

ORAL BISPHOSPHONATES AND CHRONIC KIDNEY DISEASE: PROGRESSION AND SAFETY

Background: Bisphosphonates (BPs) are contraindicated in patients Chronic Kidney disease (CKD) due to lack of knowledge about their safety.

Objective: Examine whether BP use increases risk of stage progression (SP) (including dialysis and transplant), acute kidney injury (AKI), gastrointestinal events (GIE) and hypocalcaemia.

Methods: Patients with an estimated Glomerular Filtration Rate <45 were identified from two homogenous electronic medical record datasets CPRD (UK) and SIDIAP (Spain). Those exposed to BP were calliper matched (width 0.02) to up to 5 controls using propensity scores stratified by duration in study. For each outcome, patients were censored at the first event, 210 days after the last BP prescription, switching to BPs or alternative treatment, dropout, death or 10 years. Absolute incident rates were calculated per 10,000 person years. Hazard ratios (HRs) of BP user were estimated using Cox regression. Analyses undertaken in individual datasets and combined using fixed effect meta-analysis.

Results: In CPRD 6,309 exposed patients matched to 24,966 unexposed patients. SIDIAP: 4,143 and 20,165 respectively. Balance was <0.1 in both datasets. Rates and HR (95% CI) for each dataset shown below (Table) For SP 5,078 events in CPRD and 6,357 in SIDIAP; pooled HR of 1.36 (95% CI: 1.30, 1.43). For AKI 1,848 events in CPRD and 1,456 in SIDIAP; pooled HR of 0.98 (0.88, 1.09). For GIE 891 events in CPRD and 178 events in SIDIAP; pooled HR of 1.06 (0.87, 1.30). For HC, 150 events in CPRD, and 6 in SIDIAP. No pooled HR estimated as few events in SIDIAP.

Conclusion: Bisphosphonates increase the likelihood of SP at any later time by 36% in CKD patients; the majority did not change stage. Bisphosphonates are not associated with AKI, GIE or hypocalcaemia.

Table:

Event	CPRD			SIDIAP		
	Rate BP	Rate non BP	HR (95% CI)	Rate BP	Rate non BP	HR (95% CI)
SP	797.1	509.4	1.55 (1.46, 1.65)	976.9	828.6	1.15 (1.07, 1.23)
AKI	122.3	107.7	0.87 (0.73, 1.01)	166.2	153.1	1.08 (0.93,1.25)
GIE	56.1	57.9	0.95 (0.74, 1.17)	25.2	17.3	1.53 (1.01,2.32)
HC	8.4	10.8	0.76 (0.33, 1.19)	1.4	0.5	NA