Drug Therapy for Osteoporosis

Question 1
Which of the following medications is considered first-line therapy for osteoporosis?

A. Bisphosphonates  
B. Raloxifene  
C. Calcitonin  
D. Hormone replacement therapy

Question 2
Which of the following natural products has been shown to prevent osteoporosis?

A. Isoflavones  
B. Black cohosh  
C. Soy milk  
D. None of the above
Question 3
Which of the following medications is limited for use in high-risk patients?
A. Raloxifene  
B. Calcitonin  
C. Teriparatide  
D. Ibandronate

Question 4
Which of the following does NOT have FDA indication for the prevention of osteoporosis?
A. Estrogen  
B. Alendronate  
C. Calcitonin  
D. Raloxifene

Question 5
What is the key end point of any clinical trial involving therapy for osteoporosis?
A. Patient drop out rate  
B. Effect on bone density  
C. Effect of fracture incidence  
D. Incidence of adverse events
Instructions

While viewing this multi-media program, you can control the slides and audio by using the "play", "pause", "next", and "previous" controls. You can also jump to a specific slide using the thumbnail images at the bottom of the screen.

Learning Objectives

At the conclusion of this program participants should be able to:

- Describe the appropriate use of the various pharmacotherapeutic choices to treat osteoporosis, including indication, mechanism of action, dosing, administration, adverse effects and precautions
- Explain the role of the drugs approved for osteoporosis in the management of this disease
- Educate patients about the various pharmacotherapeutic choices to treat osteoporosis and monitor their response to therapy

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Overview of Drug Therapy

The Osteoporosis Pyramid

Pharmacotherapy

Identify and Address Secondary Causes

Lifestyle Changes

Role of Drug Therapy

- Osteoporosis is preventable & treatable though not currently curable
- Available therapies can effectively prevent further disease progression and reduce disability associated with fractures

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Categories of Drugs

Drugs for Osteoporosis

Antiresorptive agents

Formation-stimulating drugs

Antiresorptive agents

Major Action: suppress bone resorption
preventing further bone loss
– Decrease in number or depth of resorptive sites
– Stops further architectural loss
– Slower turnover allows better mineralization

Resulting increase in BMD due to more complete mineralization, not increased synthesis of bone
– May increase BMD by 2-8%

Antiresorptive Agents

ERT/HRT
Alendronate (Fosamax®)
Salmon-calcitonin (Fortical®, Miacalcin®)
Raloxifene (Evista®)
Risedronate (Actonel®)
Ibandronate (Boniva®)

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Formation-Stimulating Drugs

- Major Action: stimulate formation of bone mass
  - May increase BMD by 10-20%
  - May increase cortical thickness & enhance trabecular microarchitecture

Formation-Stimulating Drugs

- Teriparatide (Forteo®)

Drug Development for Osteoporosis

Discovery of Osteoporosis
1800s

Connection between Menopause and Osteoporosis
1940

Postmenopausal & Senile Osteoporosis Clearly Distinguished
1980s

Injectable calcitonin approved for treatment
1984
Drug Development (cont.)

CEE (Premarin®) Labeling revised to indicate for treatment (early 1990s)

Miacalcin Nasal Spray® (calcitonin) Approved for treatment 1995

Alendronate (Fosamax®) Approved for prevention and treatment 1995

Raloxifene (Evista®) Approved for prevention and treatment 1997

Risedronate (Actonel®) Approved for prevention and treatment 1998

Drug Development (cont.)

CEE (Premarin®) Package labeling revised to indicate for prevention 2000

The first once weekly bisphosphonate approved 2000

Teriparatide (Forteo®) Approved for the prevention and treatment of fracture in patients at high risk 2002

FDA approves new labeling for estrogens due to WHI 2003

Ibandronate (Boniva®) Approved for prevention and treatment 2003 marketed 2005

Evaluation of Drug Therapy Effectiveness

- Effect on bone density
- Effect on fracture incidence
Fractures are the key endpoint of any clinical trial of therapy for osteoporosis.

**Estrogen Replacement Therapy (ERT) and Hormone Replacement Therapy (HRT)**

**ERT/HRT**

Indication (relative to osteoporosis):
- Prevention of osteoporosis
ERT/HRT

Mechanism of Action in Osteoporosis
- Inhibits bone resorption
- Estrogen receptors are located in osteoclasts & osteoblasts
- Estrogen accelerates the death of osteoclasts while prolonging life of osteoblasts
- Increases intestinal calcium absorption and renal calcium conservation

ERT/HRT

Efficacy
- Increases cortical BMD 1-3% & trabecular 2-5%
- Decreases vertebral fractures 34% and hip fractures 25%

Risks & Benefits of HRT in Healthy Postmenopausal Women (Women’s Health Initiative)

Patient Population: 16,608 postmenopausal women aged 50-79 y with intact uterus
- 7.7% had prior cardiovascular disease

Therapy: CEE 0.625mg + medroxyprogesterone acetate 2.5mg/d (PremPro®) or placebo

Results: On May 31, 2002 after a mean of 5.2 y of F/U, data & safety monitoring board recommended stopping the trial because statistic for breast cancer exceeded stopping boundary & global index statistic supported risks exceeding benefits
WHI Results
Among 10,000 users of HRT there were:
- 7 heart attacks
- 8 strokes
- 8 breast cancers
- 8 blood clots
- 6 colon cancers
- 5 hip fractures

20 extra adverse outcomes/yr for every 10,000 users

WHI Results
Among 10,000 users of HRT there were:
- 7 heart attacks
- 8 strokes
- 8 breast cancers
- 8 blood clots
- 6 colon cancers
- 5 hip fractures

20 extra adverse outcomes/yr for every 10,000 users

WHI Results
Among 10,000 users of HRT there were:
- 8 strokes
- 8 breast cancers
- 8 blood clots
- 6 colon cancers
- 5 hip fractures

20 extra adverse outcomes/yr for every 10,000 users
WHI Results
Among 10,000 users of HRT there were:
- +7 heart attacks
- +8 strokes
- +8 breast cancers
- +8 blood clots
- -6 colon cancers
- -5 hip fractures

20 extra adverse outcomes/yr for every 10,000 users

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**WHI Results**

Among 10,000 users of HRT there were:

- + 7 heart attacks
- + 8 strokes
- + 8 breast cancers
- + 8 blood clots
- - 6 colon cancers
- - 5 hip fractures

20 extra adverse outcomes/yr for every 10,000 users

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**WHI: Study Limitations**

- The trial tested only one drug regimen
  - Lower doses?
  - Other formulations?
- The trial does not distinguish the effects of estrogen from progestin
- Only studied a small group of women in their early 50s who were recently menopausal
WHI: Recommendations

- Estrogen & progestin therapy should not be continued or started to prevent heart disease
- Short term use for managing menopausal symptoms?
  - This use was not specifically addressed
  - Results suggest that use < 1 yr has risks for coronary heart disease & thromboembolic disease
  - Must balance severity of symptoms with small absolute risks
- Osteoporosis prevention?
  - Must balance benefits with small absolute risks
  - Alternate treatments are available

