Opioid requirement in patients with rare mutations in the mu-opiate receptor gene (OPRM1)

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Background:
Opioids are the most common analgesic medications used in patients undergoing painful procedures. They elicit analgesic effects mainly by activating the mu-opioid receptor encoded by the OPRM1 gene. Multiple single nucleotide polymorphisms (SNPs) of OPRM1 have been suggested to impair mu-opioid receptor function and possibly alter response to opioids. However, it remains unclear whether individual OPRM1 variants affect opioid requirement perioperatively. The aim of this study was to investigate the perioperative opioid requirement in patients with rare coding variants in OPRM1.

Methods:
The study population consisted of 61,019 consented participants of the MyCode Community Health initiative of Geisinger Health System (GHS), an integrated health services organization in Pennsylvania and New Jersey. Whole exome sequencing was performed on DNA samples from these patients as part of the DiscovEHR collaboration with the Regeneron Genetics Center. Protein-coding variants in OPRM1 gene were identified and annotated. Perioperative opioid requirement was compared between the patients with and without rare OPRM1 coding variants who underwent similar painful procedures.

Results:
Among 61,019 participants, we identified 85 with rare coding variants in OPRM1 (allele frequency < 0.05). Heterozygous loss-of-function (LOF) variants were identified in 6 individuals, including 4 stop-gain, 1 frameshift, and 1 splice acceptor variant. Four of the 6 patients with LOF mutations underwent one of the following procedures at a Geisinger facility: laparoscopic cholecystectomy, cataract surgery, or vaginal delivery. Compared to the general population who underwent similar procedures, individuals heterozygous for an OPRM1 LOF did not require significantly more opioids for pain control. Among the remaining 79 patients with other rare nonsynonymous variants, 58 underwent at least one procedure at Geisinger. Review of procedure and post-procedure medications for these 58 patients showed no evidence of a difference in their response to opioids when compared to general population undergoing similar procedures.

Conclusions:
Individuals with heterozygous LOF and other rare nonsynonymous variants in OPRM1 did not require significantly more opioids for perioperative pain control compared to the general population.

References:


