Session 5

골다공증의 특수 상황

좌장: 김범택 (아주의대), 이지영 (건국의대)

대한골다공증학회

제47회 연수강좌

CKD and Bone Health

이 시 훈

가천대학교 의과대학 내분비내과

MEMO

Osteoporosis

- Affects up to **200 million women** worldwide and causes **9 million fractures** annually.
- Related fracture occurs every 3 seconds. Among people over age 50, an estimated **1 in 3 women** and **1 in 5 men** will experience a fragility fracture.
- Chronic kidney disease (CKD) stages 1-4 affects up to 20 million Americans, and stage 5 disease affects about 750,000.
- To confound the diagnosis and treatment even further, as patients age, the prevalence of both osteoporosis and CKD increases.

Chronic Kidney Disease

- Pts with CKD are more likely to develop osteoporosis and fractures than age-matched controls without kidney disease.
- Risk of fracture-related mortality increases as the severity of CKD increases.
- Pts with CKD-MBD may need different treatment of fragility fractures, and standard osteoporosis therapies may be precluded in some high-risk patients.
- Examples of CKD-MBD include **osteomalacia** (decreased mineralization of newly formed bone), **secondary hyperparathyroidism**, **mixed uremic osteodystrophy**, **amyloid bone disease**, and **adynamic bone disease**.
- CKD-MBD is an independent risk factor for fragility fractures.

MEMO

Q. What tests should we pursue to make a diagnosis of renal bone disease, and which stages of CKD are we most concerned about?

- In stage 3 CKD, it's sufficient to use T-scores and/or fracture history to make the diagnosis of osteoporosis—without looking for evidence of CKD-MBD. Treatment with standard agents for osteoporosis is recommended.
- In stages 4 and 5 (eGFR <30 ml/min) where one cannot use T scores or fracture history to make the diagnosis of osteoporosis.

- In these later-stage patients, the 2 most important markers of CKD-MBD are parathyroid hormone (PTH) and bone specific alkaline phosphatase (BSAP). A high PTH (>6x the upper limit of normal) rules out adynamic bone disease and suggests hyperparathyroidism. Treating this secondary hyperparathyroidism is the goal of care to prevent fragility fractures.
- A high BSAP also goes against the diagnosis of adynamic bone disease in most patients, except in those who have just had a recent large bone fracture.
- A high BSAP may be suggestive of Paget's Disease, bone metastasis, and osteomalacia. A low BSAP in a patient not on any antiresorptive therapy may suggest adynamic bone disease. The combination of a low PTH (<150 pg/mL) and low BSAP has a high positive predictive value for adynamic bone disease. In these patients, use of antiresorptive therapy typical of osteoporosis management is not recommended, because there is little bone resorption to target.

BSALP and iPTH in CKD

High turnover *vs* Low turnover

Table 1 Brief summary of the predictive value of intact PTH and BSAP in CKD patients

Blood marker	High-turnover sensitivity / specificity	Positive predictability
BSAP > 20 ng/mL	100% / 100%	84%
BSAP > 15 ng/mL	97% / 83%	86%
BSAP > 10 ng/mL	84% / 70%	90%
iPTH > 200 pg/mL	72% / 80%	92%
iPTH > 150 pg/mL	78% / 70%	89%
BASP + iPTH > 20 ng > 200 pg/mL	100% / 80%	94%
iPTH > 300 pg/mL	58% / 77.7%	
iPTH > 9 X ULN	37% / 85.8%	
Blood marker	**Low turnover sensitivity / specificity**	**Positive predictability**
BSAP < 20 ng/mL	100% / 100%	100%
BSAP < 15 ng/mL	83% / 97%	83%
BSAP > 10 ng/mL	70% / 84%	58%
iPTH < 200 pg/mL	80% / 72%	47%
iPTH < 150 pg/mL	70% / 78%	50%
BASP + iPTH < 20 ng < 200 pg/mL	80% / 100%	100%
BSAP < 27 U/L	78.1% / 86.4%	75%
iPTH < 150 pg/mL	80.6% / 76.2%	65%
BSAP < 12.9 ng/mL	100% / 94%	72%
iPTH < 79.7 pg/mL	88.9% / 90.6%	
iPTH < 150 pg/mL	68.6% / 61.2%	
iPTH < 2 X ULN	65% / 67.3%	

Calcified Tissue International (2018) 103:111–124

MEMO

- Other important tests typically ordered in patients with CKD stages 4-5 include determinations of calcium, vitamin D, and phosphorous, as the handling of all of these important minerals is deranged in advanced CKD and plays a significant role in bone turnover, mineralization and volume.
- **CKD-MBD** and **osteoporosis** can co-exist. it is suggested by persistent hyperphosphatemia, elevated PTH and "normal" BSAP. The treatment for CKD-MBD is to manage hyperphosphatemia and secondary hyperparathyroidism, not typical osteoporosis therapies. However in high-risk patients (prior fragility fracture, T-scores <-2.5, age >65 years), once the CKD-MBD metabolic parameters are managed, osteoporosis medications can be considered.
- Regarding the occasional need for **bone biopsy** in patients with suspected renal osteodystrophy, it is only considered in patients with CKD stages 4-5 when suspected adynamic bone disease based on blood tests and needs to consider either an antiresorptive agent or, if adynamic, an anabolic agent first line in high-risk patients.

Summary

- **CKD-MBD** and **osteoporosis** may share some similar pathophysiologic processes leading to more fragile bones, but with a crucial difference in the amount of bone turnover that is occurring.
- Since many of the medications for osteoporosis are based on decreasing bone turnover, distinguishing states where no or low bone turnover is occurring, as in some forms of CKD-MBD, is important to make before considering osteoporosis therapy.
- The cohort of CKD patients where the mineral and bone disorder is most problematic is CKD stages 4 and 5.

치과치료 전후의 골다공증 관리

김 재 영

연세대학교 치과대학 구강악안면외과

2017년 대한민국은 65세 인구가 14% 이상인 고령사회로 진입하였습니다. 치과와 의과 모두 고령 환자들이 증가하고 있으며, 치과치료와 골다공증 치료 모두가 필요한 환자 군이 늘어날 수밖에 없는 상황으로 임상가들의 어려움이 가중되고 있다고 생각됩니다. 특히 이러한 환자들은 BRONJ의 발생 위험을 높일 수 있는 당뇨와 같은 다른 질환들을 같이 치료받고 있는 경우가 많아 management 가 더욱 어려워질 수 있다고 보입니다.

2003년 Marx 등에 의해 처음 보고된 비스포스포테이트 관련 약물괴사증(bisphosphonate-related osteonecrosis of the jaw, BRONJ)은 2014년 미국구강악안면외과학회에서 발표한 position paper에서 denosumab 등의 anti-angiogenic medication과 anti-resorptive medication이 추가되면서 약물관련 악골괴사증(medication-related osteonecrosis of the jaw, MRONJ)으로 그 개념이 확장되었습니다.

본 발표에서는 MRONJ 의 발생에 관련된 약제들과 치과치료에 대하여 다시 한 번 살펴보고, MRONJ 발생을 최소화하면서 치과치료를 진행하고 골다공증 관리를 할 수 있는 방법에 대해 문헌고찰과 함께 알아보고자 합니다.