Menopausal Hormone Replacement Therapy & Risk of Ovarian Cancer

*JAMA* 2002;288:334-341

- Patient Population: 44,241 postmenopausal women followed about 20 years
- Therapy: ERT or HRT
- Results:
  - Women on ERT for 10-19 yr were twice as likely to develop ovarian cancer compared to women not using hormones
  - Women in ERT for > 20 yr were three times as likely to develop ovarian cancer

ERT / HRT

What to do?
**Current Recommendations**

- **US Preventive Services Task Force**  
  - Recommends against the routine use of combined estrogen & progestin for the prevention of chronic conditions

- **Am College of Ob Gyns & N Am Menopause Society**  
  - Recommend caution in using HRT solely to prevent osteoporosis & suggest alternative therapies should be considered

- **Labeling update for estrogen products (Wyeth):**  
  - Women taking estrogen only for osteoporosis prevention should consider alternative therapies  
  - Take HRT for shortest time possible at lowest dose

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The argument against using postmenopausal hormone therapy for the prevention of chronic diseases is not that the likelihood of harm is high, but that the potential harm outweighs the potential benefit.

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**Effect of Discontinuation of Estrogen, Calcitriol & the Combo on BMD & Bone Markers**  
*J Clin Endocrinol Metab 2002;87:4914-23*

- **Patient Population:** 489 women (mean age 72) randomized to receive 3 yr course of HRT, calcitriol or combo. Subset of 178 observed for 2 yr following D/C of tx

- **Results:**  
  - Spine BMD increased 6% on HRT, 2/3 of gain was lost during 2 yr off HRT  
  - Femoral neck BMD increased 4% on HRT, 2/3 lost during 2 yr off HRT  
  - At each site, greatest decrease in BMD occurred during 1st yr off HRT
Natural Products

- Compounded dosage forms
- Food sources

Bioidentical Hormone Replacement Therapy

- Contain hormones identical to endogenous hormones (estradiol, estriol, estrone, progesterone & testosterone)
- Usually plant-based – extracted & derived from soy or yams
- Commonly used form is micronized triple estrogen (Tri-Est®) with micronized progesterone

Limitations

- Lack of well designed studies to evaluate these products. Risks & benefits, especially with long-term use, remain uncertain
- Specifically, ability to prevent osteoporosis not sufficiently studied
**Common Misconceptions**

- Natural hormones have no potential for risks or adverse effects.
- Natural hormones are obtained directly from plants with little or no processing.

**Transdermal Progesterone Cream for Vasomotor Symptoms & Postmenopausal Bone Loss**

*Obstet Gynecol* 1999;94:225-8

- **Patient Population:** 102 women within 5 years of menopause.
- **Therapy:** Placebo OR progesterone cream (Pro-Gest®) 20mg once daily (1/4 tsp). All patients receive multivitamin + calcium 1200 mg/d.
- **Results:** At one year, effects on BMD were not significantly different from placebo.

**Dioscorea Villosa (Wild Yam) Creams**

- Widely advertised as a source of natural progesterone.
- **CONCERN:**
  - Wild yam is not converted to progesterone in the body as often as claimed.
  - These creams do not contain progesterone unless a small variable amount of pharmaceutical-grade progesterone has been added.
  - Lack of information about the effectiveness or long-term safety of natural progesterone products.
**Phytoestrogens**
*(Plant Estrogens)*

- Weak estrogenic effect in the body
- Seem to mimic the action of estrogen and in other tissues they seem to block the action of estrogen

**Classification of Phytoestrogens**

- **Isoflavonoids**
  - Isoflavones
    - Over 1,000 types
    - Genistein & daidzein have highest estrogenic properties
  - Coumestans
- **Lignans**
- **Others**
  - Black cohosh
  - Red clover

**Isoflavones**

- Antioxidant activity
- Weak plant versions of estrogen
- Major source = soy beans & red clover
- Bind to estrogen receptors 100 to 1,000 times weaker than estradiol
**Isoflavones**

- **Dosage:** Not well defined. Most studies used soy isoflavones 80 mg/day

- **Food Sources:**
  - Soy flour: ¼ cup = 44 mg
  - Soy milk: 1 cup = 20 mg
  - Uncooked tofu: 4 oz = 38 mg

- **Commercial Products:**
  - One-A-Day Bone Strength = isoflavones 10 mg, calcium 500 mg & vitamin D 100 IU
  - Caltrate 600 + Soy = isoflavones 25 mg, calcium 600 mg & vitamin D 200 IU

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**Ipriflavone in the Treatment of Postmenopausal Osteoporosis**

- **Design:** Prospective, randomized, double-blind, placebo-controlled 4 yr study

- **Patient Population:** 474 postmenopausal Caucasian women, 45 – 75 yo, with BMD < 0.86 g/cm²

- **Therapy:** Randomly assigned to ipriflavone 200 mg tid or placebo; all received calcium 500 mg

- **Results:**
  - No change in annual % change from baseline in BMD at any site measured
  - No difference in biochemical markers
  - No difference in number of new vertebral fractures

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**Effect of Soy Protein Containing Isoflavones on Cognitive Function, BMD, and Plasma Lipids in Postmenopausal Women**

- **Patient Population:** 175 late menopausal women, mean of 18 years after onset of menopause

- **Therapy:** soy protein supplements (25.6 gm/day) containing 99 mg of isoflavones vs milk protein

- **Results:** 1 yr comparison with baseline values, no significant differences were found in either group in cognition, lipid levels or BMD

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**Soy Isoflavones and Bone Loss**
- Not well-studied in Caucasian women
  - No large scale, well-controlled studies
- Too early to make specific health claims for soy
- In theory, could competitively inhibit effects of ERT
- Question: should these women be given progesterone?

**Bisphosphonates**
- Alendronate (Fosamax®)
- Risedronate (Actonel®)
- Ibandronate (Boniva®)
**Bisphosphonates**

**Mechanism of Action**
- Interferes with activity of osteoclasts
  - Reduces amount of bone resorbed
  - Results in fewer & shallower resorption sites
  - Increases bone mineralization
- Resulting increases in BMD due to more complete mineralization, not increased synthesis of bone

**Bisphosphonates**

**Pharmacokinetics**
- Once absorbed, about 50% is rapidly bound to active bone remodeling sites
  - Most retained in trabecular bone
- Estimated half-life is similar to bone turnover (1-10 yr)
- Amount in skeleton gradually increases over time
  - Predicted max amt in bone after 10 y of 70 mg/wk would be 75 mg alendronate
- About ½ the alendronate in bone is removed within 3 y of discontinuation

**Bisphosphonates**

**Dosing Intervals**
- Long half-life of residence on bone surface
- Increased dosing convenience
- Increased patient acceptance/compliance
- Reduced potential for upper GI ADRs
**Bisphosphonates**

