Calcitonin prescribing criteria for the management of hypercalcemia in a community hospital

Jessica Hernandez  
*Baptist Hospital of Miami*, jessicahernan@baptisthealth.net

Radhan Gopalani  
*Baptist Hospital of Miami*, radhang@baptisthealth.net

Heidi Clarke  
*Baptist Hospital of Miami*, heidic@baptisthealth.net

Joyce Lee  
*Baptist Hospital of Miami*, joycel@baptisthealth.net

Alyssa Donadio  
*Baptist Hospital of Miami*, alyssad@baptisthealth.net

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Calcitonin Prescribing Criteria for the Management of Hypercalcemia in a Community Hospital

Jessica Hernandez, Pharm.D.
Baptist Hospital of Miami, PGY-1 Pharmacy Resident
Disclosure Statement

- The following contributors have nothing to disclose regarding any financial or nonfinancial relationships with the products described, reviewed, or evaluated in this presentation:
  - Jessica Hernandez, Pharm.D.
  - Radhan Gopalani, Pharm.D., BCPS
  - Heidi Clarke, Pharm.D., BCCCP
  - Joyce Lee, Pharm.D., BCCCP
  - Alyssa Donadio, Pharm.D., BCPS
Objective

1. Discuss the clinical impact of pharmacist interventions in implementing prescribing criteria for calcitonin at Baptist Hospital of Miami
Hypercalcemia

Clinical condition defined as serum calcium levels exceeding the upper limit of normal (10.5 mg/dL).

Classifications of hypercalcemia:

- **Mild**: Corrected serum calcium < 12 mg/dL
- **Moderate**: Corrected serum calcium 12-14 mg/dL
- **Severe**: Corrected serum calcium >14 mg/dL

Regulation of Calcium in the Plasma

- **Parathyroid Hormone (PTH)** → Increases serum calcium levels
  - Stimulates production of vitamin D within the kidney
  - Facilitates mobilization of calcium from bone
  - Maximizes tubular reabsorption of calcium within the kidney

- **1,25-dihydroxyvitamin D3 (Calcitriol)** → Increases serum calcium levels
  - Facilitates absorption of calcium from the small intestine
  - Enhances reflux of calcium out of bone

- **Calcitonin** → Reduces serum calcium levels
  - Secreted from thyroid gland in response to an increase in calcium blood concentrations
  - Promotes renal excretion of calcium

# Etiology of Hypercalcemia

<table>
<thead>
<tr>
<th>Primary hyperparathyroidism</th>
<th>Malignancy-associated hypercalcemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D intoxication</td>
<td>Medications</td>
</tr>
<tr>
<td></td>
<td>• Thiazide diuretics</td>
</tr>
<tr>
<td></td>
<td>• Lithium</td>
</tr>
<tr>
<td></td>
<td>• Calcium containing antacids</td>
</tr>
<tr>
<td>Familial hypocaliuric hypercalcemia</td>
<td>Immobilization</td>
</tr>
</tbody>
</table>
Intravenous (IV) Hydration
Recommended for mild, moderate & severe hypercalcemia

Calcitonin
Reserved for moderate (symptomatic) & severe hypercalcemia

IV Bisphosphonates
Recommended for moderate & severe hypercalcemia

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Mode of Action</th>
<th>Dose</th>
<th>Onset of Action</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV fluids</td>
<td>• Increases glomerular filtration rate • Enhances calcium excretion</td>
<td>200-500 mL/hr or 2-4 L/day</td>
<td>Immediate</td>
<td>• Volume overload • HF exacerbation</td>
</tr>
<tr>
<td>Pamidronate</td>
<td>Inhibits osteoclast activity leading to decrease bone resorption</td>
<td>60-90 mg IV over 2-4 hours X 1 dose</td>
<td>≤24 hours • Maximum effect in ≤7 days</td>
<td>• Nephrotoxicity • Flu-like symptoms</td>
</tr>
<tr>
<td>Zoledronic acid</td>
<td>Inhibits osteoclast activity leading to decrease bone resorption</td>
<td>4 mg IV over 15 minutes X 1 dose</td>
<td>≤24 hours • Maximum effect in ≤7 days</td>
<td>• Nephrotoxicity • Flu-like symptoms</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>• Inhibits osteoclast activity • Enhances calcium excretion</td>
<td>4-8 IU/kg SQ or IM every 12 hours</td>
<td>~2 hours</td>
<td>• Rebound effect • Vomiting • Cramps • Flushing</td>
</tr>
</tbody>
</table>

Thomas SA, Chung S. Jhop. 2016;6(1).
Calcitonin (Miacalcin®)

- **FDA approved indications:**
  - Postmenopausal osteoporosis
  - Hypercalcemia
  - Paget’s disease

- **Hypercalcemia Dosing:**
  - Dose: 4 units/kg IM/SQ every 12 hrs
  - May increase to 8 units/kg every 12 hrs if response is unsatisfactory

- **Concerns with overuse of calcitonin:**
  - Hypocalcemia
  - **Tachyphylaxis:** Hypocalcemic effect diminishes within 24 to 48 hours
  - **Price:** 400 units/2 mL (200 units/mL): $2,712.09
Purpose

- To assess the prescribing practices of calcitonin at Baptist Hospital of Miami (BHM) and to optimize the utilization of calcitonin in patients with hypercalcemia.

