Pain in Fibrous Dysplasia/McCune-Albright Syndrome

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Fibrous Dysplasia Foundation Patient & Family Conference 2017
# Pain in Fibrous Dysplasia: Prevalence and Treatment

<table>
<thead>
<tr>
<th></th>
<th>Adults (n=35)</th>
<th>Children (n=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Anywhere (Y/N)</td>
<td>81%</td>
<td>49%</td>
</tr>
<tr>
<td>Mean Pain Scores</td>
<td>4.1 *</td>
<td>2.8</td>
</tr>
<tr>
<td>% that used treatment</td>
<td>26%</td>
<td>44%</td>
</tr>
</tbody>
</table>

- Pain increases with age
- Pain is undertreated in children

*Kelly, Osteoporosis Int, 2007*
No correlation between amount of FD and pain

Kelly, Osteoporosis Int, 2007
Causes of Pain in FD: Many

- **Orthopedic**
  - Fractures (current or impending)
  - Bone cysts
  - Surgical hardware problems

- **Metabolic**
  - Phosphate Wasting
  - “Intrinsic” FD pain

- **Functional**
  - Abnormal gait
  - Deformities
  - Muscle weakness
  - Arthritis
Approach to Pain Management in FD

1. Prevent & treat fractures & deformities
2. Treat endocrine disease
3. Optimize physical function & strength
4. Optimize psychosocial & emotional function
5. Pharmacologic and non-pharmacologic treatments

There are no therapies that can fix the underlying problem in FD. But we can be proactive to prevent complications that lead to pain. And we can be proactive to develop skills to cope with pain.
Phosphate Wasting in FD

Low Blood Phosphorus

Renal phosphate wasting

FD + rickets

Osteomalacia, Bone Pain

o = osteoid  b = bone
FGF23 is a Hormone that Causes Phosphate Wasting in FD

FGF23 is made by FD cells

May show up during times of rapid growth (ex: infancy, puberty)
May resolve in adulthood
Hypophosphatemia Increases Fractures

(Leet, JBMR, 2004)
Hypophosphatemia: Treatment

1. Phosphorus Supplements
   - Pills, powder, or liquid
   - Short-acting, must give 3-5 times a day
   - Diarrhea, GI discomfort

2. Calcitriol
   - Prevents hyperparathyroidism (major side effect of Phosphorus supplements)
   - May increase urine calcium
     - Monitor urines and kidney ultrasounds
Pharmacologic Management of FD Pain
# FD Pain Management: Pharmacologic Therapy

<table>
<thead>
<tr>
<th>Pain Treatments</th>
<th>Adults (n=35)</th>
<th></th>
<th>Children (n=43)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% that used it</td>
<td>% reported relief</td>
<td>% that used it</td>
<td>% reported relief</td>
</tr>
<tr>
<td><strong>NSAIDs</strong></td>
<td>57%</td>
<td>56%</td>
<td>56%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Narcotics</strong></td>
<td>26%</td>
<td>47%</td>
<td>17%</td>
<td>90%</td>
</tr>
<tr>
<td><strong>Bisphosphonates</strong></td>
<td>26%</td>
<td>73%</td>
<td>17%</td>
<td>75%</td>
</tr>
<tr>
<td><strong>Alternative Treatments</strong></td>
<td>17%</td>
<td>52%</td>
<td>11%</td>
<td>No report</td>
</tr>
</tbody>
</table>
FD Pain Treatment 3 Step Ladder

1 mild
Acetaminophen
NSAIDs
± Adjuvants

2 moderate
Bisphosphonates
- Zoledronate
- Pamidronate
± Adjuvants (Gabapentin, SSRI)

3 severe
Carefully consider opioids
± Adjuvants
What about bisphosphononates?

- Synthetic analogues of pyrophosphate
- Used to treat disorders of low bone mass or high bone activity
- Taken up into skeletal matrix and inhibit osteoclasts (bone breakdown cells)
- Half life >10 years
Bone Remodeling Cycle

Osteoclasts: Break Down Bone

Osteoblasts: Build New Bone

X
Types of Bisphosphonates

**Intravenous**
- Pamidronate (Aredia)
  - 3 hr infusion, ~every 3 months
- Zoledronic acid (Reclast)
  - 30 min infusion, ~every 6 months
- Ibandronate (Boniva)
  - Rapid infusion, ~every 3 months

**Oral**
- Alendronate (Fosamax)
  - Weekly pill
- Risedronate (Actonel)
  - Daily or weekly pill
What types of patients use bisphosphonates?