**Administration Issues**
- Poor oral absorption
  - Only 1–5% is absorbed
  - Reduced further with the presence of food or calcium
    - Less than 90% with food
    - Less than 60% with coffee or orange juice
- GI irritation
  - May cause local irritation of the upper GI mucosa if not taken precisely as directed

**Administration Requirements**
- Take with a full glass of water in morning
- Do NOT eat or drink anything for at least 30 minutes after taking (Ibandronate: 60 minutes)
- Do NOT lie down for at least 30 minutes after taking and until after eating (Ibandronate: 60 minutes)

Same for all dosage forms

**Adverse Effects**
- GI upset
  - Nausea
  - Dyspepsia
  - Abdominal pain
Upper Gastrointestinal Tract Safety Profile of Alendronate

- **Patient Population:** FIT trial (3.8 years)
- **Measurements:**
  - Patient interview every 3 months
  - Review of hospital records & endoscopy reports
- **Results:**
  - Overall incidence of upper GI tract events: 47.5% with alendronate & 46.2% with placebo
  - Dyspepsia was most common event: 18.2% with alendronate & 19.1% with placebo
  - No significant difference in incidence of serious events
  - Alendronate not associated with significant increase in events among women at increased risk (age >75; previous upper GI tract diseases; NSAIDs)

Oral Bisphosphonates & Upper GI Tract Problems: What is the Evidence?

- **Methods:** Reviewed, rated & summarized published info on upper GI tract safety of bisphosphonates using principles of evidence-based medicine
- **Results:**
  - Randomized controlled trials suggest little or no increase in risk of upper GI tract problems if administered properly
  - Many ADRs reported may reflect high background incidence of upper GI complaints and increased sensitivity to detection rather than causal effect to therapy

Bisphosphonates

**Adverse Effects**

- **GI upset**
  - All oral bisphosphonates can produce GI adverse effect
  - The background incidence of GI symptoms in older women is high, even in the absence of medications
  - In clinical trials, patients treated with either alendronate or risedronate had no greater incidence of GI AEs than did the controls
  - In clinical practice, it is not obvious that there is a meaningful difference between alendronate & risedronate
Bisphosphonates

Adverse Effects

- Severe bone, joint and muscle pain
  - Described as severe, extreme, disabling pain
  - Bones, joints and muscles throughout were affected
  - Many unable to perform usual activities, some required bed rest, walkers or crutches

Bisphosphonates

Adverse Effects

- Severe bone, joint and muscle pain
  - Onset ranged from same day to 52 months.
  - Average was 14 days from therapy start
  - Most experienced relief after D/C – some had immediate improvements, others more gradual

Bisphosphonate Associated Severe Bone, Joint and Muscle Pain

- Alendronate
  - From Sept 95 to Nov 02, 118 reports
  - 74% at 10 mg daily, 18% at 70 mg weekly
- Risedronate
  - From Sept 98 to June 03, 6 reports
  - Details not published
- Serious bone, joint and/or muscle pain that begins shortly after bisphosphonate initiation should be reported
Bisphosphonates

Adverse Effects

- Osteonecrosis of the jaw (ONJ)
  - Reports of ONJ primarily in cancer patients receiving chronic IV bisphosphonates
    - These IV agents are indicated for Paget’s disease, hypercalcemia associated with malignancy, metastatic bone lesions and multiple myeloma.
    - Pamidronate (Aredia®)
    - Zoledronic acid (Zometa®)
  - Labeling for oral & IV agents now includes this class osteonecrosis risk

Osteonecrosis of the Jaw

- Jaw bone is particularly vulnerable because of tooth and gum susceptibility to infection
- The death of bone resulting in collapse of structural architecture
- Leads to bone pain, loss of function and destruction
- S/S: gum pain, swelling, poor healing, loosening of teeth, drainage and exposed bone
- Range of severity from asymptomatic to need for partial jaw removal

Bisphosphonate Associated ONJ

- FDA Adverse Event Reports
  - 139 cases of ONJ from marketing approval dates until May 2004
    - 34% pamidronate (Aredia®)
    - 24% zoledronic acid (Zometa®)
    - 42% receiving both agents
    - 8.6% alendronate (Fosamax®)
    - 1 case risedronate (Actonel®)
  - Majority occurred after a dental extraction; some occurred spontaneously
Bisphosphonate Associated ONJ

Recommendations
- Maintain excellent oral hygiene and have routine dental exams
- Dental professionals need to give careful attention to avoid soft tissue injury during routine dental cleanings
- Delay bisphosphonate therapy, if possible, to complete dental procedures with poor prognosis
- Avoid elective jaw procedures

Bisphosphonates

Adverse Effects

Ocular side effects
- Incidence is rare
- First reported with IV pamidronate (Aredia®)
- Other agents implicated include alendronate & risedronate
- Ocular problems include nonspecific conjunctivitis, scleritis & uveitis
- Onset within 6 to 48 hours after administration

Bisphosphonates and Ocular Side Effects

Nonspecific conjunctivitis
- Most common ocular effect reported
- S/S: blurred vision, mucus discharge
- Typically no treatment was needed & symptoms diminished over time with continued bisphosphonate treatment
Bisphosphonates and Ocular Side Effects

- Scleritis
  - Required D/C of pamidronate for resolution

- Uveitis
  - The most serious condition
  - If left untreated can seriously compromise vision
  - Some cases required hospitalization

Bisphosphonates and Ocular Side Effects

- Advise patients to report any symptoms of possible ocular problems such as ocular pain, blurred or diminished vision or photophobia
- Should be referred to ophthalmologist

Bisphosphonates

Adverse Effects

- CNS toxicity
  - Auditory hallucinations, visual disturbances, amnesia, confusion, depression
  - Very rare; case reports with pamidronate, etidronate & alendronate
  - Mechanism unknown
    » Does not appear to be secondary to hypocalcemia
Bisphosphonates

Considerations

- Use with caution in patients with active GI problems including dysphagia, symptomatic esophageal disease, gastritis, ulcers
- Risedronate does not have contraindications related to upper-GI disorders. Has general precaution that bisphosphonates may cause upper-GI complications
- Concurrent therapy with ASA or any NSAID compounds increase the likelihood of esophageal ulceration and will require close monitoring

Bisphosphonates

Considerations

- Safety and efficacy have not been established in pediatrics or pregnant women
- Category C

Bisphosphonates

Considerations

- Ensure patients maintain dietary and supplemental calcium intake

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**Bisphosphonates**

Patient Monitoring/Education

- Review medication administration procedure
- Review signs and symptoms suggestive of esophageal irritation
  - Difficulty swallowing
  - New or worsening heartburn
  - Retrosternal pain
- Discontinue alendronate and seek medical attention if these symptoms occur

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**Alendronate**

**Indication**

- For the prevention and treatment of osteoporosis in postmenopausal women
- For treating glucocorticoid-induced osteoporosis in men and women
- For treatment to increase bone mass in men with osteoporosis

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**Alendronate**

**Efficacy**

- Increased BMD at lumbar spine 5-10%, femoral neck 2.3-4.8%
- Reduced fracture rate at spine & wrist by 47% and hip by 51% in patients with osteoporosis
Randomized Trial of Effect of Alendronate on Risk of Fracture in Women with Existing Vertebral Fractures

