Impact of a Pharmacist-Implemented Protocol on Calcium Monitoring and Safety Outcomes with Denosumab Use in Ambulatory Patients

Rachel A. Kiehne, Pharm.D.
St. Louis College of Pharmacy
Mercy Hospital St. Louis
PGY-1 Pharmacy Practice Resident
Background

• Denosumab (Prolia®)
  – 60 mg subcutaneous injection every 6 months
  – Indicated for steroid-induced osteoporosis and osteoporosis/bone loss in men and women
• MOA: Monoclonal antibody which binds to RANKL, preventing osteoclast formation
• Severe ADRs: hypocalcemia, serious infections, atypical femoral fractures, osteonecrosis of the jaw

Background

• Hypocalcemia
  – Presentation: tingling fingertips/toes, myalgias, muscle cramps/spasms, tetany, respiratory distress, arrhythmia, seizures, psychiatric symptoms
  – Calcium level nadir typically occurs 10 days post-injection
  – Supplement all patients with calcium 1000 mg daily plus at least vitamin D 400 IU daily
  – Calcium level should be corrected before each injection
  – At-risk patients include: renal impairment/HD, hypoparathyroidism, thyroid surgery, malabsorption syndromes

Background

Retrospective Study

25.9% of patients experienced hypocalcemia

Background

Mercy Clinic – Family Medicine (MFM)
• Primary clinical site for the Mercy Family Medicine Residency
  – 18 Medical Residents
• 8-10 Attending Physicians
• Clinical Pharmacist at the clinic since 1992
• Required experience for Mercy PGY-1 Pharmacy Residency Program
• Prior research: pharmacist-physician collaboration improves osteoporosis treatment rates

Assess patient to schedule denosumab injection

- Calcium level not current
  - Order BMP

- Calcium level current
  - Normal value (8.6-10.2 mg/dL)
    - Schedule injection
      - Infusion center administration
  - Abnormal value (<8.6 or >10.2 mg/dL)
    - Refer to physician for calcium management
      - MFM administration
      - Recheck BMP

**MFM Protocol**
Developed in December 2017 by clinical pharmacist
Objective

• To determine the impact of a pharmacist-implemented protocol at Mercy Clinic-Family Medicine (MFM) compared to other Mercy East Community clinics on completion of calcium-monitoring and other safety outcomes for patients taking denosumab for osteoporosis
## Methods

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Adults &gt; 18 years of age</td>
<td>• Patients receiving denosumab for indications other than osteoporosis</td>
</tr>
<tr>
<td>• Received denosumab (Prolia®) injection between December 13&lt;sup&gt;th&lt;/sup&gt;, 2017 and December 1&lt;sup&gt;st&lt;/sup&gt;, 2019</td>
<td></td>
</tr>
<tr>
<td>• Patient of the Mercy East Community clinics</td>
<td></td>
</tr>
</tbody>
</table>

Patients identified via EPIC Electronic Medical Record using claims data for denosumab injections
Primary Outcome

Received denosumab for osteoporosis at a Mercy East Community Clinic

Non-MFM patients:
- Calcium level drawn within past 30 days
- Calcium level not drawn within past 30 days

MFM patients:
- Calcium level drawn within past 30 days
- Calcium level not drawn within past 30 days

Matched in 1:1 ratio (age & sex)
Secondary Outcomes

- Mean days since last calcium level was drawn prior to denosumab injection
- Percentage of:
  - Patients receiving documented calcium plus vitamin D supplementation
  - Patients with correctly-timed denosumab injections 180 to 210 days after the previous administration

- Incidence of:
  - Post-injection hypocalcemia within 30 days
  - Hospital admissions due to hypocalcemia within 30 days post-injection
  - Hospital admissions for infections 30 days post-injection
  - Fractures after injection and prior to next administration
Data Analysis

Chi-squared or Fisher’s exact tests

- **Primary Outcome**: Calcium level drawn within past 30 days
- **Secondary Outcomes**: Post-injection hypocalcemia, hospital admission for hypocalcemia or infection, incidence of fracture, on-time injections, calcium and/or vitamin D supplementation

Student’s t-test

- **Secondary Outcome**: Days since last calcium was drawn
Enrollment

206 patients included in retrospective analysis

- 103 MFM patients
- 103 non-MFM patients
# Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>MFM (n = 103)</th>
<th>Non-MFM (n = 103)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – yr</td>
<td>75.2 ± 9.8</td>
<td>75.3 ± 9.8</td>
<td>0.98</td>
</tr>
<tr>
<td>Female – n (%)</td>
<td>98 (95.1)</td>
<td>98 (95.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Height – in</td>
<td>62.7 ± 2.7</td>
<td>63.0 ± 3.0</td>
<td>0.42</td>
</tr>
<tr>
<td>Weight – kg</td>
<td>63.0 ± 10.8</td>
<td>67.1 ± 15.1</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Baseline Characteristics

MFM (n = 103)

- White: 89 (86%)
- Black: 7 (7%)
- Hispanic: 0 (0%)
- Asian: 4 (4%)
- Other: 3 (3%)

Non-MFM (n = 103)

- White: 102 (99%)
- Black: 0 (0%)
- Hispanic: 1 (1%)
- Asian: 0 (0%)
- Other: 0 (0%)