MEMO

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- Prolia는 치과치료 전 후 안전한 약제인가?
- 환자 평가와 치과 치료 전 후 협진 (의과 → 치과, 치과 → 의과)

치과 치료와 악골괴사증

MRONJ (AAOMS 2014)

2007 & 2009	2014
Current or previous treatment with a bisphosphonate	Current or previous treatment with antiresorptive or antiangiogenic agents
Exposed bone in the maxillofacial region that has persisted for more than 8 weeks	Exposed bone or bone that can be probed through an intraoral or extraoral fistula(e) in the maxillofacial region that has persisted for more than eight weeks
No history of radiation therapy to the jaws	No history of radiation therapy to the jaws or obvious metastatic disease to the jaws

- Ruggiero et al. *J Oral Maxillofacial Surg* (2014)- AAOMS Position paper

MEMO

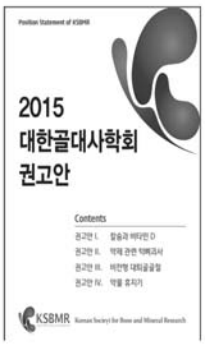
Position Papers

BISPHOSPHONATE RELATED
OSTEONECROSIS of the JAW
(BRONJ)
- Position Statement of Korea-

비스포스포네이트와 연관된
악골(턱뼈)괴사

2009.05.06 회의
2009.06.02 정리
2009.06.25 최종

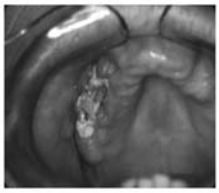
대한대문비학회
대한잔재사학회, 대한잔다공증학회, 대한구강악안면외과학회



Letter to the editor

Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic

Robert E Marx, DDS*



Incidence of MRONJ

2. 역학

1) 유병률

대부분의 국외연구에서는 0.001% 이하로 매우 낮다. 국내 15개 종합병원의 공동연구 자료에서 BRONJ의 빈도는 0.04% (1명/2,300명)로 추산되나 추가연구가 필요하다. 종양환자에서 BRONJ 유병률은 1.86%까지 보고되며 골다공증 환자에서보다 높다.

2) 발생률

경구비스포스포네이트 치료 환자에서 턱뼈괴사 발생율은 1.04-69명/100,000 patient-years, 주사제 치료 환자에서의 발생율은 0-90/100,000 patient-years 이며 약제치료기간에 따라 증가한다.

MEMO

Long duration of treatment

- 86/Female
- 2017-02 초진
  - 약 1개월 전 개인치과에서 발치 시행한 이 후 낫지 않는다는 주소로 치주과 경유 본과 의뢰됨.
  - 3개월에 한번씩 IV로 골다공증 제재 투여 중이나 정확한 약명은 모름. (Bonviva??)
  - 정확한 약명 및 치료 계획 확인 위해 해당병원 협진 의뢰
    - T-score<-4.5 이하인 환자로 2012년부터 본비바 (inj/3Ms) 사용중입니다. 당분간 약 끊으시거나 바꾸셔도 관계 없습니다.
- 2018-10 치료 종료 (PTH 투여, sequestrectomy 2회)

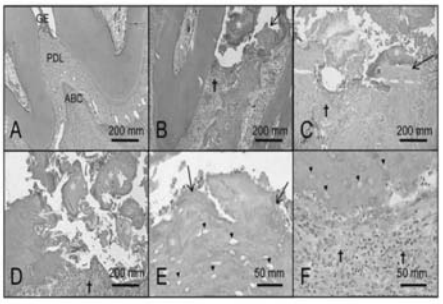
Medication related osteonecrosis of the jaw (MRONJ)

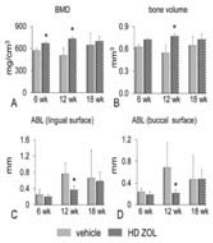
- 비스포스포네이트 투여 후 턱뼈에서만 특이적으로 골괴사가 나타나는 이유에 대하여 다양한 가설이 제시되고 있으나 파골세포 및 골대사 억제, 감염 또는 염증에 대한 국소조직의 반응에 관여, 신생혈관 형성 억제로 인한 혈류저하, 상피세포 등의 연조직에 대한 독성으로 골노출 초래, 면역체계에 대한 영향, 미세골절의 치유 억제 등 여러 기전의 복합적인 작용에 의한 것으로 추정된다.

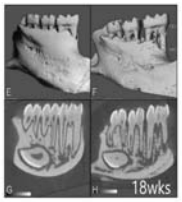
- 대한골대사학회권고안 (2015)

- Ruggiero et al. *J Oral Maxillofacial Surg* (2014)- AAOMS Position paper

Oncologic Doses of Zoledronic Acid Induce Osteonecrosis of the Jaw-Like Lesions in Rice Rats (*Oryzomys Palustris*) with Periodontitis







- HD Zol – Zolendronate 80ug/kg (once a month, IV)

- Aguirre et al. *J Bone Miner Res* (2012)

MEMO

Spontaneous Osteonecrosis of the Jaw During Bisphosphonate Therapy: An Unusual Etiology of the Numb Chin Syndrome

- A 75-year-old White woman
- Moderate renal insufficiency (Kidney Disease Outcomes Quality Initiative [KDOQI] Stage III with estimated glomerular filtration rate [eGFR] of 40 mL/min/1.73 m2)
- Multiple myeloma with several bone lesions in her thoracic and lumbar spine, which were treated with several vertebroplasties.
- Underwent an autologous stem cell transplantation in 2006, with relapsing disease in 2009.
- Currently treated with lenalidomide and low-dose dexamethasone.
- Oral bisphosphonate therapy with zoledronic acid was started in 2010 and had been interrupted 3 weeks prior to admission due to the diagnosis of a spontaneous osteonecrosis of the right jaw.
- A bone biopsy performed at that time excluded tumorous infiltration and infectious processes.

- Schumidhauser and Bardelli. *Journal of palliative and pharmacotherapy (2016)*

The effects of adjunctive parathyroid hormone injection on bisphosphonate-related osteonecrosis of the jaws: an animal study

E. H. Dayisoylu[1], F. Ç.Şenel[2], C. Üngör[3], E. Tosun[4], M. Çankaya[5], S. Ersöz[6], F. Taskesen[7]
[1]Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Baskent University, Ankara and Konya, Turkey; [2]Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Karadeniz Technical University, Trabzon, Turkey; [3]Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Hacettepe University, Ankara, Turkey; [4]Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Recep Tayyip Erdogan University, Rize, Turkey; [5]Department of Pathology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey

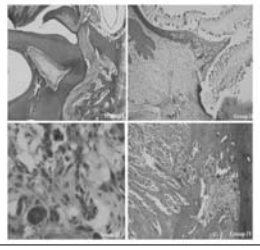
Int. J. Oral Maxillofac. Surg. 2013; 42: 1475–1480
http://dx.doi.org/10.1016/j.ijom.2013.05.001, available online at http://www.sciencedirect.com

- 0.1 mg/kg ZA (Zometa , 4 mg flacon, Novartis, Turkey)
- Intraperitoneally (i.p) – three times a week for 8 weeks

Table 4. The presence and severity of inflammation in the four study groups.

Group		No inflammation (0)	Mild to moderate inflammation (1)	Severe inflammation (2)
I	SS	100%	0%	0%[a]
II	ZA	77.7%	22.2%	0%
III	ZA + Ext	0%	0%	100%[a]
IV	ZA + Ext + PTH	22.2%	11.1%	66.6%[a]

SS, sterile saline; ZA, zoledronic acid; Ext, tooth extraction; PTH, parathyroid hormone.
[a] A statistically significant difference was observed in groups III and IV compared with group I ($P < 0.01$).



Position Paper

saving faces | changing lives
American Association of Oral and Maxillofacial Surgeons

Medication-Related Osteonecrosis of the Jaw—2014 Update

- Dentoalveolar surgery is considered a major risk factor for developing MRONJ.
- Dentoalveolar surgery
  - Tooth extraction
  - Dental implant - unknown
  - Endodontic procedure - unknown
  - Periodontal procedure – unknown

Medication-Related Osteonecrosis of the Jaw and Dental Implants Failures: A Systematic Review

- Due to the heterogeneity of the included studies and the high risk of bias, there is no evidence of the safe use of oral antiresorptive agents prior or after dental implant surgery.
- Indeed, implant failure and ONJ development can occur and represent a devastating side effect that should be considered during treatment.