- **Patient Population:** 2,027 postmenopausal women with pre-existing vertebral fracture
- **Therapy:** Placebo OR alendronate 5 mg/d for 2 years followed by 10 mg/d for 1 year
  All patients with dietary calcium < 1,000 mg/d received 500 mg/d and vitamin D 250 IU/d
- **Results:** Reduced risk of new vertebral fractures by 47%, hip fracture by 51% and wrist fracture by 47%

Alendronate Reduces Risk of Multiple Symptomatic Fractures: Results from FIT

- **Patient Population:** Subset of women from FIT
- **Therapy:** Placebo or alendronate (5 mg/d x 2 yr; 10 mg/d x 1 year) Avg f/u = 4.3 yr
- **Results:**
  - Over 3-4 years alendronate reduced occurrence rate of all symptomatic fractures by 33% and vertebral fractures by 67%
  - Benefit was seen within a few months of starting treatment

Alendronate

**How Supplied**
- Daily dosing
  » 5 mg tablet
  » 10 mg tablet
- Weekly dosing
  » 35 mg tablet
  » 70 mg tablet
  » 70 mg oral solution
  » 70 mg alendronate / 2,800 IU vitamin D
  ■ Fosamax Plus D®
**Alendronate**

**Recommended Dose**
- For the treatment of osteoporosis in postmenopausal women and men = 10 mg once daily or 70 mg weekly
- For the prevention of osteoporosis in postmenopausal women = 5 mg once daily or 35 mg weekly
- For the treatment of glucocorticoid-induced osteoporosis = 5 mg once daily or 35 mg weekly

**Contraindications**
- Severe renal insufficiency (creatinine clearance <35 ml/min)
- Abnormalities of the esophagus that delay esophageal emptying
- Hypocalcemia
- Inability to stand or sit upright for at least 30 minutes
- Hypersensitivity

**Drug/Drug Interactions**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranitidine</td>
<td>IV ranitidine doubled alendronate bioavailability. Unknown clinical significance.</td>
</tr>
<tr>
<td>Calcium supplements and antacids</td>
<td>Products containing calcium and other multivalent compounds interfere with alendronate absorption.</td>
</tr>
<tr>
<td>All medications</td>
<td>Wait at least 30 minutes after taking alendronate before taking any other drug due to absorption interference.</td>
</tr>
</tbody>
</table>
**Fosamax Plus D®**

- Alendronate 70 mg / vitamin D 2,800 IU
  - 10 mg/day + 400 IU/day = once-weekly dose
- Indications
  - Treatment in postmenopausal women
  - Treatment in men
- Dosage & Administration
  - 1 tablet once weekly
  - Same administration procedure
- Adverse Effects
  - Safety profile similar to Fosamax® 70 mg

**Risedronate**

**Indication**
- For the prevention and treatment of osteoporosis in postmenopausal women
- For the prevention and treatment of glucocorticoid-induced osteoporosis

**Risedronate**

**Efficacy**
- Increased BMD at lumbar spine 5.4%; femoral neck 1.6% & trochanter 3.3%
- Reduced fracture rate at spine by 41% and non vertebral fractures by 39% in patients with osteoporosis
Effects of Risedronate Treatment on Vertebral and Nonvertebral Fractures in Women with Postmenopausal Osteoporosis

**JAMA** 1999;282:1344-52

- **Patient Population:** 2,458 postmenopausal women with radiographic evidence of at least 2 vertebral fractures OR 1 vertebral fracture + low lumbar BMD
- **Therapy:** Placebo OR risedronate 2.5 or 5 mg/d. All patients received calcium 1,000 mg/d + vitamin D if level < 40 nmol/L
- **Results:** BMD changes: lumbar spine increased 5.4% and trochanter 3.3%
  - Decreased vertebral fractures by 41% and nonvertebral fracture by 39%

Risedronate

**Recommended Dose**

- 5 mg once daily or 35 mg weekly for all osteoporosis related indications

Actonel® with Calcium

- Co-packaged product containing risedronate 35 mg and calcium carbonate 1,250 mg (500 mg elemental calcium)
- **Indications**
  - Treatment and prevention of osteoporosis in postmenopausal women
- **Dosage and Administration**
  - Risedronate 35 mg on day 1
  - Calcium carbonate 1,250 mg on days 2 through 7
- **Adverse Effects**
  - Safety profile similar to individual agents
**Ibandronate**

**Indication**
- For the prevention and treatment of osteoporosis in postmenopausal women

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**Ibandronate**

**Efficacy**
- Increased BMD at lumbar spine 6.5% & at the hip by 3.4% after 3 yr
- Reduced fracture rate at spine by 52% after 3 yr. No statistically significant reduction in nonvertebral fractures

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**Effects of Oral Ibandronate Administered Daily or Intermittently on Fracture Risk in Postmenopausal Osteoporosis**

*J Bone Miner Res 2004;19:1241-1249*

- **Patient Population:** 2,946 postmenopausal women with osteoporosis
- **Therapy:** placebo or oral ibandronate either 2.5 mg daily or 20 mg qod for 12 doses every 3 months
- **Results:**
  - After 3 years, rate of new vertebral fractures was significantly reduced with daily (4.5%) and intermittent ibandronate (4.9%) relative to placebo (9.6%)
  - No statistically significant reduction in nonvertebral fractures
Ibandronate

Recommended Dose
– 150 mg once monthly
– 2.5 mg once daily

The compelling hip fracture data with the bisphosphonates is often justification for selecting these agents.

Alendronate Use
J Managed Care Pharm. 1998; 4:488-492

- Patient Population: 812 women, mean age 69
- Study Design: Women were interviewed an average of 8 months after starting alendronate.
- Results: During the course of treatment—
  - 56% did not comply with at least 1 instruction for taking the drug
  - 52% disregarded rules on consumption of food, liquids & other meds
  - 33% reported it caused upper GI problems
  - 30% reported discontinuing the drug within the 1st 6 months
- Based on refill records—
  - 35% discontinued the drug

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Alendronate Use

J Managed Care Pharm. 1998; 4:488-492

- Interesting point
  - In clinical trials alendronate is well tolerated with few ADRs significantly different from placebo. But outside the clinical trial setting, as reported here, there are increased reports of ADRs.
  - As part of routine healthcare, women do not receive the education, encouragement and support given to research subjects and may not be as highly motivated. As a result, improper use and adverse gastrointestinal effects are common.

