

Biphosphonates and Osteonecrosis of Jaw (BON-J)

RISK

Biphosphonates Inhibit bone remodeling. All bone is affected but necrosis seen most often in jaw as it has 10x rate of remodeling.

Defined as exposure of necrotic avascular bone in Maxilla or Mandible for more than 8 weeks in a patient that has been taking biphosphonates and has NOT had radiation

- highest cause Tooth extraction = 70%
- other causes--- Implants, Denture sores ,Periodontal disease =30%,

Other long-term risk of these drugs

Odvin J Clin Endocrinol Metab. 2005 described 9 patients on alendronate for 3- 8 years,. increased susceptibility to, and delayed healing of, nonspinal fractures

- other anecdotal reports about unusual fractures in patients on long-term or high-dose bisphosphonates

(Schneider JP, Armamento-Villareal R , Whyte MP) point to medically significant risks with long term use.

BENEFIT

Osteoporosis is a growing problem. Aggravated in part by elective cessation of hormone replacement therapy and a large demographic cohort of post menopausal females.

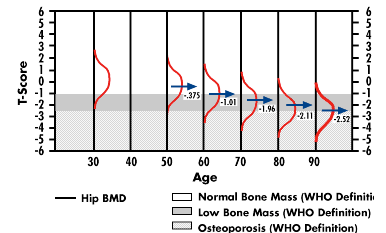
The average 50yr old Caucasian female has a 14% risk of hip fracture.

The average 80 yr old Caucasian female has lost 40% of their peak bone mass . and 70% are osteoporotic.

Benefit Fosamax cleared for use in 1995

Has shown after 2 years use...

- 59 % reduction spinal fracture
- 63% reduction in hip fracture



However several recent studies in the Medical Literature have noted limited longer term benefit of Biphosphonate treatment beyond 5 years use in management of Osteoporosis.

- Bone , Hosking et al : Ten Years experience with alendronate for osteoporosis in postmenopausal women. N Eng. J. Med. 350: 1189, 2004.

- Black , Schwartz et al FLEX research Group : Effects of continuing or stopping alendronate after 5 years . JAMA 296: 2927, 2006.

DRUG FORMS

Oral < 1% bioavailability. Used primarily for osteoporosis has moderate- low risk for BON-J

- Fosamax (alendronate)
- Bonafos (clodronate)
- Actonel (residronate)
- Didrocal (etidronate)

Intravenous = 50 % bioavailable has high BON-J Risk estimated to 10%

- Used to control hypercalcemia in forms of breast, prostate and bone cancer
- Aredia(pamidronate) & Zometa (zoledronate) =high risk
- Bonafos (clodronate) Canada = mod risk

Drug,	Potency	Form
nEtidronate (Didrocal)	1	oral
nBonafos (clodronate)	10	oral or IV
nPamidronate (Aredia)	100	oral
nAlendronate (Fosamax)	500	oral
nRisedronate (Actonel)	2000	Iv or oral
nZoledronate (Zometa)	10,000	Iv

Relative Risk & case reports of oral BP's.

- 2003-2007 over 300 case reports published on oral BP's and related jaw necrosis.

Marx, 2006 ,Miami clinic reported on 300cases of ONJ

- 10% (30) were taking oral bisphosphonate for osteoporosis

-Fosamax most common. (28 Cases) Due to potency and prevalence

- Actonel (2 Cases)

- Of oral meds only fosamax actonel, nitrogen chain BP's are potent enough to cause ONJ

Mavrokokki et al U of Adelaide, 2006.

- Frequency of bONJ cases estimated from Rx & extraction data.

158 cases of ONJ... main trigger was dental extraction (73%).

-IV forms chemo zometa/aredia . Post-Extraction risk ONJ was 8% (72% of cases)

-Oral forms osteoporotic patients (28% cases) extractions risk was 0.2%

-avg dose fosamax at onset of ONJ was 9,000 mg. (24+ months fosamax).

ADA guidelines 2006 for pts on oral BP

-Inform pts. oral B. P. risk is low estimate between 1/1000 and 1 / 10,000

-Periodontal,Extraction and Implant surgery :

Limited data. Inform for elective care ,Treat limited area

Surgery with caution and written informed consent

CHx rinse advised. For 2 mos post surgically

-Prophylactic antibiotic's pre and post dose optional.

No data on Antibiotics , empiric choice, amoxy /metro

Marx proposed screening-management with C-terminal telopeptide. (CTx),

this test is available as blood test at Calgary Med Labs.

100 Pg/ml = high risk

100-150 Pg/ml = Moderate risk

150 plus Pg/ml = low risk

Stopping oral Bp's, drug holiday leads to rebound in bone remodeling potential measured by CTx

- about 25 pg/ml per month increase

- hence the rationale for 3mos drug/holiday prior to any dental surgical procedure .

Summary

- Extractions ,Implant surgery ,Periodontal surgery

- High risk in patients on IV BP's ,

- Moderate risk with Nitrogenous oral BP's

- Low risk in non-Nitrogenous oral BP's

- Consider Drug holiday or potent oral forms .

- 3 mos cessation pre-tx & 3mos post tx

- Longer term use beyond 5 yrs may be in question.

- Remove poor teeth before Chemo-IV.

- if BON-J .in IVcase. Palliative tx only, no surgical treatment or resolution

Dr French is a Periodontist, not a medical specialist in this field. This information is provided as a courtesy to Medical and Dental Professionals. It is not a complete synopsis of Biphosphonates and Management of Osteoporosis. We advise you follow up on reference and further study of this topic to develop appropriate guidelines