- Guazzo et al. *Journal of Oral Implantology (2016)*

Bisphosphonate-Associated Osteonecrosis of the Jaws and Endodontic Treatment: Two Case Reports

- Sarathy et al. *Journal of Endodontics (2005)*

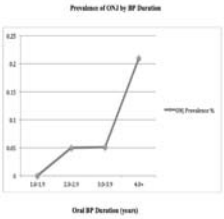
MEMO

Position Paper

American Association of Oral and Maxillofacial Surgeons

Medication-Related Osteonecrosis of the Jaw—2014 Update

- Risk factors
  - Mandible>Maxilla
  - Denture use
  - Pre-existing inflammatory dental disease (periodontital disease or periapical pathology
  - Type and Duration of Medication



MRONJ 예측 가능한가? (Biomarker)

Oral Bisphosphonate-Induced Osteonecrosis: Risk Factors, Prediction of Risk Using Serum CTX Testing, Prevention, and Treatment

of pain and clinical evidence of infection. The morning fasting serum C-terminal telopeptide (CTX) test results were observed to correlate to the duration of oral bisphosphonate use and could indicate a recovery of bone remodeling with increased values if the oral bisphosphonate was discontinued. A stratification of relative risk was seen as CTX values less than 100 pg/mL representing high risk, CTX values between 100 pg/mL and 150 pg/mL representing moderate risk, and CTX values above 150 pg/mL representing minimal risk. The CTX values were noted to increase between 25.9 pg/mL to 26.4 pg/mL for each month of a drug holiday indicating a recovery of bone remodeling and a guideline as to when

<Level of C-telopeptide>
- Less than 100pg/ml: High risk
- 100pg/ml~150pg/ml: Moderate risk
- 150pg/ml: Minimal risk

❖ Small sample size – 30 patients
❖ No control group

- Marx et al. *J Oral Maxillofac Surg* (2007)

MEMO

Yong-Dae Kwon
Joo-Young Ohe
Dong-Yoon Kim
Dong-Jin Chung
Yong-Duk Park

Retrospective study of two biochemical markers for the risk assessment of oral bisphosphonate-related osteonecrosis of the jaws: can they be utilized as risk markers?

Result: Twenty-three ONJ patients had taken alendronate for osteoporosis treatment, and the s-CTX testing results were low levels of 10–192 pg/ml (mean: 93.2 ± 49.4 pg/ml). Mean of s-CTX of the control ($n = 61$) was 125 ± 85.7 pg/ml. The duration of BP therapy ranged between 1 and 10 years (4.82 ± 2.6). The s-OC level was estimated between 0.2 and 5.4 ng/ml (1.91 ± 1.51 ng/ml). The mean s-CTX value of the control group was higher but without significance ($P = 0.12$). The s-OC values of the ONJ group were significantly lower than the lowest value of the reference range ($P < 0.001$).

Conclusion: As a result of the s-CTX and s-OC testings at the diagnosis of BRONJ, the values of the two markers were decreased. The decrease of the s-OC values implies a problem during the bone-formation process. Therefore, we can assume that in this patient group, invasive dental surgery contributes to an increase in the risk of BRONJ incidence. This result may imply that, during bisphosphonate therapy, simultaneous consideration of s-CTX showing inhibition of bone resorption and s-OC indicating the degree of bone formation might be a set of risk markers assessing risk prediction for BRONJ before invasive dental surgery.

- Kwon et al. *Clin Oral Implants Res* (2011)

Machine learning to predict the occurrence of bisphosphonate-related osteonecrosis of the jaw associated with dental extraction: A preliminary report

Table 1
Comparison of parameters between cases and controls.

BRONJ	Yes (case)	No (control)	p	
	(n = 41)	(n = 84)		
Perioperative serum CTX level (pg/mL)				
Mean ± sd	220.5 ± 220.9	255.0 ± 117.4		
Median [IQR]	163.0 [95.0; 254.0]	235.0 [174.0; 317.5]	0.003**	Mann-Whitney *U*
Lower than 150 pg/mL	20 (48.8%)	9 (10.7%)	< 0.001***	Chi square test
150 pg/mL or higher	21 (51.2%)	75 (89.3%)		

- Kim et al. *Bone* (2018)

Assessing the utility of serum C-telopeptide cross-link of type 1 collagen as a predictor of bisphosphonate-related osteonecrosis of the jaw

A systematic review and meta-analysis

JADA 147(7) http://jada.ada.org July 2016

Conclusions and Practical Implications. A systematic review of the literature with meta-analysis does not support the use of sCTX levels as a predictor of the development of BRONJ. Further prospective large sample studies are needed to understand the role of sCTX as a predictor for BRONJ.

MEMO

Biomarkers for Bisphosphonate-Related Osteonecrosis of the Jaw

Materials and Methods: Forty-eight Sprague-Dawley rats were randomly divided into the bisphosphonate group ($n = 36$), who were injected once a week with zoledronic acid, and the control group ($n = 12$), who were injected once a week with saline. After 6 weeks, surgical intervention was performed, and injections were continued up to 8 weeks. Rats in the bisphosphonate group were then further classified to the ONJ group, and the non-ONJ group, and biomarkers, including CTx, Glu-OC, TRACP 5b, RANKL, and OPG, were assessed at baseline (T0), at surgical intervention (T1), and at sacrifice (T2). Histomorphometric analysis for quantification of osteoclasts was performed.

Results: Repeated measures analysis of variance revealed that TRACP 5b levels and the RANKL/OPG ratio were significantly decreased over time in the ONJ group compared with the non-ONJ group ($p < .05$). At T2, the area under the curve was

- Kim et al. *Clin Implant Dent Relat Res* (2016)

Salivary proteomics in bisphosphonate-related osteonecrosis of the jaw

metabolism, immunological and dermatological diseases. Of all the differentially expressed proteins, we selected metalloproteinase-9 and desmoplakin for further validation. Immunoassays confirmed increased expression of metalloproteinase-9 in individual saliva (p=0.048) and serum samples (p=0.05) of BRONJ patients. Desmoplakin was undetectable in saliva. However, desmoplakin levels tended to be lower in BRONJ serum than controls (p=0.157).

- Thymbigere-Math et al. *Oral Diseases (2015)*

Biomarkers to predict the onset of biphosphonate-related osteonecrosis of the jaw: A systematic review

Conclusions: The present review suggests that no useful markers are currently available to evaluate BRONJ risk. Nevertheless, the present paper indicates that a paradigm shift from bone turnover biomarkers to angiogenesis and endocrine markers could shed light on this search.

- Lorenzo-Pouso et al. *Med Oral Patol Oral Cir Buccal* (2019)

Association between biomarkers and medication-related osteonecrosis of the jaws: a systematic review

Conclusions: Although many biomarkers have been associated with MRONJ, the present SR found scarce clinical evidence supporting the use of these biomarkers for the diagnosis and prognosis of MRONJ.

- Moraschini et al. *Oral Surg Oral Med Oral Pathol Oral Radiol* (2019)

Cessation of at-risk Medication

MEMO

Cessation of at-risk medication

- The *AAOMS Position Paper on Bisphosphonate-Related Osteonecrosis of the Jaw*, revised in 2009, recommended discontinuing oral bisphosphonates for 3 months prior to and 3 months following invasive dental surgery – systemic conditions permitting.
- However, there is currently no evidence that interrupting bisphosphonate therapy alters the risk of ONJ in patients following tooth extraction.

- Ruggiero et al. *J Oral Maxillofacial Surg* (2014)- AAOMS Position paper

Pharmacotherapeutics

self CDE continuing education

Cessation of at-risk medication

Bisphosphonate-related osteonecrosis of the jaws: a potential alternative to drug holidays

Douglas D. Damm, DDS • David M. Jones, DDS

Authors	Drug holiday
Damm and Jones et al. (2013)	• No studies to support these recommendations • Based on bone physiology and pharmacokinetics • 50% of serum BP undergoes renal excretion • Osteoclast (life span) : 2 weeks • Serum BP : The majority of free BP within the serum would be extremely low 2 months following the last dose of an oral bisphosphonate ➔ A 2 month drug free period should be adequate prior to an invasive dental procedure.
AAOMS Committee	• Level 5 evidence • Limited data to support or refute the benefits of a drug holiday • A theoretical benefit may still apply for those patients with extended exposure histories (>4 yrs) • The modified drug holiday strategy as described by Damm and Jones to be a prudent approach for those patients at risk.

- Ruggiero et al. *J Oral Maxillofacial Surg* (2014)- AAOMS Position paper

Machine learning to predict the occurrence of bisphosphonate-related osteonecrosis of the jaw associated with dental extraction: A preliminary report

- Kim et al. *Bone* (2018)

Table 1
Comparison of parameters between cases and controls.