Zoledronic Acid (Zometa®)

- Most potent bisphosphonate to be used in clinical trials
- Current indications:
  - Hypercalcemia of malignancy
  - Multiple myeloma & bone metastases of solid tumors (in addition to standard antineoplastic therapy)
- Dosing for current indications:
  - Max of 4 mg infused over no less than 15 min
  - May repeat after 7 days
- A deterioration in renal function requires careful monitoring

Intravenous Zoledronic Acid in Postmenopausal Women with Low BMD


- Patient Population: 351 postmenopausal women with low BMD
- Therapy: Placebo or IV zoledronic acid 0.25 mg, 0.5 mg or 1 mg @ 3 mo intervals. One group received 4 mg once & another 2 mg q6 mo. All received calcium (1 gm/day)
- Results:
  - Similar increases in BMD in all study groups
  - Results comparable to those with oral daily dosing with bisphosphonates
  - ADRs: most common were musculoskeletal pain, nausea and fever - generally rated mild
  - Suggest that an annual infusion of zoledronic acid might be an effective therapy
Salmon-Calcitonin

- Nasal: Miacalcin®
  - Fortical®
- Injection: (various)

Calcitonin

Indication
- For the treatment of postmenopausal osteoporosis in females greater than 5 years post menopause
Calcitonin

Mechanism of Action
- Antiresorptive agent
- Naturally occurring hormone
- Produced by the thyroid
- Inhibits production & activity of osteoclasts

Calcitonin (Miacalcin®)
- Increased BMD at the spine 3%
- Reduced vertebral fractures 36%
- Has not been studied in nonvertebral fractures

A Randomized Trial in Nasal Spray Salmon Calcitonin in Postmenopausal Women with Established Osteoporosis: the Prevent Recurrence of Osteoporotic Fracture Study (PROOF)

- Patient Population: 1,255 women with at least 1 but not > 5 vertebral fractures
- Therapy: Randomized to receive Miacalcin® 100, 200, 400 IU or placebo daily. All received 1,000 mg calcium + 400 IU vitamin D
- Results: 36% reduction in risk of new vertebral fractures with 200 IU daily
Miacalcin®: Questions Remain

- Poor trial design & execution
- Why the lack of a dose response effect?
- What is the impact on nonvertebral fractures?

Calcitonin

- Analgesic effect
  - Not well supported by medical literature
  - Mechanism of action unclear
    » Increase in blood CSF β-endorphins
    » Direct action on CNS
  - Has been used for pain management of acute vertebral compression fractures
  - Effect may begin within few weeks of therapy

Calcitonin

- Analgesic effect
  - Considerations
    » May be tried if patient does not respond to traditional pain management
    » Should be continued only if patient has documented response
    » Should not preclude starting first-line osteoporosis therapy in these high risk patients
How Supplied

- Miacalcin®
  - 2 ml bottles containing 14 doses
  - Each activation releases calcitonin 200 IU in 0.09 ml of solution
- Fortical®
  - 3.7 ml bottles containing 30 doses
  - Each activation releases calcitonin 200 IU in 0.09 ml of solution

Calcitonin

Contraindications
- Allergy to calcitonin

Drug/Drug Interactions
- None known to date
**Calcitonin**

Dosage and Administration

- 200 IU spray to one nostril daily
  - Before first dose, necessary to activate the pump
  - Place nozzle into nostril with head in upright position and depress the pump
  - Alternate nostrils daily
  - May be administered at any time during the day

**Calcitonin**

Adverse Effects

- Rhinitis
- Nasal symptoms = nasal crusts, irritation, redness, sores, nose bleed
- Back pain
- Arthralgia
- Headache

**Calcitonin**

Considerations

- Provision of adequate calcium and vitamin D in the diet or as supplements is recommended in conjunction with calcitonin
Calcitonin

Patient Monitoring/Education

- Patient should receive a nasal examination prior to the start of therapy and at any time nasal complaints occur.

Calcitonin

Patient Monitoring/Education

- Review medication administration procedure.
- It is unnecessary to inhale the spray as the medication is absorbed through the nasal mucosa.

Calcitonin

Patient Monitoring/Education

- Store unopened bottles of the nasal product in the refrigerator. Once the pump has been activated, store at room temperature.
- Unopened or opened bottles of spray left at room temperature for more than 4 weeks should be discarded.

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**Raloxifene**

*Evista®*

**Indication**
- Indicated for the treatment and prevention of osteoporosis in postmenopausal women

**Mechanism of Action**
- Selective estrogen receptor modulator (SERM)
- Actions
  - Prevents bone loss
  - Lowers serum cholesterol levels
  - Inhibits growth of breast cancer
  - Does not stimulate the endometrium

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### Raloxifene

**Efficacy**
- Increases BMD in femoral neck by 2.1% and in spine by 2.6%
- Reduces rate of vertebral fractures about 40%
- No apparent effect on nonvertebral fractures

### Reduction of Vertebral Fracture Risk in Postmenopausal Women with Osteoporosis Treated with Raloxifene

**Patient Population:** 7,705 postmenopausal women 31–80 years old with osteoporosis

**Therapy:** Randomized to 60 or 120 mg/d raloxifene OR placebo. All received supplemental calcium + cholecalciferol

**Results:**
- 2–3% increase in spine & hip BMD
- 30% reduction in risk for vertebral fracture with 60 mg; 50% reduction with 120 mg
- No change in risk of nonvertebral fracture

### Effects on Lipid Metabolism & Clotting Factors

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**Raloxifene & Cardiovascular Events in Osteoporotic Postmenopausal Women**

**Patient Population:** Secondary analysis of MORE trial

**Outcome Measures:**
- Cardiovascular events (MI, unstable angina, coronary ischemia)
- Cerebrovascular events (stroke or TIA)

**Results:**
- Raloxifene therapy for 4 yr did not significantly affect risk of CV events in overall cohort but did significantly reduce risk of CV events in subset of women with increased CV risk
- No evidence that raloxifene caused an early increase in risk of CV events

---

**Raloxifene**

**Contraindications**
- Pregnancy
- History of or active thromboembolic events including deep vein thrombosis, pulmonary embolism, retinal vein thrombosis

---

**Raloxifene**

**Drug/Drug Interactions**
- Cholestyramine – coadministration will significantly reduce absorption of raloxifene
- Warfarin – closely monitor PTs and INRs; PT decreased 10% in single-dose studies
- Protein bound drugs (clofibrate, diazepam, ibuprofen, indomethacin, naproxen) – use with caution. Raloxifene is more than 95% bound to plasma proteins
**Raloxifene**

**Dosage and Administration**
- Usual dose is 60 mg once daily without regard to meals

**Adverse Effects**
- Hot flashes
  - Most common in first 6 months
  - 7% incidence
- Leg cramps
  - Generally mild
  - 4% incidence
- Venous thromboembolic events
  - Greatest risk in first 4 months
  - 3 fold increase incidence

**Uterine cancer**
- Preliminary evidence suggests no increased risk

**Breast cancer**
- MORE results: among women taking raloxifene, incidence of all types of breast cancer decreases by 62% & incidence of invasive breast cancer decreases by 72%
Continuing Outcomes Relevant to Evista:
Breast Cancer Incidence in Postmenopausal Osteoporotic Women in a Randomized Trial of Raloxifene

*J Natl Cancer Inst* 2004; 96:1751-61

**Patient Population:** 5,000 participants from the MORE trial received an additional 4 yr of raloxifene or placebo

**Results:**
- 59% reduction in risk of invasive breast cancer
- 66% reduction in risk of invasive estrogen-positive breast cancer

**Raloxifene Considerations**

- Raloxifene is of no benefit for hot flashes. Studies show it may actually increase the incidence of hot flashes
- Safety and efficacy have not been evaluated in men

**Raloxifene**

Considerations

- Supplemental calcium should be added to the diet if daily intake is inadequate

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**Raloxifene**

**Patient Monitoring/Education**

- Review possible side effects and what to do if they occur.
  - Unexplained uterine bleeding should be reported to physician
- Review signs and symptoms of possible venous thrombosis:
  - Pain in the calves or leg swelling
  - Sudden chest pain, shortness of breath or coughing blood
  - Changes in vision

The occurrence of any of these should be reported to physician immediately and patients should stop therapy immediately.

