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- Member, Pharmacy and Therapeutics Committee, Dakotacare
- Governor appointed member of the Pharmacy and Therapeutics Advisory Committee for SD Medicaid
- Participating physician Medicare, Medicaid, IHS, VA, and Tricare

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- Speaker and/or consultant: Ferring (Euflexxa); Takeda (Uloric); Novartis (Forteo, Reclast); Roche (Boniva); Pfizer (Celebrex); Sanofi aventis and Proctor and Gamble (Actonel); Abbott (Humira); Amgen (Enbrel)

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- Current Investigator with active research: Pfizer, (OA and RA studies) Roche (RA); and Genentech (RA)
- Past research investigator: Pfizer, Wyeth, Roche, Amgen, Merck

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- No direct stock or other ownership/investment in any of these companies
- Remuneration for services rendered and expenses only

Fracture Risk Assessment and Prevention Program

James A Engelbrecht, MD
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Osteoporosis

- Compromised bone strength
- 10-12 million with osteoporosis, 80% women
- 30-34 million with low density at risk of developing osteoporosis, 70% women

Fragility Fractures

- Low trauma
- Predicts increased risk of osteoporosis
- Increased risk of future fracture by 2-3x
- With vertebral fracture, 5-fold increase risk of new fracture in 1-3 years

Fragility Fracture of the Hip

- Increased morbidity
- Functional decline
- Death


Osteoporosis: Silent Disease or Is It Screaming at Us?

BOTH!

Consider this:

- <1/3 of people with significantly low bone density are aware of it
- Vertebral fractures are often asymptomatic
- <25% of patients with fragility fracture get an evaluation of their bone status and/or preventative treatment

SEARCH citation, or a



The NEW ENGLAND
JOURNAL of MEDICINE

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Zoledronic Acid and Clinical Fractures and Mortality after Hip Fracture

Kenneth W. Lyles, M.D., Cathleen S. Colón-Emeric, M.D., M.H.Sc., Jay S. Magaziner, Ph.D., Jonathan D. Adachi, M.D., Carl F. Pieper, D.P.H., Carlos Mantales, M.D., Lars Hyldstrup, M.D., D.M.Sc., Chris Recknor, M.D., Lars Nordström, M.D., Ph.D., Kathy A. Moore, R.N., Catherine Lavocchia, M.S., Jie Zhang, Ph.D., Peter Mesenbrink, Ph.D., Patricia K. Hodgson, B.A., Ken Abrams, M.D., John J. Orloff, M.D., Zebulun Horowitz, M.D., Erik Fink Eriksen, M.D., D.M.Sc., Steven Boonen, M.D., Ph.D., for the HORIZON Recurrent Fracture Trial

Study Design

- 2111 patients, > 50 years old
- Hip fracture
- Work up for secondary causes
- Calcium/Vit D supplementation
- IV placebo vs zoledronic acid yearly
- Follow-up 3 years

Results

- Bone Density: Placebo no change to slight decline; IV Zoledronic improve 2.6-5.5%
- New Fracture within study period:
Placebo 13.9% IV Zoledronic 8.6%

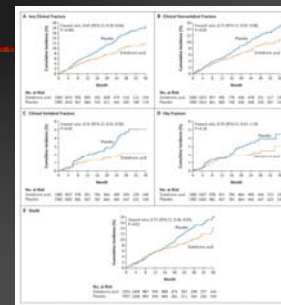
Results continued...

DEATHS during study period:

Placebo 13.3% IV Zoledronic 9.6%

A 28% reduction in post fracture mortality!

Time to Primary or Secondary End Point



Lyles K et al. N Engl J Med 2007;357:1799-1809

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Adverse Events

- Transient pyrexia, myalgias, and bone pain overall < 10%; about 3:1 treatment vs placebo group
- Risk factors for bisphosphonate toxicity were part of exclusion criteria for study

Our Concerns and Discussions

- More evidence of the impact of intervention on outcomes
- A new standard of care?
- Are patients at risk being identified?
- Are they getting evaluated and treated?
- Is anyone taking responsibility to own the bone?

Can We Do a Better Job?

