

BCCA Protocol Summary Guidelines for the Diagnosis and Management of Malignancy Related Hypercalcemia

Protocol Code

SCHYPCAL

Tumour Group

Supportive Care

Supportive Care Group Contacts

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PREVALENCE

- Highest in patients with multiple myeloma and breast cancer
- Intermediate in patients with non-small cell lung cancer and lymphoma
- Rare in patients with renal cell, colon, and small cell lung cancer

TREATMENT DECISIONS

Relate to

- Elevation of serum calcium concentration (corrected)
- Symptoms

Affected by

- Rapidity of onset
- Age of patient
- Performance status
- Site of metastases
- Renal function

Patients may tolerate chronic elevations of serum calcium between 3.0-3.5 mmol/L with few symptoms but may become acutely ill and obtunded if a rapid elevation of serum calcium concentration were to occur over days, with serum calcium concentrations less than 3.0 mmol/L.

SYMPTOMS

General

Intravascular volume contraction, weight loss, anorexia, pruritus, increased thirst

Neuromuscular

Lethargy, muscle weakness, hyporeflexia, confusion, psychosis, seizure, drowsiness, coma

Gastrointestinal

Nausea, vomiting, constipation, obstipation, ileus

Renal

Polyuria, renal insufficiency

Cardiac

Bradycardia, prolonged P-R interval, shortened Q-T interval, wide T-waves, atrial/ventricular arrhythmias

DIAGNOSIS and ASSESSMENT

- Measure serum calcium, phosphate, creatinine, urine output
- Perform EKG
- Measure blood pressure and pulse lying and standing (after 1 minute) to determine any orthostatic changes reflecting intravascular blood volume
- Observe jugular venous pressure
- Confirm corrected serum calcium
- Corrected calcium = Measured calcium (mmol/L) + [40 - serum albumin (g/L)] x 0.027

Note: Low or below normal serum phosphate may be associated with PTH like activity or may reflect concurrent 1° hyperparathyroidism

MANAGEMENT

Ideally, treating the underlying malignancy is preferred where feasible. Many cases of hypercalcemia, however, present with advanced disease which may be poorly responsive to antineoplastic therapy.

Managing hypercalcemia will be directed at reducing bone resorption and increasing urinary excretion of calcium.

General Measures

- Avoid immobilization
- Stop drugs which inhibit urinary calcium excretion
- EG, thiazides
- Stop drugs which decrease renal blood flow
- EG, cimetidine, NSAIDs
- Stop drugs containing:
 - Calcium (Tums, Rolaids, etc.)
 - Vitamin D
 - Vitamin A/ Retinoids

Determine urgency of treatment: Hospital based or Outpatient based

Hospital based Management	Outpatient based Management
Serum calcium greater than or equal to 3.0 mmol/L	Serum calcium less than 3.0 mmol/L
Altered level of consciousness	Alert and oriented
Nausea or vomiting	No significant nausea
Intravascular volume contraction	Adequate intravascular volume

Hospital based Management	Outpatient based Management
Impaired renal function	Normal renal function
Cardiac arrhythmia	Stable cardiac rhythm
Obstipation, ileus	Mild constipation
No support at home	Support at home
Limited access to medical care	Access to emergency care
<i>(from De Vita, 1997, Table 49.3-4)</i>	

Hospital based Management (See accompanying table)

1. For ALL patients

1.1. Intravenous fluids: Isotonic saline (0.9% NaCl) **at** 300-400 ml/hr (assuming previously normal renal and cardiac function) to obtain euvolemic status

2. For hypercalcemia greater than or equal to 4 mmol/L

2.1. IM/SC Calcitonin: 4-8 unit/kg q 6h x 2 days

PLUS

2.2. IV Pamidronate (started concurrently with calcitonin): 90 mg in 250 mL NS over 1 hour

OR

2.3. IV Zoledronic acid (started concurrently with calcitonin): 4 mg in 100 mL NS over 15 minutes (note: see #7)

3. For hypercalcemia greater than or equal to 3.5 mmol/L

3.1. IV Pamidronate: 90 mg in 250 ml NS over 1 hour

OR

3.2. IV Zoledronic acid: 4 mg in 100 ml NS over 15 minutes (note: see #7)

4. For hypercalcemia less than 3.5 mmol/L with symptoms

4.1. IV Clodronate 1500 mg in 500 ml NS over 4 hours , with observation over 48 hours; if no response then use Pamidronate or Zoledronic acid as above

OR

4.2. IV Pamidronate 60-90 mg in 250 ml NS over 1 hour

OR

4.3. IV Zoledronic acid 4 mg in 100 ml NS over 15 minutes (note: see #7)

5. For hypercalcemia unresponsive to other measures

- 5.1. IV Mithramycin (Plicamycin) 25 mcg/kg repeat in 48 hours if no response; 12.5 mcg/kg if pre-existing renal or hepatic dysfunction

6. Re-treatment

There are patients whose serum calcium concentrations do not completely normalize in the first 48 hours after treatment. If needed, patients receiving Pamidronate will often have a second dose of 90 mg IV administered after 48 hours. The data on Zoledronic acid does not include serum calcium concentrations at exactly 48 hours, but only approximate data at 96 hours (4 days: range: days 2-5), at which time, 45% of patients had normalized their serum calcium concentrations. A second dose of Zoledronic acid after 48 hours seems reasonable.

For those patients who relapse after initial treatment, or require routine IV therapy to maintain normal serum calcium concentrations it is recommended that the same drug used initially be continued.

7. Zoledronic Acid Dose Modification for Renal Function

Single doses of Zoledronic acid should not exceed 4 mg and the duration of infusion should be no less than 15 minutes.

Baseline Creatinine Clearance (mL/Min)	Zoledronic Acid Dose
greater than 60	4 mg
50-60	3.5 mg
40-49	3.3 mg
30-39	3 mg

Monitor serum creatinine before each zoledronic acid dose. Withhold the dose

- a) For patients with normal baseline creatinine (less than 123 micromol/L), withhold the dose if an increase of 44 micromol/L or more occurs.
- b) For patients with abnormal baseline creatinine (greater than 123 micromol/L), withhold the dose if an increase of 88 micromol/L or more occurs.

Outpatient based Management (See accompanying table)

1. Ensure adequate oral fluid and salt intake: EG. 250 mL Oxo (or similar salty broth) PO three times daily
2. If serum phosphate is low normal or below normal:

- 2.1. Consider PO phosphate (Pharmascience Phosphates Solution) 0.5 to 3 grams phosphorus (4 to 24 mL) per day as tolerated
3. For hematologic malignancies (low grade lymphomas, CLL, myeloma)
 - 3.1. Prednisone 40-100 mg PO daily
4. For breast cancer (including Tamoxifen induced "flare")
 - 4.1. Prednisone 30 mg PO daily

Call Dr. Kevin Murphy or tumour group delegate at (604) 930-4055 or 1-800-523-2885 with any problems or questions regarding this treatment program.

Date activated: 01 June 1999

Dated revised: 01 May 2009 (unsafe abbreviations and symbols replaced)

REFERENCES

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