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THE EFFECT OF ORAL BISPHOSPHONATES ON ACUTE KIDNEY INJURY, GASTROINTESTINAL EVENTS AND HYPOCALCAEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Objective: Oral bisphosphonates (oBP) are contraindicated in patients with severe chronic kidney disease (CKD), but there is a lack of data on safety in this area. We aimed to study the association between oBP use and risk of acute kidney injury (AKI), gastrointestinal events (GIE) and hypocalcaemia (HC) in patients with moderate-severe CKD.

Material and methods: Patients with stage 3B+ CKD (eGFR<45)

were identified in two primary care records databases from the United Kingdom (CPRD) and Spain (SIDIAP) linked to hospital inpatient data. Patients with CKD exposed to oBP were identified and matched to up to 5 patients from the same database using propensity score matching. Confounders included a priori defined variables: age, gender, concomitant diseases and medications. Missing data within covariates (creatine (SIDIAP), BMI, alcohol use, and smoking) were imputed using multiple imputation. First AKI, GIE and HC events were identified for each patient as the outcomes of interest. Analyses were undertaken for each outcome and each database separately. Patients were censored at the event, death, end of study or database, or 210 days after the final prescription whichever came first. Cox regression models were used. Absolute rates were calculated per 10,000 person years.

Results: In CPRD there were 9,988 exposed patients matched to 40,068 unexposed patients. In SIDIAP the numbers were 4,143 and 20,165. For AKI there were 1,668 events in CPRD and 1,456 in SIDIAP; HR (95% CIs) were 1.17 (1.04, 1.31) in CPRD and 1.08 (0.93, 1.25) in SIDIAP with absolute event rates of 132.8, 103.2, 166.2 and 153.1 for exposed and unexposed in CPRD and SIDIAP respectively. This gave a pooled HR (95% CI) of 1.14 (1.04, 1.24). For GIE there were 832 events in CPRD and 178 events in SIDIAP, with HRs of 1.03 (0.83, 1.24) and 1.53 (1.01, 2.32) respectively with absolute event rates of 52.1, 61.0, 25.2 and 17.3. This gave a pooled HR (95% CI) of 1.11 (0.93, 1.33). Finally, 137 HC events were identified in CPRD, and 6 in SIDIAP; HRs were 0.94 (0.57, 1.54) in CPRD, but not calculated in SIDIAP due to low HC events. Absolute event rates were 9.7, 8.4, 1.4 and 0.5.

Conclusion: oBP use may increase the risk of AKI by about 15% in patients with moderate-severe CKD. A 50% excess risk of GIE is seen in one of the databases but not in the other. HC was

extremely rare and not related to oBP use.