

**GUIDELINES FOR MANAGEMENT OF HYPERCALCAEMIA OF MALIGNANCY**
FEBRUARY 2008**Definition**

Hypercalcaemia is a corrected serum calcium >2.60 mmol/l.

However if corrected calcium 2.60-2.69, treatment may not be required if patient asymptomatic.

Corrected calcium >4 mmol/l is life-threatening & requires URGENT treatment.

Management

Please note: These guidelines refer to the management of hypercalcaemia due to malignancy. If patient has hypercalcaemia and is not known to have malignancy, investigate for malignancy & hyperparathyroidism (FBC, ESR, U&E's, LFT's, TFT's, PTH, plasma cortisol, vitamin D level, myeloma screen [urine for Bence-Jones protein, plasma protein electrophoresis]), commence IV fluids and seek advice from Endocrinologist regarding management.

1. Assess patient's clinical condition (are they symptomatic?) and determine if treatment is appropriate and in line with their wishes.
2. Check U&E if not already done.
3. Review and consider discontinuing any drugs which may affect renal blood flow e.g. NSAIDs, diuretics, ACE inhibitors, ARB's.
4. Prehydrate the patient with 1-3 litres of 0.9% Sodium Chloride intravenously. Aim to give 3 litres over 24 hours if possible, but volume and rate of fluid replacement should be determined by level of dehydration, age, cardiac status and ability to maintain venous access.
5. For first episode of hypercalcaemia, give pamidronate, according to chart below.
6. For recurrent or resistant hypercalcaemia, give zoledronic acid.
7. Recheck U&E & calcium levels after 5-7 days. They may be checked sooner than this to monitor need for further fluid replacement, but **DO NOT GIVE MORE BISPHOSPHONATE UNLESS AT LEAST 5 DAYS SINCE FIRST DOSE, AS IT WILL NOT HAVE HAD TIME TO WORK, AND THERE IS A RISK OF HYPOCALCAEMIA IF FURTHER BISPHOSPHONATE IS GIVEN TOO SOON.**
8. If corrected serum calcium remains elevated 5-7 days after bisphosphonate treatment, consider further dose of bisphosphonate (zoledronic acid) unless calcium level is reducing and symptoms are improving.
9. Recheck calcium level weekly as long as risk of hypercalcaemia remains or more frequently if symptoms dictate.
10. Give further doses of bisphosphonate (zoledronic acid) if calcium levels high and it is more than 3 weeks since the last dose of bisphosphonate. If it is less than 3 weeks since the last dose, seek advice from the Palliative Care Team &/or Endocrinologist.

Pamidronate

Corrected Serum Calcium mmol/L	Pamidronate Dose	If patient needs pamidronate to treat bone pain, give 90mg irrespective of corr. Ca
<3.00	30mg	
$3.00 - 3.50$	60mg	
>3.50	90mg	

- ❖ In patients with normal renal function Pamidronate should be given in 250-500ml of 0.9% Sodium Chloride at a maximum rate of 1mg/min.
- ❖ In patients with impaired renal function the rate of infusion should not exceed 20mg/hour.
- ❖ Pamidronate should not be given to patients with severe renal failure i.e. creatinine clearance <30 ml/min (GFR <10), unless careful consideration has been given and the risk to life from hypercalcaemia is so great that the benefit of treatment would outweigh the risk. SEEK ADVICE IF NECESSARY.

Zoledronic Acid

- ❖ Give Zoledronic Acid 4mg IV in 100ml of 0.9% Sodium Chloride over at least 15 mins.
- ❖ Should not be used in patients with severe renal failure i.e. creatinine clearance <30 ml/min (GFR <10).

Other agents used for the treatment of hypercalcaemia

These may be considered in the circumstances described, but advice should be sought from the Palliative Care Team &/or Endocrinologist.

Ibandronic Acid

- Appears to be safer in renal impairment than other bisphosphonates.
- Dose given is dependent upon corrected serum calcium level.
- A corrected calcium <3.00 mmol/L requires 2mg IV.
- A corrected calcium >3.00mmol/L requires 4mg IV.
- Needs to be given in 500ml 0.9% Sodium Chloride over at least 2 hours.

Clodronate

- Can be given subcutaneously if IV access proving difficult.
- Dose required is 1500mg in 500-1000ml of 0.9% Sodium Chloride given subcutaneously over 24 hours.
- If the sites are of concern, they can be injected with 150IU of Hyaluronidase.

Calcitonin

- Should only be given in exceptional circumstances where the corrected serum calcium is very high (>4 mmol/l), and there is a clinical indication warranting its rapid reduction.
- Calcitonin is administered either subcutaneously (100IU every 6-8 hours, repeated as necessary, up to a maximum of 400IU qds) or intravenously (up to 10 units/kg over at least 6 hours).
- Calcitonin should be given in addition to the bisphosphonate.
- Calcitonin is highly emetogenic, so should be prescribed with Haloperidol

References

Wigan Borough Palliative Care Pain & Symptom Control Guidelines – Version 1, May 2007

Merseyside & Cheshire Palliative Care Network Audit Group Standards & Guidelines, Third Edition 2006

www.palliativedrugs.com

Jackson GH. Renal Safety of Ibandronate. *The Oncologist* 2005; 10:14-18.

Major P, Lortholary A et al. Zoledronic Acid is Superior to Pamidronate in the treatment of Hypercalcaemia of Malignancy: a Pooled Analysis of Two Randomized, Controlled Clinical Trials. *J Clin Oncol* 2001; 19(2): 558-567.

Pecherstorfer M, Herrmann Z et al. Randomized Phase II Trial Comparing Different Doses of the Bisphosphonate Ibandronate in the Treatment of Hypercalcaemia of Malignancy. *J Clin Oncol* 1996; 14(1): 268-276.

Pecherstorfer M, Steinhauer EU et al. Efficacy and Safety of Ibandronate in the Treatment of Hypercalcaemia of Malignancy: A Randomized Multicentric Comparison to Pamidronate. *Support Care Cancer* 2003; 11: 539-547.

Purohit OP, Younger J et al. A Randomized Double-blind Comparison of Intravenous Pamidronate and Clodronate in the Hypercalcaemia of Malignancy. *Br J Cancer* 1995; 72: 1289-1293.

Ralston SH, Thiebaud D et al. Dose-response Study of Ibandronate in the Treatment of Cancer-associated Hypercalcaemia. *Br J Cancer* 1997; 75(2): 295-300.

Rosen LS, Gordon D et al. Long-term Efficacy and Safety of Zoledronic Acid Compared with Pamidronate Disodium in the Treatment of Skeletal Complications in Patients with Advanced Multiple Myeloma or Breast Cancer. *Cancer* 2003; 98(8): 1735-1743.

Stewart AF. Hypercalcaemia associated with cancer. *NEJM* 2005 352(4): 373-379