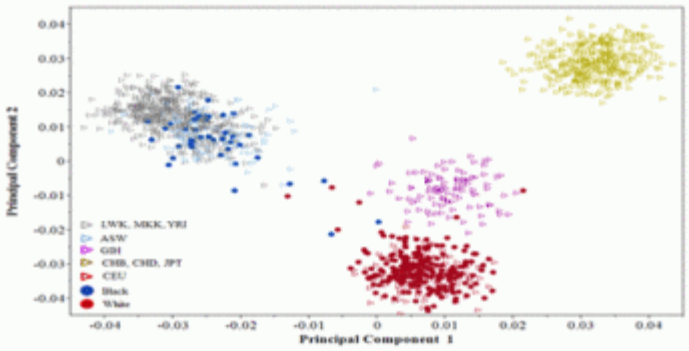

Figure 1b. PONV associations with FAAH SNPs from Omni5 GWAS array

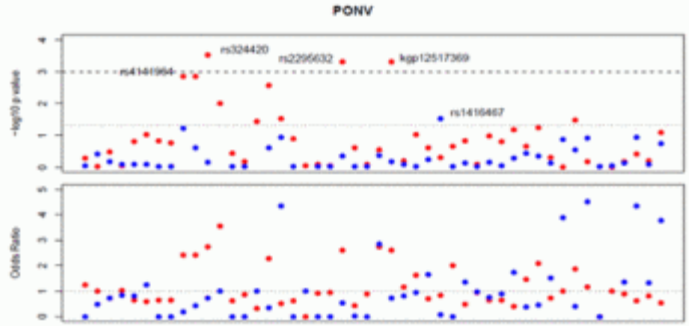

Figure 1c. Respiratory Depression associations with FAAH SNPs