- The intent of this project is to facilitate the implementation of a calcitonin prescribing criteria through pharmacist review and clinical recommendations at BHM.
Phase I:
- Retrospective chart review of all patients who received calcitonin injections at Baptist Hospital of Miami (BHM) between October 1st, 2017-September 30th, 2019.

Phase II:
- Prospective review post implementation of calcitonin prescribing criteria for the treatment of hypercalcemia.
- Resident will be on call to determine if initiation of calcitonin meets protocol criteria and make recommendations to the ordering physician as needed.
Outcomes

**Primary Outcome**

- Duration of calcitonin therapy (hrs)

**Secondary Outcomes**

- Number of pharmacy interventions
- Percentage of patients treated with IV fluids and IV bisphosphonates
Calcitonin (Miacalcin®) Prescribing Criteria for Hypercalcemia

Introduction:
Calcitonin (Miacalcin®) is a synthetic hormone with a rapid onset of action and used intramuscularly (IM) or subcutaneously (SQ) as a second-line treatment in the management of hypercalcemia. Calcitonin lowers serum calcium levels by inhibiting bone resorption and enhancing calcium excretion in the urine. However, its use is reserved for the treatment of severe and symptomatic moderate hypercalcemia. Despite its rapid onset of action, the use of calcitonin in the management of hypercalcemia is limited due to its short duration of effect and the development of tolerance that results from downregulation of calcitonin receptors after 48 hours of treatment initiation.

Etiology of hypercalcemia:
- Primary hyperparathyroidism
- Malignancy-associated hypercalcemia
- Vitamin D intoxication
- Medication induced hypercalcemia (eg. thiazide diuretics, lithium, calcium containing antacids)
- Immobilization

Dose of calcitonin for the treatment of hypercalcemia: 4 units/kg IM or SQ every 12 hours

Calcitonin Prescribing Criteria:
1. Calcitonin should be reserved for severe and symptomatic moderate hypercalcemia
2. Pharmacist to review dose, dose increases, and duration of therapy consistent with guidelines (see table below for treatment guideline recommendations)
3. Pharmacist to monitor response of calcitonin daily by reviewing labs and limit use to 48 hours.

Calcitonin – Criteria for Use in Hypercalcemia:
* Use of calcitonin in hypercalcemia should be limited to 48 hours due to diminished hypercalcemic effects beyond 48 hours

- **Severe hypercalcemia w/o symptoms** (CSC ≥ 14 mg/dL):
  - IV normal saline: 200-500 mL/h or 2-4 L/d
  - Pamidronate: 60-90 mg IV over 2-4 hours as a single dose (allow at least 7 days before re-treatment)
  - Calcitonin: 4 units/kg IM or SQ every 12 hrs

- **Moderate symptomatic hypercalcemia** (CSC 12-13.9 mg/dL):
  - IV normal saline: 200-500 mL/h or 2-4 L/d
  - Pamidronate: 60-90 mg IV over 2-4 hours as a single dose (allow at least 7 days before re-treatment)
  - Calcitonin: 4 units/kg IM or SQ every 12 hrs

- **Moderate asymptomatic hypercalcemia** (CSC 12-13.9 mg/dL):
  - IV normal saline: 200-500 mL/h or 2-4 L/d
  - Pamidronate: 60-90 mg IV over 2-4 hours as a single dose (allow at least 7 days before re-treatment)

- **Mild hypercalcemia** (CSC < 11.9 mg/dL):
  - Do not require immediate treatment
  - IV normal saline: 200-500 mL/h or 2-4 L/d

Calcitonin is not to be used in this setting

Calcitonin (Miacalcin®) Optimization Project
Principal Investigator (PI): Jessica Hernandez, PharmD, PGY-1 Pharmacy Resident

Rationale:
Calcitonin should be reserved for severe and symptomatic moderate hypercalcemia (please see Calcitonin Prescribing Criteria attachment)

Purpose:
To optimize the utilization of calcitonin in patients with hypercalcemia and reduce cost
- Prospective chart review will be conducted for every calcitonin order to determine if it meets treatment guideline recommendations
- Goal is to intervene and review chart prior to verification of calcitonin

Pharmacist's role:
- Prior to verifying any order for calcitonin, please contact Jessica Hernandez, PGY-1 Resident
- **Time frame:** January 6th – April 24th 2020
- **On Call from 7am – 7pm (including weekends):**
  - ASCOM: 54217
  - Cell: 561-685-2081
- For any orders outside of time frame:
  - List name, FIN, and room number on attached sheet and leave in designated basket in resident’s office.
  - Prior to verifying order, calculate for corrected serum calcium (CSC) for hypoalbuminemia in order to see if calcitonin is warranted.
  - **CSC = Serum calcium + 0.8 (4 – patient’s albumin)**

