OSTEOPOROSIS, WHO TO TREAT AND WHEN

JOHN ELLIOT
• Zoledronate, best given in hospital
• Cost $60, $36 for alendronate
• Implant and screw survival
• Bone density can help
• 50,000 IU D prior, maintenance?
• Calcium?
• Ongoing instructions to LMO, BMD can help
ZOLEDRONIC ACID AND CLINICAL FRACTURES AND MORTALITY AFTER HIP FRACTURE
LYLES, FOR THE HORIZON RECURRENT FRACTURE TRIAL*

NEJM 2007
ZOLEDRONATE AFTER HIP FRACTURE

**Figure 2.** Time to Primary or Secondary End Point.
ORAL ALENDRONATE/RISEDRONATE VS IV ZOLEDRONATE

• TAKE ALENDRONATE FIRST THING IN THE MORNING, AT LEAST 30 MINUTES BEFORE YOU EAT OR DRINK ANYTHING OR TAKE ANY OTHER MEDICINE. IF YOU TAKE ALENDRONATE ONLY ONCE PER WEEK, TAKE IT ON THE SAME DAY EACH WEEK AND ALWAYS FIRST THING IN THE MORNING. TAKE WITH A FULL GLASS (6 TO 8 OUNCES) OF PLAIN WATER. REMAIN UPRIGHT AFTER TAKING.

• PERHAPS 50% OF PATIENTS PERSIST WITH ORAL TREATMENT
• PATIENTS WHO DO NOT ADHERE DO NOT GET FRACTURE BENEFITS
• THE ORAL REGIME CAN POSE PROBLEMS. FASTING(ONLY 0.65% ABSORBED) GI SIDE EFFECTS.
• PATIENT PREFERENCE
Benefits and Risks

Motor Vehicle Accidents

- Wearing seat belts reduces the risk of serious crash-related injuries and deaths by about 50%

Osteoporosis

- Treatment with bisphosphonates reduces the risk of fractures by about 50%

There are about 2.3 million adults treated in ERs each year for injuries from MVAs and about 2 million osteoporotic fractures each year. The risk of seat belt injuries and serious side effects from osteoporosis treatment is very small in proportion to the benefits. Data from multiple sources.
TIMING OF THE INITIATION OF BISPHOSPHONATES AFTER SURGERY FOR FRACTURE HEALING: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Y.-T. Li & H.-F. Cai & Z.-L. Zhang, Ol 2015

• CONCLUSIONS EARLY ADMINISTRATION OF BPS AFTER SURGERY DID NOT
• APPEAR TO DELAY FRACTURE HEALING TIME EITHER RADIOLOGICALLY OR
• CLINICALLY.
BONE MASS AND PUTTING METAL SCREWS INTO CHALK.....

- CONSIDER RISK AT TIME OF SCHEDULING SURGERY
- ORDER DXA
- HIGH RISK
CONCLUSIONS IN PATIENTS UNDERGOING LOWER LIMB ARTHROPLASTY, BISPHOSPHONATE USE WAS ASSOCIATED WITH AN ALMOST TWOFOLD INCREASE IN IMPLANT SURVIVAL TIME. THESE FINDINGS REQUIRE REPLICATION AND TESTING IN EXPERIMENTAL STUDIES FOR CONFIRMATION.
• A T SCORE DIAGNOSIS
• HOW THEY COMPARE WITH OTHERS, SCREEN BOTTOM 3% FOR SECONDARY CAUSES
• VERTEBRAL FRACTURE ASSESSMENT.
• FRAX
• SOMETHING TO FOLLOW NEW FRACTURES, VERY LOW BMD STILL. CONTINUE OR CHANGE OR SPACE OUT INFUSIONS
• WHAT ADVICE DO YOU GIVE GPS RE ONGOING TREATMENT
ADVICE TO LMO

• ANNUALLY FOR 3 YEARS, CONTINUE TO 6 IF VERTEBRAL FRACTURE OR BMD STILL IN OSTEOPOROTIC RANGE HIP.
• SWITCH TO TERIPARATIDE OR DENOSUMAB OR GO FOR ANNUAL IF NEW FRACTURE
• OR ANYTHING YOU LIKE!
Opportunistic CT

- CT attenuation coefficient
  - Hounsfield units
- Estimation BMP
- Obtainable on all CT Scans
- Correlates screw pullout

<table>
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<tr>
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<th>T-Score</th>
<th>HU</th>
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<tbody>
<tr>
<td>Normal</td>
<td>&gt; - 1.0</td>
<td>133</td>
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<tr>
<td>Osteopenia</td>
<td>-1.0 to -2.5</td>
<td>108.5</td>
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<tr>
<td>Osteoporotic</td>
<td>&lt; -2.5</td>
<td>78.5</td>
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</table>
Opportunistic CT Can Derive “DXA-Equivalent” T-scores
Femoral neck BMD evaluation on routine CT

“...opportunistic use of CTXA T-scores could enhance osteoporosis screening.”

Pickhardt, et. al., J Clin Densitom. 2015 Jan-Mar;18(1):5-12
Stable Vertebral collapse……….
LOTS of CT Scans Are Being Done

Growth in # of CT scans per 1,000 Medicare beneficiaries

D Brenner, PhD; www.chapter.aapm.org

MEDPAC: Health care spending and the Medicare Program, June 2016
EFFECTS OF TERIPARATIDE ON HIP AND UPPER LIMB FRACTURES IN PATIENTS WITH OSTEOPOROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS.
DÍEZ-PÉREZ A BONE. 2019

- META-ANALYSIS RESULTS SHOWED AN OR (95% CI) FOR HIP FRACTURES OF 0.44 (0.22-0.87; P = 0.019) IN PATIENTS TREATED WITH TERIPARATIDE COMPARED WITH CONTROLS.

