GUIDELINE ON THE MANAGEMENT OF HYPERCALCAEMIA OF MALIGNANCY IN ADULTS

University Hospitals of Leicester NHS
NHS Trust

Trust ref: B23/2015

1. Introduction

This guideline is for the investigation and management of hypercalcaemia secondary to malignancy.

2. Scope

This guideline is for the use of medical and nursing staff in the University Hospitals of Leicester NHS Trust, who are caring for adults aged 18 years and above. Patients with hypercalcaemia of malignancy may present to Oncology, Haematology, the Emergency Department, Medicine and Surgery. If the patient does not have a known malignancy, other causes of hypercalcaemia need to be explored and specialist advice obtained. (See Acute Hypercalcaemia Guideline).

3. Recommendations, Standards and Procedural Statements

Hypercalcaemia is a metabolic emergency and a common complication of cancer, which occurs in 20 to 30% of patients. Hypercalcaemia of malignancy can occur in patients with both haematological and solid malignancies. It most commonly occurs in patients with breast, lung, prostate, renal cancers and multiple myeloma.

Patients with hypercalcaemia of malignancy often have a poor prognosis. There are three major mechanisms that can cause hypercalcaemia of malignancy:

a) Osteolytic metastases cause 20% of cases of hypercalcaemia, and can occur commonly in breast cancer. Bone destruction in these metastases is through osteoclast activity, which is stimulated by cytokines released by the tumour.

b) Tumour secretion of parathyroid hormone-related protein (PTHrP) is common in squamous cell carcinoma of the lung, head or neck, and in renal and ovarian malignancies. Secretion of endogenous parathyroid hormone is suppressed, so the serum parathyroid hormone concentration is usually very low. This should be suspected as the cause of hypercalcaemia in patients with a solid tumour in the absence of bony metastases. Typically these patients have very advanced disease and an associated poor prognosis.

c) Tumour secretion of 1,25-dihydroxyvitamin D (calcitriol) causes most cases of hypercalcaemia in patients with Hodgkins Lymphoma

Patients often present with generalised but extremely distressing symptoms. The severity of these symptoms often reflects the speed of onset of hypercalcaemia. Presenting symptoms include constipation, nausea and vomiting, confusion, muscle weakness, and polyuria. Calcium levels will continue to rise if left untreated and symptoms can progress rapidly to coma or death.