BRONJ	Yes (case)	No (control)	p	
	(n = 41)	(n = 84)		
Drug holiday before dental extraction				
Mean ± sd	24.5 ± 65.3	111.6 ± 106.1	< 0.001***	Mann-Whitney *U* test
Median [IQR]	0.0 [0.0; 0.0]	95.0 [14.0; 168.0]		
3 months or shorter	37 (90.2%)	39 (46.4%)	< 0.001***	Chi square test
Longer than 3 months	4 (9.8%)	45 (53.6%)		

The effect of bisphosphonate discontinuation on the incidence of postoperative medication-related osteonecrosis of the jaw after tooth extraction

- Kang et al. *J Korean Assoc Oral Maxillofac Surg* (2020)

Controversial

Results: The BP-continuation (BPC) and BP-discontinuation (BPDC) groups included 179 and 286 patients, respectively. One patient in the BPC group and no patients in the BPDC group developed MRONJ (P=0.385). The patients in the BPDC group stopped receiving BP therapy at a mean of 39.0±35.5 months prior to tooth extraction.

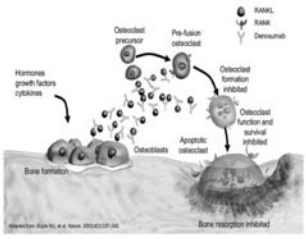
Conclusion: The possibility of pre-existing MRONJ in the extraction area must be considered during the extraction procedure. Routine discontinuation of BP medications for several months before the extraction procedure should be carefully considered, as evidence of its efficacy in reducing the development of post-extraction MRONJ is limited.

MEMO

Denosumab 은 안전한 약제인가?

Google image (fiercepharma.com)

RANK ligand inhibitor (denosumab) is an antiresorptive agent that exists as a fully humanized antibody against RANK ligand (RANK-L) and inhibits osteoclast function and associated bone resorption. When denosumab treatment of multiple myeloma. Interestingly, in contrast to bisphosphonates, RANK ligand inhibitors do not bind to bone and their effects on bone remodeling are mostly diminished within 6 months of treatment cessation.



- Lipton et al. *Clinical Medicine Insights: Oncology* (2012)

- Ruggiero et al. *J Oral Maxillofacial Surg* (2014)- AAOMS Position paper

Australian Dental Journal

Denosumab and osteonecrosis of the jaws – the pharmacology, pathogenesis and a report of two cases

M O'Halloran,* NM Boyd,† A Smith‡

- Overall incidence of ONJ in cancer patients receiving denosumab was 1.7% [95% CI: 0.9~3.1%]. (Qi et al. 2014)

- Patient #1
  - 60-year-old male / Metastatic carcinoma of the prostate
  - 120mg Xgeva® / monthly
  - No history of BPs or Radiotherapy
  - Spontaneous development
- Patient #2
  - 72-year-old male / Prostate cancer
  - 120mg Xgeva® / monthly
  - Prednisolone (10mg/daily)
  - Extraction

MEMO

Medication-related osteonecrosis of the jaw associated with bisphosphonates and denosumab in osteoporosis

J Bagan[1,2], A Peydró[3], J Calvo[4], M Leopoldo[5], Y Jiménez[6], L Bagan[7]

OBJECTIVE: To describe the clinical characteristics and evolution of our series of medication-related osteonecrosis of the jaws (MRONJ) associated with denosumab in osteoporotic patients.

MATERIAL AND METHODS: We present 10 new cases of MRONJ in patients receiving denosumab for osteoporosis. We describe the mean doses of denosumab, previous bisphosphonate intake, and the clinical characteristics associated with the osteonecrosis, such as local contributing factors, symptoms, and evolution after treatment.

RESULTS: The mean number of denosumab doses was 3.4 ± 2.2. In 90% of patients, there was *a prior* history of oral bisphosphonate intake, with a mean duration of 46.78 ± 25.11 months. The most common local factor was dental extraction (6 cases; 60%), and most cases had necrotic bone exposure (9/10, 90%). Sclerosis of the bone was the most common radiographic finding. Stage I was the most common ONM stage, found in 80%. 'Cure' after conservative treatments was obtained in 71.4%.

CONCLUSIONS: Most of our cases were in the early stages of MRONJ, and the success rate after conservative treatment was high.

Oral Diseases (2016) **22**, 324–329

Case	Age	Gender	Disease	Drug	Doses	Previous bisphosphonate treatment	
						Drug	Months
1	55	F	Osteoporosis	Denosumab	3	–	–
2	59	F	Osteoporosis	Denosumab	2	Ibandronate	52
3	78	F	Osteoporosis	Denosumab	1	Ibandronate	43
4	73	F	Osteoporosis	Denosumab	3	Risedronate	12
5	75	F	Osteoporosis	Denosumab	4	Alendronate	61
6	62	F	Osteoporosis	Denosumab	2	Ibandronate	9
7	90	F	Osteoporosis	Denosumab	6	Alendronate	52
8	77	F	Osteoporosis	Denosumab	1	Risedronate	84
9	86	F	Osteoporosis	Denosumab	8	Ibandronate	36
10	82	F	Osteoporosis	Denosumab	4	Risedronate	12
						Alendronate	60

Denosumab: 60 mg subcutaneously every six months.

- Bagan et al. *Oral Diseases* (2016)

Journal of Cranio-Maxillo-Facial Surgery 46 (2018) 1515–1525

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Osteonecrosis of the jaw in patients treated with denosumab: A multicenter case series

Suad Aljohani [a, b, *], Robert Gaudin [c], Julian Weiser [d], Matthias Tröltzsch [a], Michael Ehrenfeld [a], Gabriele Kaeppler [a], Ralf Smeets [d], Sven Otto [a]

[a] Department of Oral and Maxillofacial Surgery, Ludwig-Maximilians-Universität, Head: Prof. Dr. Med. Dr. Med. Dent. Michael Ehrenfeld, Lindwurmstrasse 2a, 80337, Munich, Germany
[b] Department of Oral Basic & Clinical Sciences, King Abdulaziz University, Al Sulaimaniyah, 21589, Jeddah, Saudi Arabia
[c] Department of Oral and Maxillofacial Surgery, Charité University, Aßmannshauser Str. 4-6, 14197 Berlin, Germany
[d] Department of Oral and Maxillofacial Surgery, University Medical Center Hamburg-Eppendorf, Martinistraße 52, 20251 Hamburg, Germany

