The Impact of Bone Mineral-Reducing Medications Following Open Reduction Internal Fixation of Ankle Fractures: A Propensity Score-Matched Analysis

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Purpose: Bone mineral-reducing medications (BMRM) are commonly prescribed for chronic conditions such as osteoporosis, epilepsy, and psychiatric disorders. However, their effects on fracture healing and surgical outcomes remain unclear. This study evaluates the impact of the ten most frequently prescribed BMRMs on postoperative complications following open reduction and internal fixation (ORIF) of ankle fractures.

Methods: Patients undergoing ORIF for ankle fractures were retrospectively identified using the TriNetX database, requiring a minimum of 2 years of postoperative follow up. Perioperative medication exposure was defined as at least two documented doses within 6 months pre- or post-surgery. The ten most common BMRMs analyzed included proton pump inhibitors (PPI), glucocorticoids, loop diuretics, thiazolidinediones, calcineurin inhibitors, aromatase inhibitors, selective serotonin reuptake inhibitors (SSRI), first-generation antipsychotic (FGA) medications, second-generation antipsychotic (SGA) medications, and anti-epilepsy medications.

Results: In total, 32,199 patients who underwent ORIF for ankle fractures were identified; of these, 25,043 (77.7%) had documented perioperative BMRM use. A total of 4414 patients in each was identified after 1:1 propensity score matching for age, sex, race, demographics, and other comorbidities that included diabetes mellitus, chronic obstructive pulmonary disease (COPD), liver diseases, chronic kidney disease (CKD), heart failure, hypertensive diseases, nicotine dependence, and body mass index (BMI). Exposure to specific BMRMs was associated with higher complication rates. Anti-epilepsy medications were linked to amputation (0.97% vs 0.12%, $p<0.001$) and nonunion (1.38% vs 0.45%, $p<0.001$). Glucocorticoids were associated with revision ORIF (5.14% vs 2.40%, $p<0.001$), deep infection (2.36% vs 1.53%, $p<0.001$), and nonunion (1.11% vs 0.36%, $p<0.001$). PPIs increased rates of revision ORIF (4.64% vs 2.06%, $p<0.001$), deep infection (3.07% vs 1.34%, $p<0.001$), and amputation (0.86% vs 0.28%, $p<0.001$). Among psychiatric medications, FGAs had the highest risk for deep infection (5.01% vs 1.21%, $p<0.001$) and revision ORIF (7.39% vs 2.07%, $p<0.001$).

Conclusion: Perioperative use of BMRMs is associated with an increased risk of postoperative complications following ankle ORIF. Patients taking anti-epilepsy medications, PPIs, glucocorticoids, and loop diuretics exhibited the highest risk for nonunion, revision surgery, infection, and amputation. Additionally, patients taking multiple BMRMs experienced compounded adverse effects.