[PR2-119] OPRM1 genetic variant predicts risk of morphine induced respiratory depression in adolescents with idiopathic scoliosis following spine fusion

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Introduction: Respiratory depression is the most serious adverse effect of opioids as it could lead to hypoxic brain injury and fatality (1). 50% of postoperative respiratory failure events involve patients receiving opioids, likely due to unpredictable inter-patient variations in opioid responses and narrow therapeutic indices of these drugs (2). Opioid receptor μ1 (OPRM1) gene which encodes the receptor may be a candidate gene for variation in pain perception and response to opioids (3). The 118AG variant of OPRM1 results in decreased μ-receptor binding potential in the brain (4). We hypothesized that this variant will affect susceptibility to morphine induced respiratory depression (MIRD) in post-surgical children receiving morphine via patient controlled analgesia (PCA).

Methods: After IRB approval and consent, a prospective genotype blinded study was conducted in 88 non-obese adolescents with idiopathic scoliosis who underwent posterior spine fusion under propofol-remifentanil total intravenous anesthesia. All patients received morphine PCA after surgery. They were followed for 48 hours for MIRD outcome (defined as postoperative occurrence of RR<8/minute for >3 minutes requiring corrective actions), morphine consumption, postoperative pain scores, use of diazepam and other analgesics. Patients were genotyped for OPRM1 A118G variant. Regression analysis for factors affecting OIRD included race, sex, morphine requirement, and genotype. Pain scores and related variables in genotype sub-groups were compared.

Results: Subjects enrolled were 11-19 years old; 59 were female, and 85% Caucasian. Based on OPRM1 genetic variant, 67 were homozygous for wild-type (AA) and 21 were heterozygous/homozygous for variant (AG/GG). 37% with AA genotype had MIRD on POD1/2 while only 9% of those with GG/AG genotype had MIRD (Fig 1A). Risk for MIRD in patients with AA genotype was significantly higher (>5 fold) compared to patients caring G allele (OR 95% CI:1.5-40.6, p=0.027) after adjusting for variables (Fig 1B). Compared to AA genotype, children with AG/GG genotypes had significant higher pain scores (p=0.02) and higher morphine requirement on POD1/2 (Fig 1C).

Conclusion: This is the first prospective clinical trial showing the risk of respiratory depression is higher in the OPRM1 AA genotype despite less morphine requirement than AG/GG genotypes. Presence of the G allele at A118G variant has a protective effect against MIRD. This genotype-respiratory depression association is an important step in predicting children at higher risk and personalizing the use of morphine in children to maximize pain relief while minimizing the likelihood of serious adverse effects.

References:
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Influence of *OPRM1* rs1799971 variation on Morphine Induced Respiratory Depression (MIRD) and pain outcomes on postoperative days 1&2