The Plan

- Orthopedics and Rheumatology
- Informal program of evaluation and follow up designed
- Began to review patients in mid 2008
- Initial patient data review was compelling
- Formal program initiated in Spring 2009

Fracture Risk Assessment and Prevention Program (FRAPP)

- Our findings, outcomes, and experience thus far
- What we have learned
- The valuable take home messages

FRAPP

- Total patients: 72
- Male: 9, all with fragility or stress fractures
- Female: 57, all with fragility fractures, bone issues but no fracture found in 4, traumatic fractures (MVA) with non-healing in 2

FRAPP: Males

- Average age 73.4 (55-86)
- 4 femoral neck
- 1 femur/pelvis
- 1 metatarsal
- 3 vertebral (low T, upper L)
- Chronic liver disease/steroid (1)
- Endocrinopathy (testosterone) (1)
- Multiple Myeloma (1)
- Low Vitamin D levels (4)

FRAPP: Males

- DEXA scores (lumbar or femoral neck)
- T < -2.5 (5); T between -1 and -2.5 (3); >-1 (1)
- Previously known low density with no work up but on treatment (oral bisphosphonate) (3); no treatment (1)
- DEXA scores all same or worse

FRAPP: Males/Treatment

- Restorative only (0)
- Restorative plus IV bisphosphonate (7)
- Other problems addressed (2)

FRAPP/males: What Can We Learn?

- Dexa screening certainly by mid-70s, earlier if risk factors
- Thorough work up needed for any low density or fragility fracture: specific cause identified in over 50% of males
- Vitamin D issues do occur in men
- Most will need some type of intervention

FRAPP: Females

- Average age 66.8 (34-92)
- Fragility or stress fracture in all: hip (10), wrist (13), vertebral (12), pelvic or sacral (5), metatarsal stress (5)
- Other fractures: tibial stress (2), ankle or tibia/fibula (4), humerus (4), femur (2), calcaneus (1)
- A few multiple sites, eg wrist/humerus, counted as wrist

FRAPP: Females: Diagnosis other than idiopathic

- Hyperthyroid (1)
- Hyperparathyroid (1)
- Multiple Myeloma (1)
- Radiation therapy for colon cancer (1)
- Glucocorticoids (2)
- Low Vit D (19)

FRAPP: Females

- DEATH within the first year: 2, one age 75 with humeral fracture and one age 78 with fractured femur

FRAPP: Females

- Known osteopenia or osteoporosis already on some form of therapy (15)
- Of these 15, 11 either had no formal follow-up or we found previous declining T scores
- Of the remaining 4, they had stable or improved T scores

FRAPP: Females

- Of the patients with declining densities on treatment we found low D, absorption/adherence problems, lack of any formal clinical follow up or monitoring, and no previous work up could be identified

FRAPP: Females/ Dexa Scores

- T < -2.5: 23
- T -1 to -2.5: 23
- T -1 or better: 8
- 2 not able to do, 1 lost to f/u

FRAPP: Females/intervention

- First focused on the underlying problem identified in the work up: thyroid, parathyroid, myeloma, steroids, etc
- Restorative treatment only (15)

FRAPP: Females/intervention

- Restorative plus meds: (31)
- Bisphosphonate: Oral (10) IV (16)
- Other: calcitonin (1), estrogen (1), raloxifene (1), teriparotide (2)
- Several are being monitored with possible later intervention pharmacologically

FRAPP: Females: What Can We Learn?

- Significant number with previously identified low bone density: Many with no formal work up or evaluation as to etiology; Medication often prescribed without work-up; Variable monitoring and lack of clinical follow-up

FRAPP: Females: More Lessons

- Although average age was 67, less than one third had previous DEXA
- Several previous studies were of questionable technical adequacy (wrong scan speed, improper positioning, incorrect weight factor)
- Vitamin D deficiency a major concern

Dr E's Bone Rules

- You have to think of it or you won't find it. Think silent disease, general health, "an ounce of prevention...."
- When there is a fracture someone must own the bone.
- If you think metabolic bone disease or osteoporosis is a simple problem, THINK AGAIN.

Rules, Continued

- You must have quality, reliable, and reproducible bone density data.
- All low bone density is not osteoporosis, and not all osteoporosis is primary or idiopathic. Give some thought to secondary causes and work up prn.
- Establish basic bone health before drugs.

A Few More Rules....

- Understand the risks, adverse effects, and especially contraindications of the drugs.
- Know the potential benefits and how to assess efficacy of the drugs.
- You must engage the patients on an ongoing basis. This is health maintenance not a one time problem.

The Last Rule:

If your not sure, there are plenty of resources to help...just ask!

References and Resources

- Lyles, K. et al. NEJM 357:1799-1809; Nov 1, 07
- Fitzpatrick, LA. "Secondary Causes of Osteoporosis" Mayo Clin Proc: 2002: 77: 453-468
- Mankin HJ and Mankin CJ. "Taking a closer look at metabolic bone disease" JMuscMed:24(3): 98-107 March 2007

References and Resources

- www.shef.ac.uk/FRAX (info on use of the FRAX in patient assessment)
- www.nof.org website of National Osteoporosis Foundation
- www.iscd.org website for the Int Society of Clinical Densitometry