Table 1
Summary of the clinical characteristics

Case	Age	Sex	Primary disease	Drug dose	Number of doses	Pts of BPs	Comorbidities	Local factors
1	58	F	OP	60 mg/6 months	1	Yes	Allergy	Extr
2	68	F	OP	60 mg/6 months	2	No	RA, allergy, hypothyroidism	Extr, P, PI
3	67	M	Prostate ca	120 mg/4 weeks	...	Yes	CI, DM II, CHD	Scaling and RP, P
4	61	M	Prostate ca	120 mg/4 weeks	...	Yes	RA, CI	Extr
5	75	F	OP	60 mg/6 months	...	No	HT, COPD, CVD	Extr
6	66	M	Prostate ca	120 mg/4 weeks	10	No	HT, hypothyroidism	Extr
7	66	F	Breast ca	120 mg/4 weeks	22	No	Allergy, DM II	Local trauma
8	76	F	Lung ca	120 mg/4 weeks	5	Yes	HT	Extr
9	56	F	Breast ca	120 mg/4 weeks	7	Yes	Allergy	Extr, local trauma
10	69	M	Prostate ca	120 mg/4 weeks	20	Yes	HT	Extr
11	70	M	Prostate ca	120 mg/4 weeks	...	Yes	CVD	Extr
12	67	F	Breast ca	120 mg/4 weeks	7	No	OP, CI	Extr
13	76	F	OP	60 mg/6 months	8	Yes	RA, CI	P
14	78	M	Prostate ca	120 mg/4 weeks	13	No	DM II, CI	Extr
15	80	F	Breast ca	120 mg/4 weeks	29	No	HT, RA	P
16	65	M	Prostate ca	120 mg/4 weeks	36	Yes	Allergy, CI	Extr
17	58	F	Breast ca	120 mg/4 weeks	35	Yes	Allergy	None
18	65	F	Melanoma	120 mg/4 weeks	...	No	HT, RA, allergy, hypothyroidism	Extr
19	56	F	Breast ca	120 mg/4 weeks	5	Yes	CVD, allergy	Extr
20	74	M	Thyroid ca	120 mg/4 weeks	8	Yes	COPD, allergy, Asthma	P
21	50	F	Breast ca	120 mg/4 weeks	24	No	CVD	Extr
22	74	F	Breast ca	120 mg/4 weeks	45	Yes	HT, allergy	None
23	76	F	Breast ca	120 mg/4 weeks	18	No	None	Extr, local trauma
24	64	F	Breast ca	120 mg/4 weeks	8	Yes	OP, allergy	Extr
25	63	F	Breast ca	120 mg/4 weeks	3	Yes	DM II, allergy	Local trauma
26	72	M	Prostate ca	120 mg/4 weeks	36	No	DM II, HT	None
27	52	F	Breast ca	120 mg/4 weeks	24	No	Allergy	None
28	79	F	Breast ca	120 mg/4 weeks	17	No	DM II	Extr, P
29	67	M	Breast ca	120 mg/4 weeks	10	No	Hypothyroidism, allergy	Extr, local trauma
30	78	M	OP	60 mg/6 months	8	Yes	HT, hypothyroidism	Local trauma
31	71	M	Breast ca	120 mg/4 weeks	...	No	CVD, hypertension	None
32	74	F	Kidney ca	120 mg/4 weeks	6	Yes	HT, RA, CI, Rheumatoid	Local trauma
33	72	F	OP	60 mg/6 months	5	Yes	CVD, allergy	P
34	67	F	Breast ca	120 mg/4 weeks	30	No	HT	None
35	78	M	Prostate ca	120 mg/4 weeks	35	Yes	DM II	Extr, P
36	82	F	OP	60 mg/6 months	8	No	CVD, CBD	Extr, P
37	65	M	Prostate ca	120 mg/4 weeks	...	Yes	COPD, DM II	P
38	66	M	MM	120 mg/4 weeks	...	Yes	Hypothyroidism, HT, CVD	Extr
39	80	F	Breast ca	60 mg/3 months	3	Yes	RA, CI	Extr
40	48	F	Breast ca	120 mg/4 weeks	30	No	None	Extr
41	73	F	Breast ca	120 mg/4 weeks	3	Yes	CVD, allergy, hypothyroidism	None
42	71	F	Breast ca	120 mg/4 weeks	22	Yes	OP	None
43	74	F	Breast ca	120 mg/4 weeks	28	Yes	CVD, allergy	P
44	60	F	Breast ca	120 mg/4 weeks	24	No	None	Extr
45	67	M	Prostate ca	120 mg/4 weeks	22	No	None	Extr
46	74	F	Breast ca	120 mg/4 weeks	...	Yes	Renal insufficiency II	None
47	86	F	Breast ca	120 mg/4 weeks	...	Yes	None	Extr
48	84	F	MM	120 mg/2 months	...	No	DM II	Extr
49	73	F	OP	60 mg/6 months	...	Yes	HT	Extr
50	52	M	Kidney ca	120 mg/4 weeks	24	No	Cholesterol nephrosclerosis	Extr
51	74	F	OP	60 mg/6 months	1	No	COPD, HT	Extr
52	55	F	Breast ca	120 mg/4 weeks	48	Yes	None	Extr
53	56	M	Prostate ca	120 mg/4 weeks	...	No	HT	None
54	74	M	Prostate ca	120 mg/4 weeks	6	No	HT	None
55	73	M	Kidney ca	120 mg/4 weeks	12	No	None	Site of implant
56	72	M	Thyroid Ca	120 mg/4 weeks	30	No	HT	PI
57	86	M	Prostate ca	120 mg/2 months	10	Yes	HT, history of kidney cancer	Site of implant
58	77	M	Prostate ca	120 mg/4 weeks	...	No	HT	None
59	73	M	Prostate ca	120 mg/4 weeks	24	Yes	None	Extr
60	83	M	Prostate ca	120 mg/3 months	...	No	DM II	None
61	82	F	Breast ca	60 mg/6 months	5	No	COPD, CVD, HT	Bridge augmentation
62	85	M	Kidney ca	120 mg/4 weeks	12	No	CBD, HT	Extr
63	75	F	Breast ca	120 mg/4 weeks	...	No	HT	Extr

Drugs: denosumab, Pts: history, BPs: bisphosphonates, ... : missing data, M: male, F: female, OP: osteoporosis, MM: multiple myeloma, HT: hypertension, RA: rheumatoid arthritis, DM II: type 2 diabetes mellitus, CCI: cardiocerebrovascular, CVD: coronary vascular disease, COPD: coronary obstructive pulmonary disease, CBD: chronic renal disease, Extr: extraction, P: periodontitis, PI: peri-implantitis, RP: root planing.

Osteonecrosis of the jaw in patients treated with denosumab: A multicenter case series

Suad Aljohani [a, b, *], Robert Gaudin [c], Julian Weiser [d], Matthias Tröltzsch [a], Michael Ehrenfeld [a], Gabriele Kaeppler [a], Ralf Smeets [d], Sven Otto [a]

MEMO

Osteonecrosis of the jaw in patients treated with denosumab: A multicenter case series

Suad Aljohani [a, b, *], Robert Gaudin [c], Julian Weiser [d], Matthias Tröltzsch [e], Michael Ehrenfeld [f], Gabriele Kaeppler [g], Ralf Smeets [d], Sven Otto [d]

Case	Age	Sex	Primary disease	Dmab dose	Number of doses	Hx of BPs	Comorbidities	Local factors
2	68	F	OP	60 mg/6 months	2	No	RA, allergy, hypothyrodism	Extr, P, PI
5	75	F	OP	60 mg/6 months	...	No	HT, COPD, CVD	Extr
36	82	F	OP	60 mg/6 months	6	No	CVD, CRD	Extr, P
51	74	F	OP	60 mg/6 months	1	No	COPD, HT	Extr

Case	Drug Holiday (M)	Treatment	Follow-up (M)	Treatment outcome
2	6	Surgical	16	Healing
5	6	Surgical	7	No healing
36	7	Surgical	3	Healing
51	unknown	Surgical	3	Healing

- Clinical chracteristics and treatment outcomes were not significantly different between patients with and without previous treatment intake of bisphosphonate

Vol. 125 No. 1 January 2018

Rapid onset of osteonecrosis of the jaw in patients switching from bisphosphonates to denosumab

Noam Yarom, DMD,[a,b] Towy Sorel Lazarovici, DMD,[c] Sara Whitefield, BDS,[b] Tal Weissman, DMD,[c] Oshri Wasserzug, MD,[d] and Ran Yahalom, DMD[e]

Table I. Demographic characteristics

	BP and denosumab (N = 22)	*Denosumab (N = 9)*	*P value*
Age, y (mean ± SD)	67.3 ± 8.3	65.3 ± 10.60	.58
Gender, n			
Male	9 (41%)	8 (89%)	.021
Female	13 (59%)	1 (11%)	
Underlying disease, n			
Breast cancer	9 (40.9%)	1 (11.1%)	.035
Prostate cancer	6 (27.3%)	7 (77.8%)	
Lung cancer	1 (4.5%)	1 (11.1%)	
Osteoporosis	6 (27.3%)	—	
Diabetes mellitus	5 (22.7%)	2 (22.2%)	1.00
Smoking, n	0 (0%)	0 (0%)	1.00

BP, bisphosphonates; *SD*, standard deviation.

Table II. Clinical features

Characteristic	*BP and denosumab (n = 22)*	*Denosumab (n = 9)*	*P value*
Mean no. of denosumab doses until symptom onset (median)	8.5 (4.5)	19.1 (12)	.025
Mean accumulative dose of denosumab until symptom onset, mg	982	2293	.018
Triggering event, n (%)			
Dentoalveolar surgery	6 (27.3)	2 (22.2)	1.00
Spontaneous	16 (72.7)	7 (77.8)	
Location of ONJ, n (%)			
Mandible	15 (68.2)	4 (44.4)	.45
Maxilla	6 (27.3)	4 (44.4)	
Both	1 (4.5)	1 (11.1)	

BP, bisphosphonates; ONJ, osteonecrosis of the jaw.