Thank you!
### Baseline Demographics

<table>
<thead>
<tr>
<th></th>
<th>Phase I (N=94)</th>
<th>Phase II (N=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age, years</strong></td>
<td>69</td>
<td>68</td>
</tr>
<tr>
<td><strong>Gender – male, n (%)</strong></td>
<td>53 (56.4)</td>
<td>4 (25)</td>
</tr>
<tr>
<td><strong>Mild Hypercalcemia, n (%)</strong></td>
<td>13 (13.8)</td>
<td>7 (43.8)</td>
</tr>
<tr>
<td><strong>Moderate Asymptomatic Hypercalcemia, n (%)</strong></td>
<td>9 (9.6)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td><strong>Moderate symptomatic Hypercalcemia, n (%)</strong></td>
<td>31 (33)</td>
<td>4 (25)</td>
</tr>
<tr>
<td><strong>Severe Hypercalcemia, n (%)</strong></td>
<td>41 (43.6)</td>
<td>3 (18.8)</td>
</tr>
</tbody>
</table>
Demographics

- **Phase I:**
  - Indication
    - Hypercalcemia of Malignancy: 88.3%
    - Primary Hyperparathyroidism: 7.4%
    - Other: 4.3%

- **Phase II:**
  - Indication
    - Hypercalcemia of Malignancy: 93.8%
    - Primary Hyperparathyroidism: 6.2%
Demographics

- **Phase I:**

- **Phase II:**

  - Ordering Provider Specialty
  - Internal Medicine
  - Nephrology
  - Oncology
  - Other

  Phase I:
  - Internal Medicine: 48.9%
  - Nephrology: 30.9%
  - Oncology: 17.0%
  - Other: 3.2%

  Phase II:
  - Internal Medicine: 56.3%
  - Nephrology: 31.2%
  - Oncology: 12.5%
  - Other: 3.2%
Results: Primary Outcome

Duration of Calcitonin Therapy

Phase I: ≤ 48 hrs, 71.30%; > 48 hrs, 28.70%
Phase II: ≤ 48 hrs, 100%

≤ 24 hrs | > 24 hrs
--- | ---
68.8% | 31.2%

*p = 0.0107*
Results: Secondary Outcomes

- Number of pharmacy interventions = 16
  - 75% acceptance rate

- Usage of first-line therapy:

<table>
<thead>
<tr>
<th></th>
<th>Phase I (N=94)</th>
<th>Phase II (N=16)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV Fluids – n (%)</td>
<td>76 (81)</td>
<td>16 (100)</td>
<td>p = 0.0689</td>
</tr>
<tr>
<td>IV Bisphosphonates – n (%)</td>
<td>83 (88)</td>
<td>16 (100)</td>
<td>p = 0.3613</td>
</tr>
</tbody>
</table>
Pharmacist Interventions

<table>
<thead>
<tr>
<th>Severity of Hypercalcemia</th>
<th>Discontinuation of Calcitonin</th>
<th>Shorten Duration of Therapy</th>
<th>Declined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (n=7)</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Moderate Asymptomatic (n=2)</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Moderate Symptomatic (n=4)</td>
<td>N/A</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Severe (n=3)</td>
<td>N/A</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

\[
\frac{12 \text{ interventions accepted}}{16 \text{ total interventions}} = 75\% \text{ acceptance rate}
\]
Results: Secondary Outcomes

- Phase II:

  Total dose adjustments per severity of hypercalcemia

<table>
<thead>
<tr>
<th>Severity</th>
<th>Number of calcitonin doses initially ordered</th>
<th>Number of doses dispensed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>27</td>
<td>13</td>
</tr>
<tr>
<td>Moderate asymptomatic</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Moderate symptomatic</td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td>Severe</td>
<td>12</td>
<td>7</td>
</tr>
</tbody>
</table>

Reasons for dispensing calcitonin for mild hypercalcemia:
- Presence of symptoms
- Failure to first-line therapy
- Delayed notification to the PI of order
Results: Secondary Outcomes

- **Phase II:**

  - # of doses reduced by 45%
  - # of vials saved: 18
  - Calculated cost savings ~$48,000 cost savings
  - Extrapolated BHM cost savings ~ $158,000/year
Discussion

**Limitations:**
- Low volume of calcitonin orders due to short duration of phase II
- Inability to accurately assess for presence of symptoms for hypercalcemia
  - e.g., fatigue due to hypercalcemia vs. underlying disease
  - Lack of documentation of symptoms

**Opportunities:**
- Educate pharmacists on optimal calcitonin use and monitoring
- Establish prescribing criteria to facilitate utilization of calcitonin across Baptist Health-System
- Develop electronic order-sets for the treatment of hypercalcemia based on severity level
Implementation of a calcitonin prescribing criteria through active pharmacist review and recommendations can facilitate the optimization of calcitonin use in patients with hypercalcemia at BHM and potentially lead to cost savings.
Which of the following classifications of hypercalcemia is calcitonin recommended for?

A. Moderate symptomatic hypercalcemia
B. Severe hypercalcemia
C. Asymptomatic moderate hypercalcemia
D. A & B


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