MFM versus non-MFM

<table>
<thead>
<tr>
<th>MFM versus non-MFM</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black</td>
<td>0.01</td>
</tr>
</tbody>
</table>
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Smoking Status – n (%)</th>
<th>MFM (n = 103)</th>
<th>Non-MFM (n = 103)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current</td>
<td>8 (7.8)</td>
<td>6 (5.8)</td>
<td>0.78</td>
</tr>
<tr>
<td>Past</td>
<td>41 (39.8)</td>
<td>44 (42.7)</td>
<td>0.67</td>
</tr>
<tr>
<td>Alcohol use* – n (%)</td>
<td>5 (4.9)</td>
<td>1 (1.0)</td>
<td>0.21</td>
</tr>
<tr>
<td>Hx of CKD – n (%)</td>
<td>27 (26.2)</td>
<td>23 (22.3)</td>
<td>0.52</td>
</tr>
<tr>
<td>CrCl – mL/min</td>
<td>51.9 ± 25.0</td>
<td>53.6 ± 18.6</td>
<td>0.58</td>
</tr>
<tr>
<td>&lt;30 mL/min – n (%)</td>
<td>17 (16.5)</td>
<td>9 (8.7)</td>
<td>0.14</td>
</tr>
<tr>
<td>≥30 mL/min – n (%)</td>
<td>86 (83.5)</td>
<td>94 (91.3)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

* > 3 drinks/day
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>MFM (n = 103)</th>
<th>Non-MFM (n = 103)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hx steroid use</strong> – n (%)</td>
<td>9 (8.7)</td>
<td>3 (2.9)</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Hx bisphosphonate use</strong> – n (%)</td>
<td>78 (75.7)</td>
<td>55 (53.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Admin Location</strong> – n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary care clinic</td>
<td>99 (96.1)</td>
<td>99 (96.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Infusion center</td>
<td>4 (3.9)</td>
<td>0 (0)</td>
<td>0.12</td>
</tr>
<tr>
<td>Specialty care clinic</td>
<td>0 (0)</td>
<td>4 (3.9)</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>10-year FRAX score</strong> – %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major osteoporotic fracture</td>
<td>21.2 ± 12.1</td>
<td>20.0 ± 11.0</td>
<td>0.46</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>8.4 ± 8.5</td>
<td>8.6 ± 9.4</td>
<td>0.62</td>
</tr>
</tbody>
</table>

* Prednisone 5 mg/day or equivalent for > 90 days
## Results

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th>MFM (n = 103)</th>
<th>Non-MFM (n = 103)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium drawn in last 30 days – n (%)</td>
<td>88 (85.4)</td>
<td>49 (47.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary Outcomes</th>
<th>MFM (n = 103)</th>
<th>Non-MFM (n = 103)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time since last calcium level – days</td>
<td>24.3 ± 46.1</td>
<td>97.8 ± 110.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Calcium supplement – n (%)</td>
<td>76 (73.8)</td>
<td>65 (63.1)</td>
<td>0.10</td>
</tr>
<tr>
<td>Vitamin D supplement – n (%)</td>
<td>89 (86.4)</td>
<td>80 (77.7)</td>
<td>0.10</td>
</tr>
<tr>
<td>Correctly timed injections* - n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Within 180 to 210 days from previous injection
## Results

<table>
<thead>
<tr>
<th></th>
<th>MFM (n = 103)</th>
<th>Non-MFM (n = 103)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-injection hypocalcemia</td>
<td>4 (3.9)</td>
<td>6 (5.8)</td>
<td>0.75</td>
</tr>
<tr>
<td>Post-injection hospitalization for hypocalcemia</td>
<td>1 (1.0)</td>
<td>4 (3.9)</td>
<td>0.37</td>
</tr>
<tr>
<td>Post-injection hospitalization for infection</td>
<td>0 (0)</td>
<td>3 (2.9)</td>
<td>0.25</td>
</tr>
<tr>
<td>Fracture</td>
<td>2 (1.9)</td>
<td>6 (5.8)</td>
<td>0.28</td>
</tr>
</tbody>
</table>
Results

Calcium drawn in last 30 days

- Pharmacist on-site (n = 77): 87.0%
- Pharmacist not on-site (n = 26): 80.8%

Correctly-timed injections

- Pharmacist on-site (n = 54): 78.6%
- Pharmacist not on-site (n = 23): 56.5%

Statistical significance:
- Calcium drawn in last 30 days: p = 0.521
- Correctly-timed injections: p = 0.037
Discussion

Strengths
• Similar baseline characteristics between groups
• Assess benefit of clinical pharmacist involvement and success of clinic protocols

Limitations
• Small study population limits analysis of rare safety outcomes
• Post-injection hypocalcemia difficult to capture
• No pharmacist at MFM from August 2018 to February 2019
Conclusions

• The pharmacist-implemented protocol at MFM significantly improved the frequency of calcium monitoring before denosumab administration

• This difference was not shown in secondary safety outcomes

• Pharmacists can have a significant impact on the appropriate monitoring of denosumab
Impact of a Pharmacist-Implemented Protocol on Calcium Monitoring and Safety Outcomes with Denosumab Use in Ambulatory Patients

Rachel A. Kiehne, Pharm.D.
St. Louis College of Pharmacy
Mercy Hospital St. Louis
PGY-1 Pharmacy Practice Resident