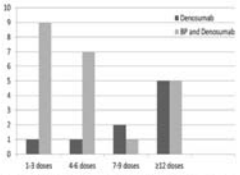


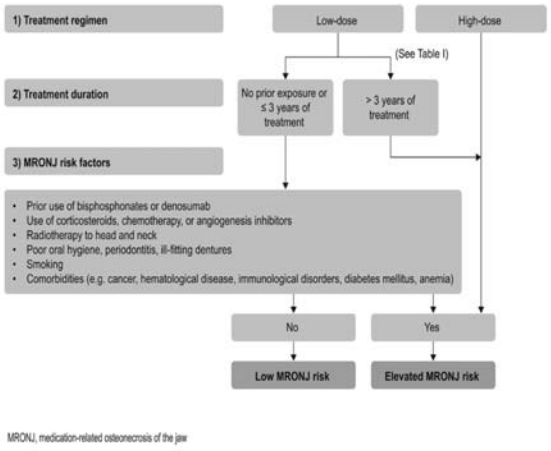
Fig. 1. Number of denosumab doses before the onset of symptoms of osteonecrosis of the jaw.

Conclusions. Denosumab-induced ONJ might develop rapidly in patients previously treated with BP. ONJ developed spontaneously in most patients treated with denosumab. In light of our sample being small, there is need for further investigation on our conclusions. (Oral Surg Oral Med Oral Pathol Oral Radiol 2018;125:27–30)

- Yarom et al. *Oral Surg Oral Medicine Oral Pathol Oral Radiol* (2018)

Patient evaluation and Management

MEMO



- Nicolatou-Galitis et al. *Oral Surg Oral Med Oral Pathol Oral Radiol* (2019)

Prophylactic dental treatment

- Prophylactic dental treatment should be carried out on all high-risk patients to minimize the probability of its development.
- Extraction of partially embedded teeth; Conservative endodontic and prosthodontic therapies of teeth with good prognosis; Periodontal stabilization splints for teeth with grade 1 or 2 mobility in patients with good dental hygiene, Extraction of such teeth in patients whose dental hygiene is poor; Identification and treatment of occult pockets of infection

- Nicolatou-Galitis et al. *Oral Surg Oral Med Oral Pathol Oral Radiol* (2019)
- Ruggiero et al. *J Oral Maxillofacial Surg* (2014)- AAOMS Position paper

Initiation or Restart of bisphosphonate or denosumab

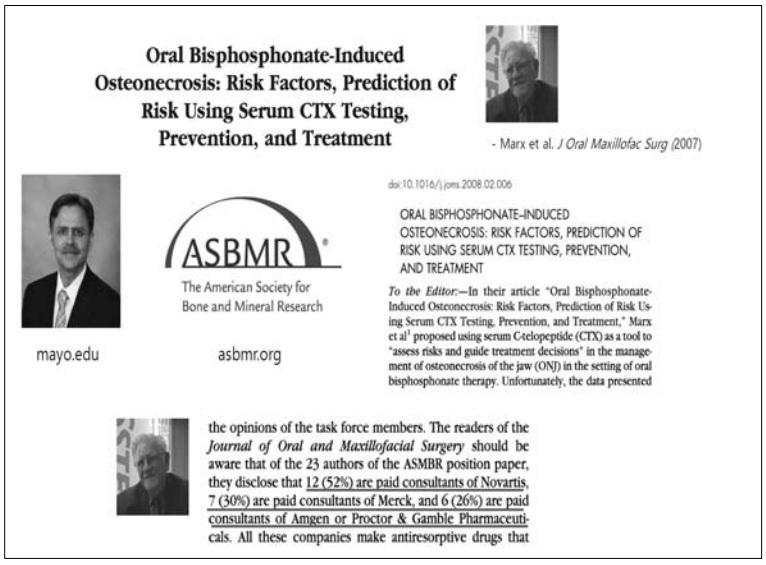
- In our opinion, bisphosphonate or denosumab therapy should not be initiated before the mucosa has healed and adequate bone remodeling has occurred; this is unlikely to happen within 1 month of dental treatment.

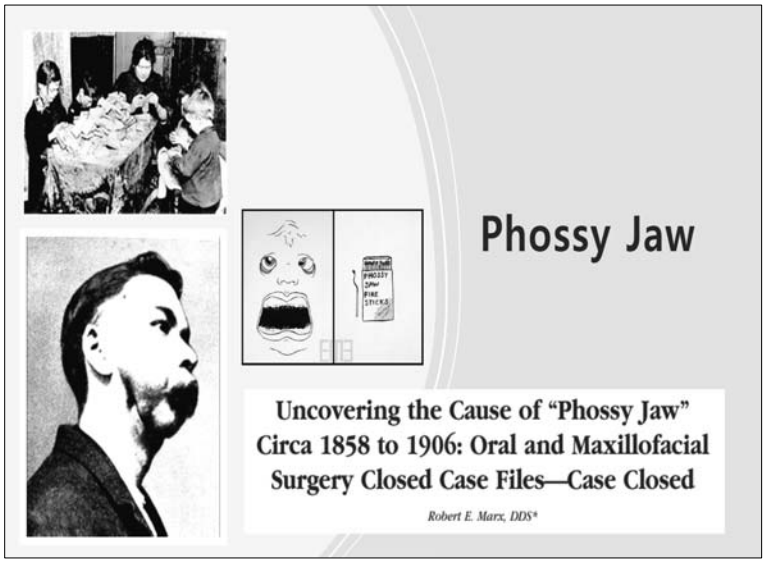
- Nicolatou-Galitis et al. *Oral Surg Oral Med Oral Pathol Oral Radiol* (2019)

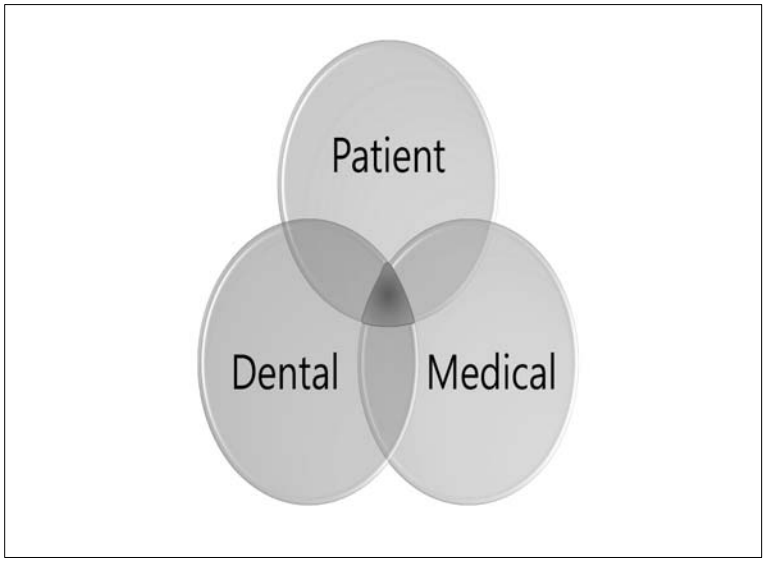
- The antiresorptive should not be restarted until osseous healing has occurred.