• FDA-approved for treatment of adults with:
  – Osteoporosis
  – Paget’s disease
  – Bone tumors and bone metastases
  – High blood calcium levels

All other uses are “off-label”
Bisphosphonates in FD

• Early case reports
  – Most show improvement in pain
  – Conflicting reports about radiographic effects on FD lesions

• Clinical trial in alendronate (oral form) at NIH:
  – 40 patients
  – Placebo-controlled
Placebo-Controlled Trial of Alendronate in FD

Compared to placebo, alendronate decreased markers of bone resorption in the blood
Alendronate Did Not Improve FD Appearance
Placebo Controlled Trial of Alendronate in FD

Alendronate did not improve pain

Boyle, JCEM 2014
Side Effects of Bisphosphonates

- **Flu-like symptoms** *(first 1-2 doses)*
  - Temporary, manageable with Tylenol/Motrin

- **Low blood calcium**
  - Adequate dairy, vitamin D and calcium supplements

- **GI disease** *(reflux, ulcerations): Oral forms*
  - Can be severe!
  - STOP drug if developing symptoms
Osteonecrosis of the Jaw

- Loss of blood supply to jaw bone
- Assoc w long-term, high dose, IV infusions, invasive dental procedures
- At NIH: 76 patients treated with bisphosphonates, 4 developed ONJ (5%)

- Use lowest dose and interval needed to control pain
- See dentist & complete planned dental work prior to starting treatment
- On treatment: Excellent dental hygiene, regular dental checkups
Non-Pharmacologic Management of FD Pain
Chronic Pain Cycle

Activity Avoidance

Anxiety, Fear, Anger

Increased Perception of Pain

Depression & Social Avoidance

Progressive Deconditioning

More Pain with Activity

PAIN

Physical\n
Psychological
Chronic Pain Cycle

Physical
- Activity Avoidance
- More Pain with Activity
- Progressive Deconditioning

Psychological
- Anxiety, Fear, Anger
- Depression & Social Avoidance
- Increased Perception of Pain
- "X" marks the point where pain leads to avoidance, perpetuating the cycle.

"PAIN" at the center of the cycle, showing the bidirectional flow from physical to psychological and back again.
Physical Activity

• Low/no impact weight bearing exercise as tolerated
  – Improve muscle strength and range of motion
  – Improve coordination, prevent falls
  – Improve non-FD bone health
  – Psychological benefits
Rehabilitation (PM&R, Physiatry): Function & Mobility

• Orthotics
• Assistive ambulation (cane, crutches, wheelchairs)
• Coordinate with PT: strength, range-of-motion
• Coordinate with OT: activities of daily living, self care
Rehabilitation: Hydrotherapy

- Water is
  - Buoyant
  - Shock absorbing
  - Pain relieving
  - A force which resists bodily movement

- Can participate at any age
- Both swimming and upright activities are beneficial
Psychological Management in Chronic Pain

- Recognition of stress and negative emotion
- Problem solving
- Coping skills
  - Mindfulness
- Behavioral
  - Relaxation training
  - Biofeedback
- Play therapy
- Individual, group, family
Psychological Therapy is Effective for Treatment of Chronic Pain

Cochrane Review, 2012

Risk Ratio
M-H, Fixed, 95% CI

Less effective More effective
Energy conservation and work simplification

• Metabolic bone diseases are tiring. Endurance can be a problem

• Be mindful about activities so you get the most bang for your buck
  – Sit rather than stand
  – Keep frequently used items within easy reach
  – Plan the steps of an activity starting and be flexible
  – Consider adaptive equipment, school accommodations
Orthopedic Surgery

• Goals:
  – Correct fractures
  – Correct and prevent deformity

• May need to use specialized techniques
Pharmacologic and Non-Pharmacologic Pain Treatments: General Principles

• It’s a balancing act
  – **Risks** (known & unknown)
  – **Benefits** (certain & uncertain)
  – **Cost** (money, time, & energy)
Health-Related Quality of Life for FD Patients and US Population
Health-Related Quality of Life for FD Patients and US Population

Children

- Physical Function *
- Role-Physical *
- General Health *
- Bodily Pain *
- Role-Emotional *
- Parental Emotional *
- Self Esteem
- Mental Health
- Behavior
- Parental Time

US Population
FD Patients
Questions?