TITLE: Use of oral bisphosphonates and bone mineral density changes in moderate-severe (Stage 3B+) chronic kidney disease: an open cohort multivariable and propensity score analysis from Funen, Denmark.

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PURPOSE In addition to safety concerns, there is a paucity of data for oral bisphosphonates (oBP) to improve bone mineral density (BMD) in patients with moderate or severe chronic kidney disease (CKD). We linked all BMD measurements in the Funen area (pop 478,000, Denmark) to biochemistry, national health registries, and filled prescriptions to study the association between oBP use and BMD changes.

METHODS

Design and participants Cohort including all subjects aged 40 years or older, with an estimated glomerular filtration rate of <45 (CKD stage 3B+), and with at least 2 BMD measurements 2 or more years apart. Previous users of oBP, and those with >1 year between closest renal and BMD measurement were excluded.

Setting Regional BMD database covering all DXA-based routine measurements in Funen, Denmark between 08/17/1999 and 02/23/2016.

Exposure, follow-up, and outcome Dispensation of oBP therapy was the main exposure. Subjects were followed from first BMD to the latest of subsequent ones. oBP non-users were identified using incidence density sampling with replacement. Outcome was annualized % change (relative to previous/baseline) in total hip BMD.

Statistical Analyses Multivariable linear regression models adjusted for age, sex, body mass index, baseline eGFR, fracture history, co-morbidities (Charlson index and renal problems), hospital contacts in previous year, and relevant treatment/s history (number of ATCs in previous year, use of steroids, aromatase inhibitors, anti-diabetics, etc.) were fitted to model BMD change according to oBP use. In addition, propensity scores (ps) were calculated using the same confounders, and linear regression stratified by ps deciles was used in a sensitivity analysis to minimise confounding by indication.

RESULTS Use of oBP was rare in this group of patients: 81 oBP users and 282 non-users with stage 3B+ CKD (as in the 1 year before DXA) were included. Whilst oBP users gained an average 0.59% total hip BMD per year, non-users lost an average 1.98% per annum. Multivariable adjusted mean difference was +1.81% (95%CI 0.99% to 2.63%), which was enhanced in the ps adjusted analysis at +2.44% (1.80% to 3.07%) in favour of oBP users.

CONCLUSION In a cohort including >360 subjects with stage 3B+ CKD, use of oBP appears associated with a significant improvement of about 2% per year in total hip BMD. More data are needed on both anti-fracture effectiveness and safety of oBP therapy in moderate-advanced CKD patients.