- Ruggiero et al. *J Oral Maxillofacial Surg* (2014)- AAOMS Position paper

MEMO


Oral Bisphosphonate-Induced Osteonecrosis: Risk Factors, Prediction of Risk Using Serum CTX Testing, Prevention, and Treatment
- Marx et al. J Oral Maxillofac Surg (2007)
mayo.edu
ASBMR
The American Society for Bone and Mineral Research
asbmr.org
doi:10.1016/j.joms.2008.02.006
ORAL BISPHOSPHONATE-INDUCED OSTEONECROSIS: RISK FACTORS, PREDICTION OF RISK USING SERUM CTX TESTING, PREVENTION, AND TREATMENT
To the Editor:—In their article "Oral Bisphosphonate-Induced Osteonecrosis: Risk Factors, Prediction of Risk Using Serum CTX Testing, Prevention, and Treatment," Marx et al[1] proposed using serum C-telopeptide (CTX) as a tool to "assess risks and guide treatment decisions" in the management of osteonecrosis of the jaw (ONJ) in the setting of oral bisphosphonate therapy. Unfortunately, the data presented
the opinions of the task force members. The readers of the Journal of Oral and Maxillofacial Surgery should be aware that of the 23 authors of the ASMBR position paper, they disclose that 12 (52%) are paid consultants of Novartis, 7 (30%) are paid consultants of Merck, and 6 (26%) are paid consultants of Amgen or Proctor & Gamble Pharmaceuticals. All these companies make antiresorptive drugs that


Phossy Jaw
Uncovering the Cause of "Phossy Jaw" Circa 1858 to 1906: Oral and Maxillofacial Surgery Closed Case Files—Case Closed
Robert E. Marx, DDS*


Patient
Dental
Medical

Take Home Message

- 치과치료 전·후 골다공증 약제의 중단에 대해서는 보다 많은 연구가 필요하다.
- 약물관련 악골괴사증을 예측할 수 있는 biomarker 에 대해서도 보다 많은 연구가 필요하다.
- 가능하다면 골다공증 치료 전 예방적 치과치료가 추천된다.
- Denosumab이 완전히 안전한 약제인지에 대해서도 보다 많은 연구가 필요하다.
- 환자의 현재 상태에 대한 치과와 의과 사이에 보다 활발한 의사소통이 필요하다.

MEMO

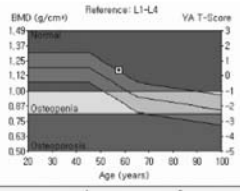
일차 진료에 필요한 취약성 척추 골절의 진단 및 관리

송 광 섭

중앙대학교 의과대학 정형외과

Vertebral Fragility Fracture (VFF)

✓F/58 기침하다 발생한 허리 통증으로 내원



Region	BMD (g/cm²)	Young-Adult (%)	T-Score	Age-Matched (%)	Z-Score
L1	0.991	93	-0.6	101	0.0
L2	1.157	102	0.2	111	0.9
L3	1.189	105	0.4	113	1.1
L4	1.274	112	1.1	121	1.8
L1-L2	1.076	98	-0.2	106	0.5
L1-L3	1.121	101	0.1	109	0.8
L1-L4	1.165	104	0.3	112	1.0
L2-L3	1.175	104	0.3	112	1.0
L2-L4	1.211	107	0.6	115	1.3
L3-L4	1.234	108	0.8	117	1.5

MEMO

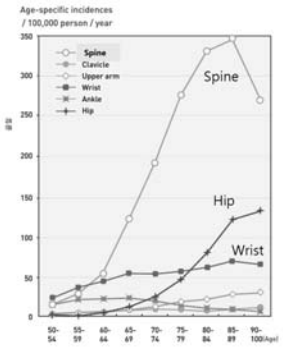
Vertebral Fragility Fracture (VFF)

- Definition
  - ✓Developed because of a minor injury (a force equivalent to a fall from a standing height or less) or in the absence of a recognized cause
- Prevalence
  - ✓Increases with advancing age
  - ✓Scandinavia (26%), Eastern Europe (18%), North America (20–24%)
  - ✓Age-standardized rates in studies combining hospitalized and ambulatory vertebral fractures are **highest in South Korea, USA, and Hong Kong and lowest in the UK**

Ballane G, Cauley JA, Luckey MM, et al.
Worldwide prevalence and incidence of osteoporotic vertebral fractures. Osteoporos Int 2017;28(5):1531e42.

MEMO

Age-specific incidence of Fragility fractures in S. Korea



Spine
- Increases rapidly at 60s

Hip
- Increase rapidly at 70s

Health Insurance review and Assessment Service report 2008-2009, Korea

Vertebral Fragility Fracture (VFF)

- Clinical significance
  - ✓Impact on quality of life (QOL) of the older population
  - ✓Pain, decrease mobility and physical function, sleep loss, increased mortality

Salaffi F, Cimmino MA, Malavolta N, et al.
J Rheumatol 2007;34(7):1551e60.

  - ✓Economic burden reaching £12 million per year in the UK or $113 million per year in Australia in direct medical costs

Ballane G, Cauley JA, Luckey MM, et al.
Osteoporos Int 2017;28(5):1531e42.

  - ✓Having previous vertebral fractures can increase the risk of a future fracture 5-fold

Lindsay R, Silverman SL, Cooper C, et al.
JAMA: J Am Med Assoc 2001;285(3):320e3.

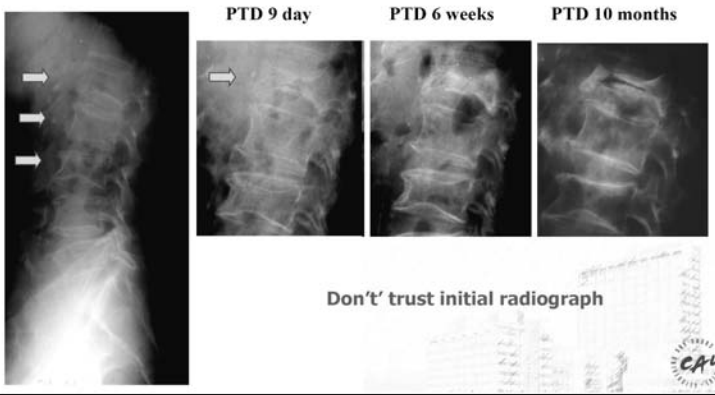
VFF – Difficulties in diagnosis

- Acute vertebral fracture
  - ✓Occurs even **without or minor trauma**
  - ✓Sometimes **has no specific symptoms**
  - ✓Missed by physicians → legal problem
- Delayed initial diagnosis
  - ✓**Results in non-union**
  - ✓**Kyphotic deformities**
  - ✓Poor prognosis
- Confirmation tests
  - ✓MRI
  - ✓CT
  - ✓Serial plain radiographs

MEMO

VFF – Difficulties in diagnosis

✓M/72, 버스가 급정거하면서 바에 부딪힘, 허리가 조금 아프다.



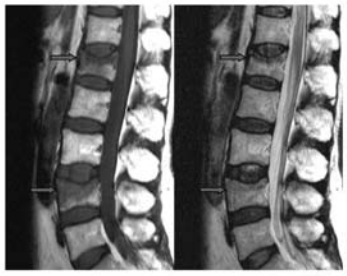
Don't' trust initial radiograph

Diagnosis – Difficulties in diagnosis

✓F/72, 외상력 없이 허리 통증

Diagnosis – Difficulties in diagnosis

✓Mainstay of Dx:
- MRI (T1 image, low signal)
- Bone scan..
- X-ray



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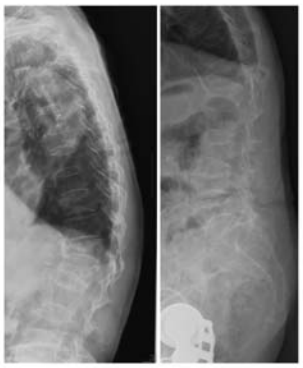
Diagnosis – Difficulties in diagnosis

✓F/84 intractable back pain for 1 month.



Diagnosis – Difficulties in diagnosis

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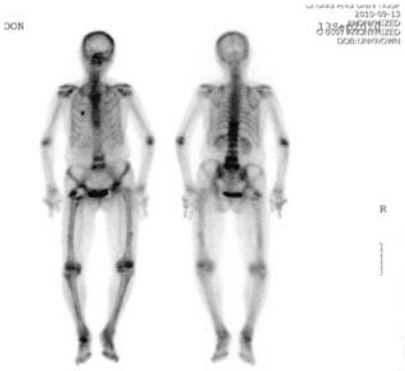

Diagnosis – Clinical suspicion

- What is the most reliable P/E finding to suspect VFF?

✓Tenderness ?

