ZOLENDRONATE
a case report

Wendy Schwarz, RN
Clinical Resource Nurse
Endocrine Clinic
AB Children's Hospital
Calgary, AB

Disclosures

- I have nothing to disclose related to this presentation

Objectives

- Present a case report on a patient that received Zoledronate
- Illicit discussion about the case
- Find out if others have had similar experiences
Zoledronic Acid

- Zoledronic acid slows down bone reabsorption (osteoclasts), allowing the bone-forming cells time to rebuild normal bone and allowing bone remodelling

- Zoledronate has shown significant benefits versus placebo over three years, with a reduced number of vertebral fractures and improved markers of bone density[1].


Zoledronic Acid

- Reclast, Zometa (Canada), Aclasta (Australia)

- From Monograph in >10% of patients
  - Bone pain (55%)
  - Nausea (29-46%)
  - Fever (32-44%)
  - Fatigue (39%)

Side Effects

- Side-effects can include fatigue, anemia, muscle aches, fever, and/or swelling in the feet or legs. Flu-like symptoms (myalgia, arthralgia, and headache) are commonly experienced after the first zoledronate infusion, although not subsequent infusions, and are thought to occur because of its potential to activate human γδ T cell (gamma/delta T cells)

- Rare adverse effects include renal dysfunction, hypocalcemia, atrial fibrillation, and osteonecrosis of the jaw
Case Study

- Dec 2010
  - 6y6m old boy with hx of 7 fractures of lower limbs, all considered fragility fractures
    - 1: (R) tibia, at age 8mos, sitting down
    - 2: (R) tibia 22mos, getting off the bed
    - 3: (L) 5th metatarsal, 4yr, jumping off bottom stair
    - 4: (R) ankle, 5yr, running
    - 5: 4th metatarsal, 6yr, no clear mechanism
    - 6: (R) big toe while still in cast for 5th break
    - 7: previous week 2nd & 3rd metatarsals, piano bench

History cont’d

- Adopted, no family history available
- Parents and one younger sibling in the home
- No significant dental issues, no evidence of dentinogenesis imperfecta
- Blue sclera noted on exam
- Denies back pain, even with palpation
- MSK – hypermobility of the joints
- Grade 1, gifted program
- Umbilical hernia repair 2009, biopsy done at the time for OI
- No steroid, antiepileptic drug or heparin use

Plan

- Screening blood work (all normal)
- Pros and cons of bisphosphonate treatment was discussed with the parents including flu-like symptoms following the first injection as well as the remote risk of osteonecrosis of the jaw
- Parents opted to hold on the treatment
Bone Density Z scores

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Follow up

- From our initial visit in Dec 2010....
  - 2011 -2 further fractures, dx w/cold urticaria
  - Genetic testing results; neg for the COL1A1 and COL1A2 gene, skin fibroblast electrophoresis was normal
  - 2013 - No further fractures- therefore no tx recommended
  - Jan 2015 (no follow up for 2 years) 5 new fractures 7 ribs, compression T7-8, in back brace, missing significant days of school, sclera now just faintly grey

Plan

- Due to an increase in fracture history, compression fractures and declining bone density scores bisphosphonate treatment was recommended
  - Parents didn’t want him missing school every 3-4 mos therefore Zolendronate versus Pamidronate was offered (once a year infusion). Parents elected to wait until summer holidays before starting
  - July 2015 Zolendronate 4mg given
Aftermath of Treatment

- Major myalgia, nausea, vomiting and fever. Lasting 10 days. This was felt to be attributed to cytokine release.
- Improved over the summer but with intermittent mild back pain remaining.
- October 2015 – complaint of worsening back pain, worse in the morning, gets better for ½ day at school then starts worsening in the afternoon. Missing some days of school. Advil/Tylenol not working.
- O/E – c/o pain when bending over and on palpation. Plan to start a trial of Naproxen and Prevacid.

- Nov 2015 - Calls from Mom, at least twice a week.
- Now missing almost all of school.
- Can’t sit or lay in one position for any length of time.
- Mom states this is affecting all of the family now.
- Urgently seen in December by Endocrine for re-evaluation.
  - O/E: walking with limp, holding spine in protected position. c/o local tenderness at L4-5, + Trendelenberg sign.
- Pharmacy manufacturer contacted re: reporting a possible adverse reaction. Of note, none on record according to the company.

- Urgent referral to Chronic Pain Clinic (Rheumatology, Anaesthesiology, Physio, Pharmacist).
- All possible inflammatory markers were normal.
- Trial of Prednisone was initiated for 10 days.
- Bone scan ordered – uptake appeared symmetric.
- Diagnosed with: Right localized severe sacroiliac pain with a neuropathic component.
- Rx oxcarbazepine to deal with the neuropathic component.
**Latest update**

- End of Jan 2016 Mom feels that pain is improved with oxcarbazepine. Starting back at half days of school. With goal to increase to full days by end of Feb


- Normal – no abnormality of the lumbosacral spine and sacroiliac joints

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**Questions for the Audience**

- Are other centres using Zolendronate?

- Has anyone had a similar experience with Zolendronate?

- Any suggestions with the case study management?
• Thank you