---

**Raloxifene**

**Patient Monitoring/Education**

- Assess adherence with calcium intake plan
- Review what to do in the event of prolonged immobilization.
  - Discontinue drug at least 72 hours prior to and during prolonged immobilization (post-surgical recovery, prolonged bed rest)
  - Avoid prolonged restrictions of movement such as during travel

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**Formation-Stimulating Drugs**

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**Drug Therapy for Osteoporosis**

- Antiresorptive Agents
- Formation-Stimulating Drugs

**Teriparatide**

*Forteo®*

**Indication**

- For the treatment of postmenopausal women with osteoporosis who are at high risk for fracture
- To increase bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fracture
Teriparatide
Mechanism of Action
- Recombinant human parathyroid hormone (PTH)
  - Identical sequence to 34 N-terminal amino acids of 84-amino acid PTH
- Actions of PTH:
  - Regulation of bone metabolism
  - Regulation of renal tubular resorption of calcium & phosphate
  - Regulation of intestinal calcium absorption

Calcium Homeostasis
- Serum calcium stimulates parathyroid glands
- Parathyroid hormone promotes activation of vitamin D
- Increases calcium reabsorption in renal tubule
- Calcium absorption in GI tract
- Calcium release

Teriparatide
Mechanism of Action
- Skeletal effects depend upon pattern of systemic exposure
- Intermittent low-dose
  - Increases osteoblastic activity
  - Increases BMD and reestablishes connectivity

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Teriparatide

Efficacy
- Increased BMD at lumbar spine 9% and femoral neck 3%
- Reduced fracture rate at the spine by 65% and nonvertebral fractures by 53%

Effect of Parathyroid Hormone on Fractures & BMD in Postmenopausal Women with Osteoporosis


- Patient Population: 1,637 postmenopausal women with prior vertebral fractures
- Therapy: Randomly received parathyroid hormone (1-34) 20 mcg or 40 mcg OR placebo administered subcutaneously daily by the women for about 18 months. All received calcium & vit D
- Results:
  - Occurrence of new vertebral fractures: 14% on placebo, 5% on 20 mcg & 4% on 40 mcg
  - Occurrence of new nonvertebral fractures: 6% on placebo, 3% on 20 & 40 mcg
  - Compared to placebo, 20 & 40 mcg increased BMD by 9% & 13% in lumbar spine and 7% & 6% in femoral neck

Teriparatide

Drug Interactions
- None known
- None anticipated
**Teriparatide**

**Dosage and Administration**
- 20 mcg once daily administered as subcutaneous injection into thigh or abdominal wall
- Take at any time of the day
- Supplied as a pre-assembled disposable pen device with 28 doses
- After 28 days discard the pen even if it still contains unused solution
- Use for longer than 2 yrs not recommended due to lack of safety & efficacy data

**Teriparatide**

- Store under refrigeration at all times. Time out of refrigerator should be minimized
- Dose may be delivered immediately following removal from refrigerator
- After the 2 year point, patient should be started on antiresorptive treatment to maintain gains in BMD

**Teriparatide**

**Adverse Effects**
- Dizziness
- Leg cramps
- Transient orthostatic hypotension
  - Infrequent event seen within first several doses
  - Begins within 4 hr of dosing and then resolves
- Transient increases serum calcium
Teriparatide

Adverse Effects

- Increased incidence of osteosarcoma in rats
  - Black Box Warning
    » Do not use in patients with:
      ■ Paget’s disease
      ■ Unexplained elevation of alkaline phosphatase
      ■ Open epiphyses
      ■ Prior skeletal radiation

Teriparatide

FDA Requirements

- RPh must give patients FDA-approved information sheet each time drug is dispensed
- Eli Lilly must fund 10-year study
- Can not advertise directly to consumers & must restrict free samples
- Eli Lilly must do physician education program

Teriparatide

Patient Monitoring/Education

- Review possible side effects & what to do if they occur
  » Orthostatic hypotension
    ■ Initial admin should occur where patient can sit or lie down
  » Hypercalcemia
    ■ Notify health care provider if persistent s/s
    - N&V
    - Constipation
    - Lethargy
**Teriparatide**

- **Patient Monitoring/Education**
  - Review drug administration
    - Use new needle for each injection
    - Prime pen prior to each dose
    - Store under refrigeration
    - Discard pen after 28 days
    - Administer at same time each day
  - Ensure adequate calcium & vitamin D intake
  - Do NOT store with needle attached
    - Solution may leak from cartridge and permit air bubbles to form in cartridge

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**Sodium Fluoride**

*Major Action* = increases number of osteoblasts

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**Sodium Fluoride**

*Concerns*
- The bone formed is poor quality and more fragile than normal bone.
- Primarily affects trabecular bone increasing BMD and appears to have the opposite effect on cortical bone mass.
- Adverse experiences with sodium fluoride are numerous.
  - Gastrointestinal side effects (epigastic pain, nausea and vomiting)
  - Lower extremity pain syndrome
Sodium Fluoride

Possible strategies for improvement —

- Lower the dose
- Use a slow-release preparation
- Addition of calcium supplements
- Cyclic/intermittent dosing regimen
- Addition of estrogen

The Effect of Sodium Monofluorophosphate Plus Calcium on Vertebral Fracture Rate in Postmenopausal Women with Moderate Osteoporosis


**Patient Population:** 200 postmenopausal women with osteoporosis

**Therapy:**
- Sodium fluoride 20 mg/d + 1,000 mg calcium OR
- 1,000 mg calcium

**Results:**
- 10% increase in BMD of spine was found for fluoride and calcium
- 7.6% decrease in vertebral fractures

Sodium Fluoride

- The use of sodium fluoride is considered experimental because of insufficient data on long-term use, effective dosage, and duration of therapy
Other Therapy Considerations

- Thiazide diuretics
- HMG-CoA reductase inhibitors

Thiazide Diuretics

- Thiazide diuretics promote a decrease in renal calcium excretion and thus reduce bone resorption
- Recent population-based case controlled studies have shown a reduction in risk of hip fracture when thiazide was used for more than 6 years