A. Assessment and Investigation

Assessment and Investigation

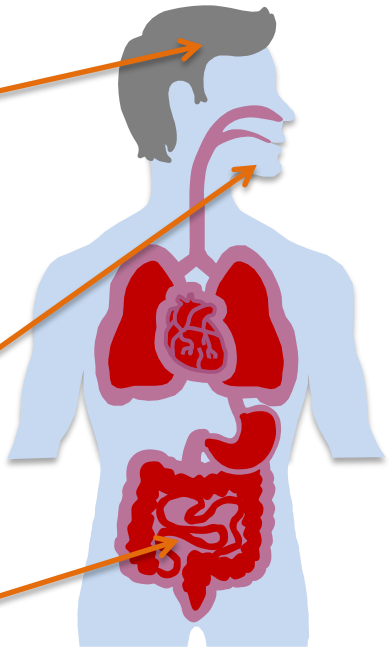
History

Clinical Examination

Lethargy
Cognitive dysfunction
Confusion
Mood disturbance
Muscle weakness

Polydipsia
Anorexia
Nausea & vomiting

Abdominal pain
Constipation
Polyuria



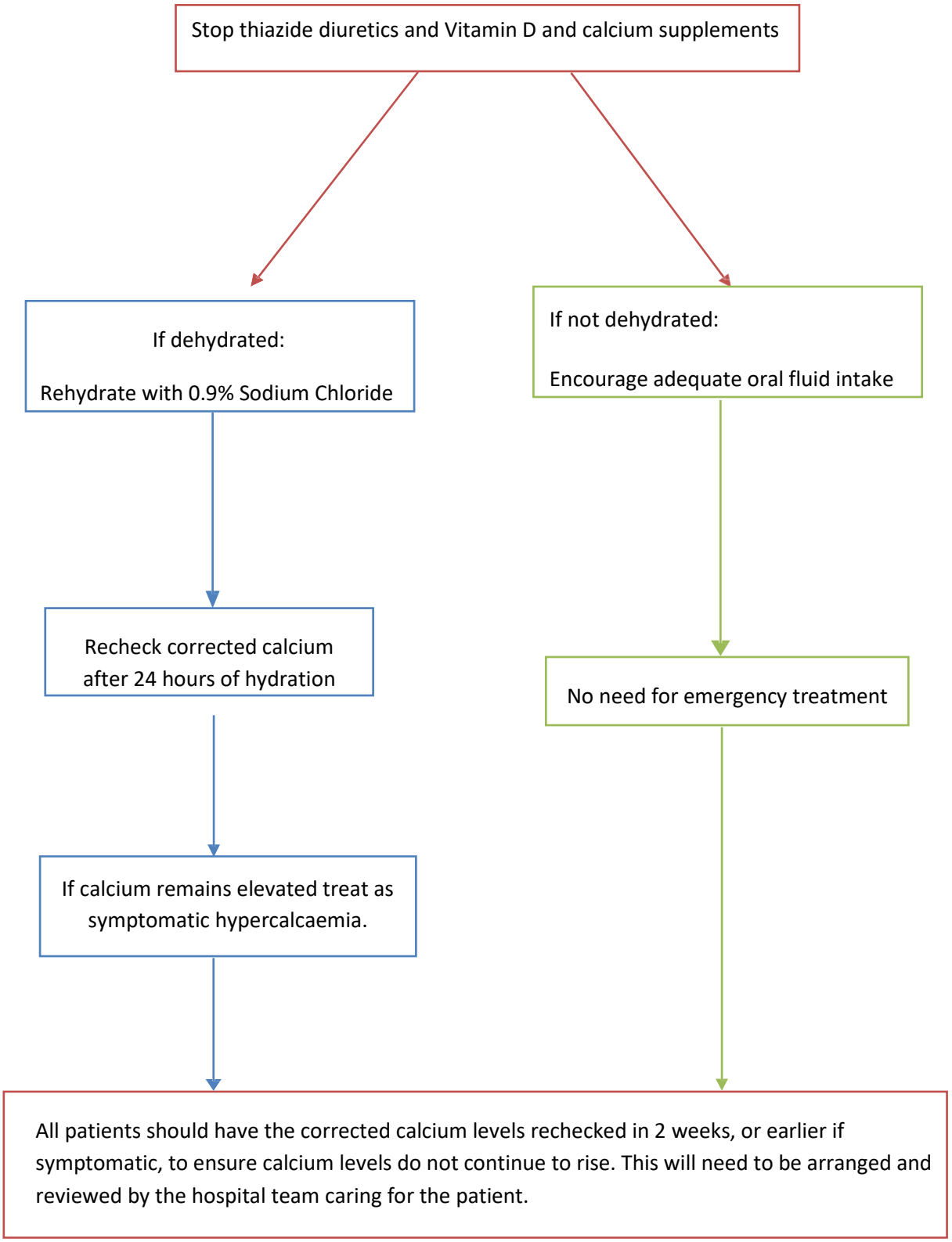
Clinically dehydrated
Look for Hypertension
Possible reduced GCS
Document MMSE

Investigations: U&E, bone profile, LFTs, PTH, vitamin D, bicarbonate, ECG

If corrected Ca >3.0mmol/L
OR <3.0mmol/L but rapidly rising
OR patient clinically unwell
Go to section C (page 4)

If corrected Ca <3.0mmol/L and patient clinically well
Go to section B (page 3)

B. Asymptomatic Hypercalcaemia with a corrected calcium of <3.0mmol/L



C. Symptomatic Hypercalcaemia or a corrected calcium of >3.0mmol/L

Stop thiazide diuretics and Vitamin D and calcium supplements

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Consider stopping any nephrotoxic drugs – Other diuretics, ACE inhibitors, NSAIDS

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Give intravenous 0.9% Sodium Chloride - 3 litres over 24 hours, aiming for a urine output of 100-150ml/hour.