- THE FOLLOWING WERE NOT STATISTICALLY SIGNIFICANT (P > 0.05).
  - HUMERUS [1.02 (0.50-2.08)]
  - FOREARM [0.53 (0.26-1.08)]
  - AND WRIST FRACTURES [1.21 (0.72-2.04)]

- THIS META-ANALYSIS PROVIDES EVIDENCE OF EFFICACY OF TERIPARATIDE IN REDUCING HIP FRACTURES BY 56% IN PATIENTS WITH OSTEOPOROSIS.
COSMAN F, ET AL.

EFFECTS OF INTRAVENOUS ZOLEDRONIC ACID PLUS SUBCUTANEOUS TERIPARATIDE [RHPTH(1-34)] IN POSTMENOPAUSAL OSTEOPOROSIS. J BONE MINER RES 2011;26:503–511.
Changes in Wrist BMD and Wrist Fracture Reduction: Abaloparatide vs. Teriparatide vs. Placebo
(Miller et al. Endo Society 3-15)

Ultra-Distal Radius BMD

K-M Estimated Incidence Rate Wrist Fracture (ITT Population)

Abaloparatide

*p < 0.001 vs placebo
*p = 0.0013 vs TP

HR 0.28* (95%CI = 0.09 - 0.84)

-72%

N=10
1.2%

N=4
0.5%

N=15
1.8%

Placebo | Abaloparatide | Teriparatide

* Vs. TPTD, p=0.015
DENOSUMAB

- GIVEN 6 MONTHLY INJECTION
- ADVERSE RESPONSES SIMILAR TO PLACEBO EXCEPT SLIGHT INCREASE IN ECZEMA, LOW CALCIUM, CELLULITIS
- $800 NZD PER YEAR
WHATS THE BEST AND COMBINATIONS

• FOR MOST
  • ZOLEDRONATE
  • ALENDRONATE/RESIDRONATE THE CHEAPEST
  • MOST BENEFIT IS IN THE FIRST 3 YEARS, BUT IF YOU STOP BMD WILL FALL

• FOR VERY LOW BMD
  • TERIPARETIDE BEST AT SPINE/AXIAL SKELETON BUT INCONVENIENT AND CAN ONLY DO 18 MONTHS AND NOT GOOD AT THE HIP EARLY AND PERHAPS NOT WRIST EVER.
  • TERIPARTEIDE THEN ZOLEDRONATE OR TOGEATHER
  • ALBALOPARETIDE THEN DENOSUMAB
  • DENOSUMAB IS A CONTENDER AVAILABLE NOT FUNDED
  • DEMOSUMAB THEN ZOLEDRONATE/ALENDRONATE ? TIMING
  • ROMOSUZUMAB THEN DENOSUMAB THEN ZOLEDRONATE…
MONTHLY HIGH-DOSE VITAMIN D TREATMENT FOR THE PREVENTION OF FUNCTIONAL DECLINE: A RANDOMIZED CLINICAL TRIAL
HEIKE A. BISCHOFF-FERRARI, MD, JAMA 2016

• CONCLUSIONS

• COMPARED WITH A MONTHLY STANDARD-OF-CARE DOSE OF 24 000 IU OF VITAMIN D3, TWO MONTHLY HIGHER DOSES OF VITAMIN D (60 000 IU AND 24 000 IU PLUS CALCIFEDIOL) CONFERRED NO BENEFIT ON THE PREVENTION OF FUNCTIONAL DECLINE AND INCREASED FALLS IN SENIORS 70 YEARS AND OLDER WITH A PRIOR FALL EVENT.

• THEREFORE, HIGH MONTHLY DOSES OF VITAMIN D OR A COMBINATION WITH CALCIFEDIOL MAY NOT BE WARRANTED IN SENIORS WITH A PRIOR FALL BECAUSE OF A POTENTIALLY DELETERIOUS EFFECT ON FALLS.
CUMULATIVE INCIDENCE OF TIME TO FIRST FRACTURE OR FALL

CALCIUM AND CARDIOVASCULAR DISEASE

- Is calcium an important part of the treatment programme?  **No**
- Should you aim for RDA?  **Enough but not too much**
- Is it better or safer to obtain calcium from diet or supplements?  **Probably Diet**
- Is there really a CV risk associated with prescribing calcium supplements?  **Maybe**
- If you are on treatment do you need calcium?  **Probably not**
CONCLUSIONS

• Zoledronate IV is the std of care, annually
• Give prior to discharge
• Bone density can add information, guide need for additional tests, diagnose vertebral fractures, guide follow up down the track,
• Vitamin D 1.25mg prior to infusion, maintenance once a month
Opportunistic CT Values at the Hip Can be Entered into FRAX

<table>
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<tr>
<th>ROI</th>
<th>BMD (g/cm²)</th>
<th>T-Score</th>
<th>WHO Classification</th>
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<tr>
<td>Femoral Neck</td>
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<tr>
<td>Trochanter</td>
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<tr>
<td>Intertrochanter</td>
<td>1.029</td>
<td>-0.49</td>
<td></td>
</tr>
<tr>
<td>Total Hip</td>
<td>0.807</td>
<td>-0.99</td>
<td>Normal</td>
</tr>
</tbody>
</table>

BMI: 26.4
The ten year probability of fracture (%)

with BMD

- Major osteoporotic: 6.1
- Hip Fracture: 0.9