Renal bone disease is a common complication of CKD and Denosumab is not indicated for this condition. CKD patients with osteoporosis who are treated with Denosumab are at increased risk of hypocalcaemia. Caution and regular monitoring is required when administering this medication in this patient subgroup. Clear documentation of Denosumab administration and calcium supplementation in a patient’s medical history is important in identifying adverse drug reactions.

Case series; hypocalcaemia requiring hospitalisation following administration of Denosumab in Chronic Kidney Disease (CKD) patients

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**Objective**

This case series aims to raise awareness of the risk of hospital admission due to hypocalcaemia in this patient subset and highlight the role of the pharmacist in patients receiving denosumab.

**Background**

**Denosumab:**

- Indications include; treatment of osteoporosis, to increase bone mass density with androgen deprivation therapy for prostate cancer. ¹,²,³
- Monoclonal antibody with high affinity and specificity for RANK Ligand. ¹,²,³ Inhibition of osteoclast formation and activity decreases bone resorption thus increasing bone mass and strength. ²,³
- Does not require dose adjustment in renal impairment. ²,³
- Increased risk of hypocalcaemia with CrCl <30mL/min and dialysis; monitoring calcium concentrations is recommended with calcium nadir usually occurring 8-11 days after administration. ²
- It can be missed off patient dispensing history and medication records as it is administered six monthly by the GP.

**Clinical features**

Three individuals presented to our facility with severe hypocalcaemia after administration of denosumab; one with stage 4 CKD, one stage 5 CKD and the third receiving haemodialysis.

In each instance, recent administration of Denosumab by the patient’s GP was identified by the pharmacist, in one case during the CKD clinic and the others during admission to the emergency department.

<table>
<thead>
<tr>
<th>Patient</th>
<th>No. of days post Denosumab</th>
<th>Calciotriol/Calcium supplement dose on admission</th>
<th>Inpatient LOS</th>
<th>CKD Stage</th>
<th>Calciotriol/Calcium supplement dose on Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3 days</td>
<td>1.60 Calcium 2 BD (Phosphate Binder) Calciotriol 1 man</td>
<td>2 days</td>
<td>ESKD HD</td>
<td>Calcium 2 TDS Calciotriol 2 man</td>
</tr>
<tr>
<td>2</td>
<td>7 days</td>
<td>1.67 Nil</td>
<td>4 days</td>
<td>Stage 5 CKD</td>
<td>Calcium 1 man</td>
</tr>
<tr>
<td>3</td>
<td>10 days</td>
<td>1.44 Nil</td>
<td>6 days</td>
<td>Stage 4 CKD</td>
<td>Calcium 1 man</td>
</tr>
</tbody>
</table>

**Interventions, case progress and outcomes**

The patients were treated with intravenous calcium and discharged on oral calcium supplements. Close monitoring of calcium levels was required both during the admission and on discharge.

On discharge, Denosumab was ceased or with-held pending further review by their GP. In all 3 instances the suspected adverse drug reaction was reported to the Therapeutic Goods Administration.

**The pharmacist’s role:**

- Identified denosumab as probable cause of hypocalcaemia
- Assisted management of calcium replacement.
- Counselling patients on importance of taking calcium supplements away from food when used for supplementation rather than as a phosphate binder.
- Follow-up management of fracture risk with patient and GP

**Conclusions**

Renal bone disease is a common complication of CKD and Denosumab is not indicated for this condition. CKD patients with osteoporosis who are treated with Denosumab are at increased risk of hypocalcaemia. Caution and regular monitoring is required when administering this medication in this patient sub-group. Clear documentation of Denosumab administration and calcium supplementation in a patient’s medical history is important in identifying adverse drug reactions.

**References**


SHPA National Conference 2018, RBWH Symposium 2018