Bisphosphonate related osteonecrosis of the jaw – clinical features, prevention, treatment

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07.29.2010., MWIA, Münster
The use of bisphosphonates
(alendronat, olpadronat, risedronat, neridronat, incadronat, pamidronat, ibadronat, zoledronat, etc.)

- Since 1970. (oral/iv.)
- 2008.: 190 million prescriptions
- 2003.: First article about osteonecrosis

1. Malignant osteolytic bone events (i.v.)
   - Myeloma multiplex
   - Metastatic neoplasmas
   - Lymphomas
2. Osteoporosis (oral/i.v.)
3. Paget disease
4. Other metabolic bone diseases
Bisphosphonates affect through the apoptosis of osteoclasts

**Benefits**

1. Decrease of bone resorption
2. Inhibiting the development of bone metastasis
3. Decrease of bone pain

**Risks**

1. Inhibiting the remodelling of the bone
2. Decrease the ability of bone healing
3. OSTEONECROSIS OF THE JAW (BIONJ/BRONJ)!
Definition of bisphosphonate releated/ induced osteonecrosis of the jaw (BRONJ/ BIONJ)


1. Exposed bone for more than 8 weeks
2. Bisphosphonate therapy in the past
3. There is no radiotherapy in the past
Bisphosphonate-related induced osteonecrosis of the jaw (BRONJ/ BIONJ)
Clinical stages and treatment

**Stage 0**
Swelling, pain, mucosa hyperaemia
Therapy: regular control, increased oral hygiene

**Stage 1**
The bone is exposed, no pain, the mucosa is not inflamed
Therapy: regular control, increased oral hygiene
+ antiseptic rinses
**Stage 2**
The bone is exposed, pain, inflammed mucosa
Therapy: regular controll, increased oral hygiene, antiseptic rinses
+ **Antibiosis** (Penicillin, Clyndamycin, Doxycylin, Fluorokinolon, Metronidazol), **Antianalgetic**

**Stage 3**
The bone is exposed, pain, non healig mucosa inflammatio, pathologic fracture, fistulas
Therapy: regular controll, increased oral hygiene, antiseptic rinses, Antibiosis, Antianalgetic + **Surgery** (bone resection, debridement)
Prevention!

**Serum Beta Cross Laps/CTX Test**

Osteoclast collagenase enzyme $\rightarrow$ Octapeptid $\rightarrow$
detect from the serum

Remodelling capacity?
Bone healing?
Risk of osteonecrosis
Beta Cross Laps – Risk of osteonecrosis

Less than 100 pg/ml - High risk
100-150 pg/ml - Medium risk
200-300 pg/ml - Low risk
Above 300 pg/ml - No risk

Drug holiday - 25pg/ml increase/ month
Materials and methods

- Datas of the last one year
- Age
- The kind of bisphosphonate
- The length of bisphosphonate therapy
- \( \beta \)-Cross Laps
### Results - Osteoporosis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Bisphosphonate</th>
<th>Length of the therapy (years)</th>
<th>ß-Cross Laps</th>
</tr>
</thead>
<tbody>
<tr>
<td>75 years old woman</td>
<td>Boniva</td>
<td>2</td>
<td>34</td>
</tr>
<tr>
<td>60 y.o. woman</td>
<td>Boniva</td>
<td>6</td>
<td>180</td>
</tr>
<tr>
<td>58 y.o. woman</td>
<td>Calcisedron</td>
<td>4</td>
<td>-</td>
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<tr>
<td>75 y.o. man</td>
<td>Calcisedron</td>
<td>3</td>
<td>185</td>
</tr>
<tr>
<td>80 y.o. woman</td>
<td>Bonviva</td>
<td>-</td>
<td>843</td>
</tr>
<tr>
<td>62 y.o. man</td>
<td>Calcisedron</td>
<td>0.5</td>
<td>474</td>
</tr>
<tr>
<td>69 y.o. woman</td>
<td>Actonel</td>
<td>4.4</td>
<td>655</td>
</tr>
<tr>
<td>68 y.o. woman</td>
<td>Actonel</td>
<td>3</td>
<td>270</td>
</tr>
<tr>
<td>55 y.o. woman</td>
<td>Bonviva</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>67 y.o.</td>
<td>Calcisedron</td>
<td>2</td>
<td>64</td>
</tr>
<tr>
<td>55 y.o. woman</td>
<td>Bonviva</td>
<td>5</td>
<td>30</td>
</tr>
</tbody>
</table>
## Results - Malignant osteolytic bone events

<table>
<thead>
<tr>
<th>Patient</th>
<th>Bone disease</th>
<th>Bisphosphonate</th>
<th>Length of therapy (years)</th>
<th>β-Cross Laps</th>
</tr>
</thead>
<tbody>
<tr>
<td>59 y.o. man</td>
<td>Prostate cancer</td>
<td>Zometa</td>
<td>3,5</td>
<td>Less than 10</td>
</tr>
<tr>
<td>75 y.o. man</td>
<td>Prostate cancer</td>
<td>Zometa</td>
<td>3,5</td>
<td>129</td>
</tr>
<tr>
<td>69 y.o. woman</td>
<td>Breast cancer</td>
<td>Zometa</td>
<td>5</td>
<td>Less than 40</td>
</tr>
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<td>57 y.o. man</td>
<td>Prostate cancer</td>
<td>Zometa, Bonefos</td>
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<td>87</td>
</tr>
<tr>
<td>62 y.o. woman</td>
<td>Breast cancer</td>
<td>Zometa</td>
<td>1</td>
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<tr>
<td>67 y.o. man</td>
<td>Prostate cancer</td>
<td>Zometa</td>
<td>3</td>
<td>112</td>
</tr>
</tbody>
</table>
Conclusions

- Above 300pg/ml – absence of BIONJ
- Severity of BIONJ correlates to the β-CL
- Above 300pg/ml the chance of healing is increased
- In most of the cases BIONJ develops after tooth extraction
- Drug overdose?
- Our results correlate to the international datas
Thank you for your kind attention!