Bisphosphonate use and risk of severe acute kidney injury: A self-controlled case series in frail elderly patients in the UK

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Background: Oral bisphosphonates (BP) are commonly used in the elderly, but conflicting renal safety trumps their use in frail patients.

Objectives: To assess the risk of severe acute kidney injury (AKI) associated with BP use in frail elderly patients.

Methods: We used UK's CPRD GOLD primary care dataset, linked to Hospital Episode Statistics (HES) inpatient and the Office for National Statistics mortality data. We included all subjects aged >65 at start date (01/01/2010), with electronic frailty index ≥3, and with no BP use 1 year before study start.
We conducted a self-controlled case series (SCCS) to compare AKI rates between BP-exposed and non-exposed time for each patient with AKI recorded during follow-up.
Patients were followed up from start until the earliest of: patient leaving practice, practice last collection date, end of HES linkage coverage, death or date of data extraction.
Severe AKI was identified based on main diagnosis leading to hospitalization in HES (ICD-10 N17 and N19), with 30-day washout to avoid duplicates. BP were identified using product-specific codes in CPRD. Treatment durations were combined to continuous episodes, allowing for a maximum interval of 90 days between one another. A 90-day period was added to the end of each continuous treatment episode.
Incidence rate ratios (IRR) were calculated comparing event rates between exposed and non-exposed periods. Our main model was adjusted for age, with the following sensitivity analyses: 1) adding a 6-month pre-exposure washout period, 2) using only the first AKI per patient; and 3) restricting to only patients who survived during follow-up.

Results: We identified 94,364 eligible frail elderly patients and followed them for a median of 4.33 years. Of these, 3,023 (3.2%) experienced severe AKI during follow-up and among these, 307 (10%) were exposed to BP. 3,132 and 171 events were recorded during non-exposed and exposed patient time, respectively. 1,783 (59%) patients died during follow-up. The main SCCS model showed an IRR of 1.65 [95%CI 1.25, 2.19]. Sensitivity analyses including 1) a pre-exposure washout (IRR 1.85 [95%CI 1.35, 2.52]), 2) using the first event only (IRR 1.72 [95%CI 1.29, 2.30]) and 3) excluding patients who died during follow-up (IRR 1.51 [95%CI 1.03, 2.22]) were consistent with our main results.

Conclusions: Our study found a 65% increased risk of severe AKI associated with BP use in frail elderly patients. Future studies should further investigate the risk-benefit of BP in susceptible patients.