Effect of Opioid Activation Inhibitors on Prescription Fill Rates Following Lower Extremity Surgery

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Purpose: Unpredictable postoperative pain response to oral opioid therapy following injury remains a challenge. Insufficient pain control can increase length of stay, readmission rates, and impair postoperative outcome. Impaired activation of oral opiates via genetic predisposition or inhibitors of the activating pathway, CYP2D6, can result in increased dose and treatment time. Length of exposure to opiates is a strong predictor of negative outcomes such as addiction and overdose. Thus, we examined the impact of CYP2D6 inhibitors on prescription fill rates and hydrocodone administration following lower extremity surgery or injury.

Methods: All orthopaedic patients with lower extremity injuries at 3 urban hospitals were screened, both trauma and elective cases, with pain managed on hydrocodone and <15 days of opiate use in the past 6 months. Patients were excluded if they had factors that could affect sensation of pain or drug metabolism, such as hepatic, renal, spinal, or brain injuries. Enrolled patients had samples for plasma concentrations of opioids and metabolites collected, admission medications were recorded, and their prescription history was queried for opiate prescriptions filled for at least 2 months prior and 6 months after the injury. Total days were queried between the date of injury and the last contiguous date an opioid prescription was filled related to the injury.

Results: 129 patients fulfilled all requirements to be included in the study. 61/129 (47.3%) were on inhibitors of the activating opioid pathway while 68/129 (52.7%) were not. Patients not on inhibitors filled opiate prescriptions on average 23.7 days after injury. Patients on inhibitors filled opiate prescriptions for an average of 100.3 days after injury ($P = 0.002$). Thus, patients on inhibitors received >4 times the exposure to opiates as those not receiving inhibitors at the time of initial presentation. Further, of the 68 patients not on inhibitors, 3/68 (4.4%) attended pain clinics after injury and 0/68 (0.0%) listed pharmacotherapies for addiction in the prescription record. Of the 61 patients given at least 1 inhibitor during their admission, 7/61 (11.5%) attended pain clinics and 3/61 (4.9%) were prescribed pharmacotherapies for addiction.

Conclusion: Interactions with patients' home medications and those during admission could result in long-term opiate exposure. Health-care providers should become familiar with the inhibitors of CYP2D6 to maximize analgesic benefit while reducing risk of addiction.