Correspondence to “Denosumab-induced hypocalcemia in patients with osteoporosis: can you know who will get low?”

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Editor,

We read with great interest the study by Tsvetov [1] which has reported higher actual rates of denosumab-induced hypocalcaemia and recommend serum calcium monitoring in high-risk patients for early detection of severe hypocalcaemia.

Denosumab is used in the treatment of osteoporosis in patients whom first-line agents are ineffective, poorly tolerated, or contraindicated such as in chronic kidney disease. Hypocalcaemia is a well-reported serious adverse effect of denosumab, particularly in those with chronic kidney disease. There is no clear recommendation on adequacy of vitamin D and calcium supplementation and the monitoring of calcium levels in patients on denosumab.

We agree with the study that the manifestation of hypocalcaemia in elderly patients may be atypical and easily missed. We also concur that hypocalcaemia can develop not only after the first dose but also after subsequent dose over more than 2 years of ongoing treatment. Hence, in our institution, we routinely monitor the serum calcium 10–14 days after each denosumab administration for patients who are at high risk for hypocalcaemia.

A retrospective study was performed in our institution in year 2018 with fifty-six osteoporotic fracture elderly patients to examine the safety of denosumab in the elderly and calcium level post-denosumab injection. All fifty-six patients had replete vitamin D levels (> 30 ug/L) and were on calcium supplementations prior to denosumab administration. In the study, there was no statistically difference in pre- and post-denosumab mean corrected calcium levels even in the subgroup analysis of patients

with poor creatinine clearance of less than 35 ml/min. Post-denosumab administration, 4 cases had a drop in their calcium levels of 0.20–0.23 mmol/L from their baseline but were asymptomatic and were statistically insignificant when compared with their baseline calcium levels. Although this study is limited by its sample size, the results suggest that denosumab can be given safely to the elderly if they are adequately replaced with calcium and vitamin D.

Although the study did not correlate chronic kidney disease with denosumab-induced hypocalcaemia, we believe that this group of patients are at risk. Since implementing our pilot study, we have revised our clinical practice when managing elderly patients with osteoporosis and chronic kidney disease. Vitamin D levels of patients with creatinine clearance of less than 35 ml/min has to be adequately repleted (> 40 ug/L) first, before checking PTH level. If the PTH level is elevated, calcitriol will be prescribed. With this workflow, elderly patients with poor creatinine clearance of up to 20 ml/min has demonstrated no significant drop in their calcium levels indicating safety of denosumab in this group of patients.

We will examine our results for future publications comparing calcium levels post-replacement with vitamin D versus calcitriol in elderly osteoporotic patients with poor creatinine clearance. Risk factors for denosumab-induced hypocalcaemia will also be examined, and we hope to develop specific monitoring algorithms applicable to the local setting.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Reference

1. Tsvetov G, Amitai O, Shochat T, Shimon I, Akirov A, Diker-Cohen T (2020) Denosumab-induced hypocalcemia in patients with osteoporosis: can you know who will get low? *Osteoporos Int*. 31(4):655–665. <https://doi.org/10.1007/s00198-019-05261-7>

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This study is not based on any previous communication to any society or meeting.

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