Low-Dose HCTZ & Preservation of BMD in Older Adults


- **Patient Population:** 320 normotensive adults ages 60–79 with normal BMD
- **Therapy:** HCTZ 12.5 mg/d; 25 mg/d OR placebo
- **Results:** After 3 years, BMD at hip
  - Placebo: - 0.3%
  - HCTZ 12.5 mg: + 0.5%
  - HCTZ 25 mg: + 0.6%
  - No significant difference in BMD at spine or total body BMD
HMG-CoA Reductase Inhibitors

- Several observational and animal studies suggest they may increase BMD
- Proposed MOA:
  - Bisphosphonates & statins inhibit synthesis of mevalonate
  - Mevalonate is a precursor in synthesis of cholesterol & certain compounds in regulation of osteoclast activity
  - Statins may increase bone formation

An Overview of the Pathway of Cholesterol Biosynthesis

Acetyl CoA → HMG-CoA → Mevalonate → Farnesyl pyrophosphate → Squalene → Cholesterol

Statin Use, BMD and Fracture Risk

- *Patient Population:* Case-control evaluation of 1,375 women from Australia; 573 with fractures & 802 without
- *Results:*
  - Statin use associated with 3% greater adjusted BMD at femoral neck. BMD at spine & whole body greater but not statistically significant
  - 60% reduction in fracture risk associated with statin use
More Research Needed

- All the studies to date are observational
- Unknowns:
  - Any differences between specific agents in the class
  - Optimal dose & duration
- Need randomized controlled clinical trials

Summary

- ERT/HRT
  - Prevention indication
  - Guidelines suggest it should not be used to prevent chronic disease
- Alendronate, Risedronate, Ibandronate
  - Prevention & treatment indication
  - Decreases fractures
    - Vertebral – Alendronate, Risedronate, Ibandronate
    - Nonvertebral – Alendronate, Risedronate
  - Generally considered first line therapy

Summary

- Calcitonin
  - Treatment indication
  - Vertebral fracture data only
  - Safe but somewhat less effective
- Raloxifene
  - Prevention & treatment indication
  - Decreases vertebral fractures; no effect on nonvertebral fractures
  - Role in therapy unclear
- Teriparatide
  - Treatment indication
  - Decreases vertebral & nonvertebral fractures
  - Use limited to high risk patients
Bisphosphonates

- Produce the greatest increases in BMD of all available antiresorptive therapies
- Rapidly decreases risk of vertebral fractures
- The only approved antiresorptive agents that have demonstrated antifracture efficacy at the hip are Alendronate and Risedronate

Case: Postmenopausal Woman

- TR, a 67-year old female in generally good health, is concerned about osteoporosis due to a family history of hip fracture in her grandmother and kyphosis in her mother
- She has not suffered any fractures and has no history of secondary causes of bone loss
- TR’s T-scores
  - Spine: -2.9
  - Hip: -2.7
- TR was started on calcium, vitamin D and risedronate 35 mg weekly

Questions for Case

- How do you interpret the bone density findings in this case?
- What are your treatment recommendations?
**Approach to Treatment**

- **AACE Guidelines**: Women who may benefit from pharmacologic treatment
  - Women with BMD T-scores ≤ 2.5 & below
  - Women with BMD T-scores ≤ 1.5 & below with risk factors
  - Nonpharmacologic preventive measure were ineffective
- **NOF Guidelines**: Initiate therapy to reduce fracture risk in women with
  - Prior vertebral or hip fracture
  - BMD T-scores ≤ -2 in the absence of risk factors
  - BMD T-scores ≤ -1.5 if other risk factors are present

**Therapeutic Options**

- Calcium, vitamin D and exercise are minimums, but not sufficient
- Patient has no known contraindications to therapies for osteoporosis

**Case Variation**

Q: How would your treatment approach change if TR had a BMD T-score of ≤ 1.5 and a history of compression or fragility fractures?

A: Treatment should be offered, despite BMD, as previous fractures are the strongest predictor of future fractures
Application Exercise #3
Therapy Assessment

Case Presentation
- Toni Baloney is a 76-year old Caucasian female who was started on Alendronate about 2 years ago
- She wants to know if this is working for her
- Mrs. Baloney is in good health and enjoys playing with her grandchildren

Medical History
- Current medical problems
  - Hypertension: well controlled on HCTZ 25 mg
  - Arthritis: occasional knee pain
  - Osteoporosis: diagnosed 2 years ago; T-score = -2.5
- Current medications
  - HCTZ 25 mg once daily
  - OTC ibuprofen 200 mg, 2 tabs prn joint pain
  - Alendronate 70 mg once weekly
  - Via activ® 1 twice daily
Risk Factor Assessment
- Non-smoker
- Non-drinker
- Unknown family history of osteoporosis
- Drinks about 2 cups of coffee every morning and occasionally drinks sweet tea
- Current weight: 135 lb
- No history of fracture

BMD Results
- Mrs. Baloney had central DEXA test about 2 years ago
- T-score = -2.5

According to WHO diagnostic categories, where does Mrs. Baloney’s T-score fall?

- A. Normal
- B. Osteopenia
- C. Osteoporosis
WHO Diagnostic Categories

- Normal = BMD > -1.0 SD of young adult mean
- Osteopenia = BMD > -1 SD but < -2.5 SD below young adult mean
- Osteoporosis = BMD -2.5 SD or more below young adult mean

Is alendronate 70 mg weekly an appropriate drug choice for this patient?

A. Patient does not appear to have any contraindications however she should be on 35 mg weekly
B. This is a good choice for this patient
C. Calcitonin would be a better choice in view of patient's age
D. Teriparatide would be a better choice in view of patient’s T-score

Best Answer

B. This is a good choice for this patient
- Indication: treatment of osteoporosis in postmenopausal woman
- 70 mg weekly is the dose for this indication
- No known contraindications
- Calcitonin is age really has nothing to do with selecting this drug. Considered less effective than bisphosphonates
- Teriparatide is NOT appropriate since this is not a high risk patient
Drug Therapy Assessment

- Administration procedure
- Tolerability (adverse effects)
- Adherence

What key points should you assess regarding the patient’s administration procedure?

A. Wait 60 minutes before eating or lying down
B. Wait 30 minutes before eating or lying down
C. Take with a full glass of water in the morning
D. Do not take with coffee or orange juice

Best Answer

B. Wait 30 minutes before eating or lying down
   - *Ibandronate* = wait 60 minutes
   - *Alendronate and risedronate* = wait 30 minutes
C. Take with a full glass of water in the morning
D. Do not take with coffee or orange juice
If patient complains of GI upset while on bisphosphonate, what additional information do you need?

- Did you have these complaints before starting the drug?
- What do you do when this happens?
- Is it mild, moderate or severe?
- What administration procedure do you follow when taking this drug?

“What do you do during the 30 (or 60) minutes after you take your dose and before you eat?”

Assessing Patient Adherence

- “How many times a month do you think you miss a dose?”
- “What do you do to help you remember your dose?”
- Is anything possibly interfering with drug absorption?
What should the patient do if she missed a dose of her alendronate?