Proceed with caution in patients at risk of fluid overload with 1 to 2 litres over 24 hours.

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After adequate rehydration (usually 12-24 hours of fluid) treat with Zolendronic acid intravenous infusion at the dose appropriate for the renal function below:

Egfr> 60ml/min -4mg in 100ml 0.9% Sodium Chloride over 15 minutes
Egfr 50-60ml/min -3.5mg in 100ml 0.9% Sodium Chloride over 15 minutes
Egfr 40-50ml/min -3.3mg in 100ml 0.9% Sodium Chloride over 15 minutes
Egfr30-40ml/min -3mg in 100ml 0.9% Sodium Chloride over 15 minutes
Egfr< 30ml/min – not routinely recommended. Seek specialist advice.

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Recheck corrected calcium in 4 days to monitor the effect of the Zolendronic Acid. Continue rehydration during this period, and recheck U& E if there are concerns with electrolyte balance or renal impairment.

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If hypercalcaemia continues at day 4, please seek specialist advice regarding further management.

Once the corrected calcium level has normalised, this should be rechecked in 2 weeks, or earlier if symptomatic, to ensure calcium levels do not continue to rise. This will need to be arranged and reviewed by the hospital team caring for the patient.

D. Specialist input and further measures

- For hypercalcaemia which remains 7 days after treatment with Zolendronic acid: a repeat dose can be considered, under specialist advice. Please contact Oncology/Haematology as appropriate.
- If eGFR<30ml/min:

- consider the role of renal replacement therapy if appropriate, contact Renal team. RRT may also be indicated in very severe hypercalcaemia (>4.5mmol/L) irrespective of renal function
- consider using Pamidronate as an alternative to Zolendronic acid, contact Haematology/Renal team
- consider using Denosumab; this is an unlicensed indication and should be done under specialist advice. Note that denosumab has a higher rate of inducing hypocalcaemia than bisphosphonates. Denosumab can also be useful in hypercalcaemia that is refractory to bisphosphate therapy.

- Treatment of the underlying malignancy can help in the management of hypercalcaemia, contact Oncology/Haematology team regarding a change in systemic therapy
- Calcitonin is occasionally used in severe hypercalcaemia as a means to temporarily lower the calcium level prior to onset of action of Zolendronic acid. Please contact Pharmacy and Consultant Biochemist.
- If recurrent resistant hypercalcaemia in advanced disease, this may be an indication that a patient is approaching last few months of life. If this is the case please consider contacting Palliative Care team for managing hypercalcaemia in the community e.g. LOROS team for support.

4.Education and Training

None

5.Monitoring and audit criteria

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Medical compliance with guideline	Yearly Audit	Oncology Head of Service	Yearly	Present in Departmental Audit Meeting.

6.Supporting documents and key References

BNF May 2015 6.6.2 Bisphosphonates and other drugs affecting bone metabolism

Shane E, Berenson JR. Treatment of hypercalcaemia. UpToDate (Accessed on August 11, 2020)

Walsh, J et al Society for Endocrinology – Emergency management of acute hypercalcaemia in adult patients (Accessed on August 11, 2020)

7 .Key Words

Calcium, Hypercalcaemia, Malignancy, Cancer, Bisphosphonate

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

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REVIEW RECORD			
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05/02/2021	3	Dr Thiagarajan Sridhar	*Page 2 inserted – assessment and investigation aid; further section added on specialist input and further measures on page 5*

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