

# Palliative Care Emergencies

## Guideline: Hypercalcaemia

### Pathophysiology and symptoms

Malignancy is the most common cause of hypercalcaemia (tumour induced hypercalcaemia). This frequently occurs with; breast, lung, genito-urinary and haematological malignancies, but can occur with any. It is caused by the release of parathyroid hormone related protein (PTHrP) by malignant cells and therefore can occur in the absence of bone metastases.

The symptoms are usually insidious and easily overlooked. They include:

- Drowsiness
- Confusion
- Coma
- Nausea and vomiting
- Thirst
- Polyuria
- Constipation

Most patients with low grade hypercalcaemia present with gradual and insidious symptoms. However, patients with renal impairment and patients with rapidly advancing disease are susceptible to aggressively rising hypercalcaemia with dehydration and pre-renal failure. These patients with decompensated hypercalcaemia may be severely dehydrated, and the priority for treatment is urgent rehydration before bisphosphonate therapy.

### Diagnosis

This is confirmed via blood sample, checking for:

Total calcium corrected for albumin Normal range: <2.65mmol/L

(Corrected calcium mmol/L = measured calcium + 0.02 (40 - albumin g/L)

Ionised calcium (Sunderland Royal Hospital) Normal range: 1.19-1.29 mmol/L

If patient does not have a raised calcium level but is experiencing symptoms check level again after 1 week.

### Pharmacology

Bisphosphonates bind strongly to hydroxyapatite crystals in bone mineral, thereby preventing their growth and dissolution. Bisphosphonates are quickly taken up by the skeleton (especially where the mineral is more exposed, bone resorption) and can remain there for weeks or months. They stop osteoclast function and bring about programmed cell death. They interfere with cell metabolic pathways and decrease the production of pro-inflammatory cytokines (reduction in bone pain)

## Treatment

- Rehydration with 0.9% sodium chloride (see above comments on decompensated hypercalcaemia)
- IV bisphosphonate (Table 1)
- Recheck electrolytes and ionised/total calcium one week after treatment

Table 1

<b>Bisphosphonate/ Characteristic</b>	<b>Zoledronic Acid</b>	<b>Disodium Pamidronate</b>
<b>Initial IV dose</b>	4mg♣	30-90mg♠
<b>IV diluent</b>	100ml of 0.9% sodium chloride or 5% glucose	Concn of not greater than 60mg/250ml of 0.9% sodium chloride
<b>Infusion time</b>	15 mins	Rate not greater than 1mg/min
<b>Initial oral dose</b>	N/A	N/A
<b>Onset of effect</b>	<3 days	<3 days
<b>Maximum effect</b>	4-7 days	5-7 days
<b>Duration of effect</b>	5 weeks	3 weeks
<b>Restoration of normocalcaemia</b>	90%	70%
<b>Maintenance</b>	IV infusion 4-8 wks	IV infusion 3-4 wks
<b>Cost</b>	£195/4mg vial	£170.45/90mg vial

- ♣ In patients who do not respond or relapse then 8mg can be given.
- ♠ In hypercalcaemia, initial dose is dependant on ionised calcium level. Dose can be repeated after a week if initial response inadequate

## Current recommendations

In light of the above table it can be seen that **zoledronic acid** is the most potent bisphosphonate as safe as the others and comparable in cost. **Zoledronic acid** should therefore be first-line of the bisphosphonates.

## Cautions

- **Serious drug interactions:** Aminoglycoside antibiotics causing symptomatic hypocalcaemia.
- **Renal impairment:** Avoid in moderate to severe renal impairment, unless benefits outweigh risks. Renal function should be monitored in all patients.
- **Dehydration:** patients must be adequately hydrated before treatment.

➤ **Side effects:**

- *Very common:* transient pyrexia (1g paracetamol po can be given before administration to try and prevent this) and influenza-like symptoms (not clodronate), hypocalcaemia, hypophosphataemia. Oral preps: dyspepsia, abdominal pain, diarrhoea and constipation.
- *Common:* anaemia, headache, nausea, vomiting, lymphocytopenia, transient bone pain, arthralgia, myalgia, generalised pain, hypomagnesaemia, renal impairment.
- *Rare:* pancytopenia (< 0.1%)

Other uses

This class of drugs are also used to treat bone pain and prophylactically they are indicated to reduce the incidence of pain and pathological fracture in breast cancer and myeloma. Zoledronic acid is probably the most effective of these drugs for bone pain, including (occasionally) prostate cancer.