A. No action necessary. Just be sure to take your dose the next week
B. Take 2 tablets the following week
C. Take the dose on the morning after you remember & then return taking 1 tablet once weekly on your original chosen day

Best Answer

C. Take the dose on the morning after you remember & then return taking 1 tablet once weekly on your original chosen day
   - Do not take 2 doses the same day

Summary of Mrs. Baloney’s Experience with Alendronate

- Reports excellent adherence
  - Takes dose on Mondays; written on calendar as reminder
- Consistently follows correct administrative procedure
  - Spends the 30 minutes doing the crossword puzzle in the paper
- Tolerating well; denies GI complaints
General Preventive Strategies

- Physical activity
- Calcium
- Vitamin D

Physical Activity History

Mrs. Baloney’s physical activity consists of doing routine housework and working her garden.

What is your assessment of Mrs. Baloney’s physical activity in terms of bone health?

A. Meets recommendations for her age
B. Needs to start resistance exercise 2-3 times weekly for 30 – 60 minutes
C. Should consult with a professional to design an appropriate physical activity regimen
Best Answer

C. Should consult with a professional to design an appropriate physical activity regimen
   – In view of osteoporosis diagnosis, age and current lack of activity

Calcium Intake Assessment for Mrs. Baloney

- Takes Viactiv® 1 twice daily
- Generally does not eat calcium rich foods

What is Mrs. Baloney’s current daily calcium intake?

A. 400 mg
B. 600 mg
C. 800 mg
D. 1,000 mg
Best Answer

D. 1,000 mg
- Each Viactiv® contains 500 mg elemental calcium as calcium carbonate, 100 IU vitamin D and 40 mcg vitamin K

What is your recommendation regarding Mrs. Baloney’s calcium intake?

A. Increase Viactiv® dose to 1 three times daily
B. Add a MVI
C. Change to a calcium citrate product and take a dose that provides 1,200 mg of elemental calcium daily

Best Answer

C. Change to a calcium citrate product and take a dose that provides 1,200 mg of elemental calcium daily
- In view of patient’s age, calcium citrate is a better choice due to the decrease in GI acidity that comes with age
- Dose needs to be increased to at least 1,200 mg elemental calcium daily
Vitamin D Intake Assessment for Mrs. Baloney

- No longer taking Viactiv®
- May receive some sun exposure while working in the garden but unlikely to produce enough due to age

How much vitamin D should Mrs. Baloney receive on a daily basis?

A. 200 IU  
B. 400 IU  
C. 600 IU  
D. 800 IU

Best Answer

D. 800 IU daily
- NOF recommends that the elderly ingest 800 IU of vitamin D daily
How could Mrs. Baloney meet her vitamin D intake requirement?

A. Drink 8 glasses of milk daily
B. Take 2 multivitamin tablets daily
C. Take a calcium supplement that also contains vitamin D
D. Switch to Fosamax Plus D® and take 1 multivitamin tablet daily

Best Answer

C. Take a calcium supplement that also contains vitamin D

or

D. Switch to Fosamax Plus D® and take 1 multivitamin tablet daily

Fall Prevention Plan

- Essential component for individuals with osteoporosis
- Ask patient about fall history
  - Mrs. Baloney denies falling
Fall Prevention Checklist

- Remove or firmly anchor rugs
- Have good lighting throughout. Do not try to walk in the dark
- Keep electrical and telephone cords away from walking areas
- Equip bathroom, halls and stairways with handrails
- Reduce slipperiness of tub or shower floor
- Adjust seating and bed so easy to get into and out of

Address Mrs. Baloney’s concern

“Is this alendronate working for me?”

Monitoring Response to Therapy

- Response to therapy can be assessed by fracture history and repeat BMD testing
- Although repeat BMD tests are not required in someone on therapy, it may serve as reassurance to the clinician and patient that the therapy has had impact
Monitoring Response to Therapy

- Use the same machine at the same center and test the same site
- Error of precision
  - Changes must exceed about 4% in the spine and 6% in the hip to be considered significant
  - May take medications several years to produce changes of this magnitude
- Do not repeat testing any more often than every 2 years

Interpreting Monitoring Results

- Magnitude of increase in BMD does not correlate directly with fracture protection
  - Fracture protection benefit may be realized before BMD gains are detected
  - In clinical trials, raloxifene & calcitonin produced modest improvements in BMD yet significant vertebral fracture reduction
- Regression to the mean pattern

Monitoring Osteoporosis Therapy With Bone Densitometry

- **Patient Population:**
  - FIT patients on alendronate 5 mg/d with 2 yr of BMD monitoring
  - MORE patients on raloxifene 60 or 120 mg/d with 2 yr of BMD monitoring
- **Measure:** Baseline, 12 & 24 month hip & spine BMD
- **Results:**
  - Women with greatest loss of BMD during 1st yr of treatment were most likely to gain BMD during continued treatment
  - This phenomenon occurred with 2 drugs & measurements at 2 sites
Regression to the Mean

Principle: Individuals who have measurements that differ from the mean for a population tend to have repeat measurements closer to the mean. This tendency is greatest for measurements farther from the mean.

Practice Implications

- Treatment should be continued in patients who appear to lose BMD initially because most patients will gain it with continued treatment.
- The gains usually exceed losses of 1st year.
- When patients make unusually large gains the 1st year, they will likely lose or have modest gains during the 2nd year.

Practice Implications

- NIH Consensus Panel: Lack of improvement in BMD does not justify stopping treatment strategies in patients with osteoporosis.
### Possible Causes for a True Decrease in BMD

- Nonadherence
- Poor drug absorption
- Improper dosing
- Secondary causes of bone loss
- True nonresponse

### Summarize Assessment of Mrs. Baloney

- Consider consulting with a professional about safe & effective ways to increase physical activity for bone health
- Consider switching to a calcium citrate supplement
- Consider switching to Fosamax Plus D® and adding a multivitamin or selecting a calcium supplement that also contains vitamin D
- Consider talking to her physician about having her DXA scan repeated to assess response to therapy

### Osteoporosis Care Certificate Program

**Drug Therapy for Osteoporosis**

- Overview
- ERT and HRT
- Bisphosphonates
- Salmon-Calcitonin
- Raloxifene
- Formation - Stimulating Drugs
Describe the appropriate use of the various pharmacotherapeutic choices to treat osteoporosis, including indication, mechanism of action, dosing, administration, adverse effects and precautions.

Explain the role of the drugs approved for osteoporosis in the management of this disease.

Educate patients about the various pharmacotherapeutic choices to treat osteoporosis and monitor their response to therapy.

Take time to review if necessary.

Describe the appropriate use of the various pharmacotherapeutic choices to treat osteoporosis, including indication, mechanism of action, dosing, administration, adverse effects and precautions.

Explain the role of the drugs approved for osteoporosis in the management of this disease.

Educate patients about the various pharmacotherapeutic choices to treat osteoporosis and monitor their response to therapy.

Thank you for your participation. Click below to proceed to the Post-Test.

Post-Test Button