✓Sudden back pain (within 2wks)
✓Emergency room or outpatient clinic

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Diagnosis – clinical suspicionculties in diagnosis

- Prospective study in 4 independent institutions
- Inclusion
  - ✓Aged over 60 years
  - ✓Sudden back pain (within 2wks)
  - ✓Outpatient clinic
- Exclusion
  - ✓Hx. of high-energy trauma
- Evaluations
  - ✓Suggested physical exams - 8
  - ✓Confirmatory exams: MRI, CT, serial plain radiographs

Physical examination for VFF – Results

- Total 179 cases
  - ✓Male : female (35 : 144)
  - ✓Mean age: 73.96 (95% CI 72.84-75.08)
  - ✓Fracture : Non-fracture (106 : 73)
  - ✓Confirmation test
    Serial x-ray : 74, CT scan : 23, MRI : 82
  - ✓Tenderness (Y: 66, N: 113)
  - ✓Midline pain (Y: 150, N: 29)
  - ✓Paraspinal pain (Y: 145, N: 34)
  - ✓Hight(cm): 156.16 (95% CI 154.85-157.47)
  - ✓Weight(kg): 57.83 (95% CI 56.28-59.38)
  - ✓BMD (Lumbar, g/cm²): 0.907 (95% CI 0.882-0.933)
  - ✓BMD (Femur neck, g/cm²): 0.672 (95% CI 0.653-0.690)
  - ✓BMD (Total hip, g/cm²): 0.711 (95% CI 0.690-0.732)

Physical examination for VFF - Methods

- **Forward bending test in supine**

- **Backward bending test in supine**

- **Forward bending test in sitting**

- **Backward bending test in sitting**

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Physical examination for VFF - Methods

- Sitting for 5 seconds

- Stand to sitting, sitting to stand
- Tenderness in sitting position

- Standing for 5 seconds

- Walking 10 steps

Evaluation of Diagnostic value of each test - by McNemar's test

Test	P-value
Forward bending (supine)	0.072
Backward bending (supine)	<0.001
Sitting for 5 seconds	<0.001
Forward bending (sitting)	<0.001
Backward bending (sitting)	<0.001
Standing for 5 seconds	<0.001
Sitting to standing & standing to sitting	<0.001
Walking 10 steps	<0.001
X-ray reading (observer 1 #1)	0.401
X-ray reading (observer 1 #2)	0.118
X-ray reading (observer 2 #1)	0.031
X-ray reading (observer 2 #2)	0.086

Sensitivity, specificity, PPV, NPV of each test

Test	Sensitivity (%)	Specificity (%)	Positive predictive value (PPV, %)	Negative predictive value (NPV, %)
Forward bending (supine)	90.6	71.2	82.1	83.9
Backward bending (supine)	22.6	93.2	82.8	45.3
Sitting for 5 seconds	14.2	100.0	100.0	44.5
Forward bending (sitting)	27.5	89.3	75.8	
Backward bending (sitting)	3.3	98.6	75.0	
Standing for 5 seconds	2.2	98.6	66.7	
Sitting to standing & standing to sitting	21.3	88.9	70.4	
Walking 10 steps	2.2	97.2	50.0	44.6
X-ray reading (observer 1 #1)	72.6	69.9	77.8	63.8
X-ray reading (observer 1 #2)	66.0	68.5	75.3	58.1
X-ray reading (observer 2 #1)	66.0	74.0	78.7	60.0
X-ray reading (observer 2 #2)	70.8	75.3	80.6	64.0

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Key steps for diagnosis for VFF

- History taking
  - ✓Onset
  - ✓Trauma history
  - ✓Aggravating or Relieving factors
- Physical examination
  - ✓Deep tenderness
  - ✓**Forward bending test in supine position**
- Warning for delayed diagnosis
  - ✓Self protection from legal problems
  - ✓Consider confirmation tests

Treatment for VFF

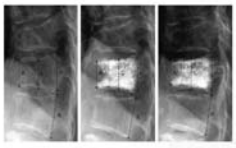
- Conservative management
  - ✓**Golden standard,** Significant reduction of pain in the first 4 weeks
  - ✓Analgesics
    NSAIDs, opioids, ...
  - ✓Braces
    Rigid or **semi-rigid braces** ?
    For 3 months ?
  - ✓ **Avoiding back flexion activities**

Suzuki N, Ogikubo O, Hansson T.
months. Eur Spine J 2008;17(10):1380e90.

Rzewuska M, Ferreira M, McLachlan AJ, et al.
Eur Spine J 2015;24(4):20

Treatment for VFF

- Interventional treatment: VP or KP
  - ✓When non-invasive, conservative care fails to improve patients' symptoms, interventional approaches, including balloon **kyphoplasty** or **vertebroplasty**, are often recommended.
  - ✓ Internal splinting role to reduce pain
  - ✓ **Integration to bone in VB? , FB**



Buchbinder R, Johnston RV, Rischin KJ, et al.
2018;11:CD006349.
Clark W, Bird P, Gonski P, et al.
Lancet 2016;388(10052):1408e16.

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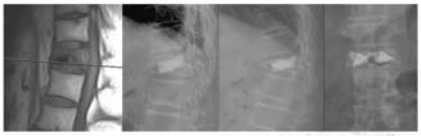
Treatment for VFF

- Interventional treatment: VP or KP

✓Complications?

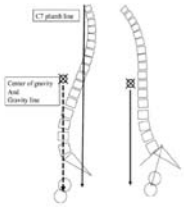
Due to cementing: embolic events, neural damages related with leakage

Cement itself : destructive source



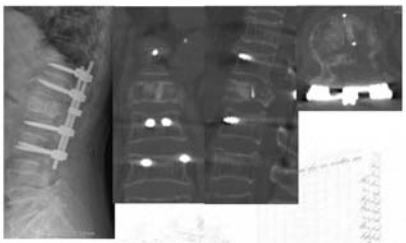
Treatment for VFF

- Surgical management
  - ✓ **Thoraco-lumbar : Myelopathy**



Treatment for VFF

- Surgical management
  - ✓ **Thoraco-lumbar : Myelopathy**



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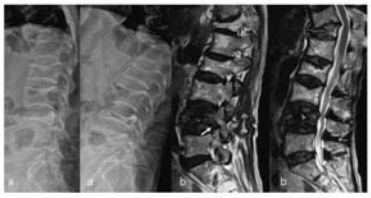
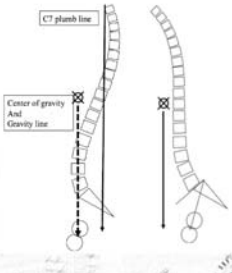
Treatment for VFF

- Surgical management: Lumbar spine
  - ✓ **Radiculopathy due to FS**
  - ✓ **Aggravation at standing**



Treatment for VFF

- Prevention of secondary fracture
  - ✓One of the most important aspect of management of VFF
  - ✓ Anti-osteoporosis medication
  - ✓ Extension exercise, limiting flexion activities
  - ✓ Weight bearing exercise.....



Black DM, Bauer DC, Schwartz AV, et al.
N Engl J Med 2012;366(22):2051e3

Key points for treatment for VFF

- Conservative management
  - ✓Analgesics
  - ✓Braces
  - ✓**Limiting flexion activities**
- Surgical treatment
  - ✓Vertebroplasty, Kyphoplasty
  - ✓Instrumentation ± Fusion
- Prevention of secondary fracture
  - ✓Anti-osteoporosis medication
  - ✓Extension exercise, limiting flexion activities

MEMO

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https://doi.org/10.3346/jkms.2020.35.e116
eISSN 1598-6357·pISSN 1011-8934

JKMS

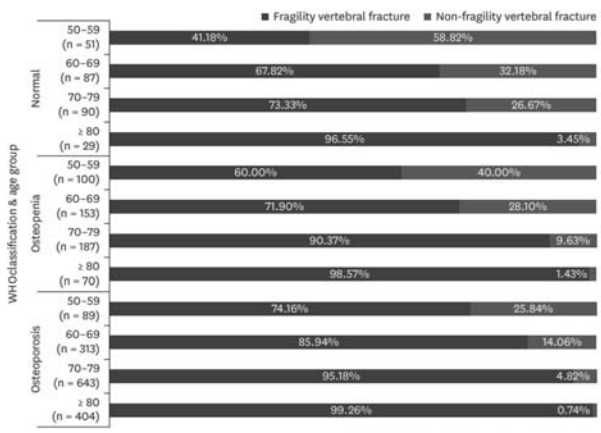
Original Article
Musculoskeletal Disorders, Rehabilitation & Sports Medicine

Check for updates

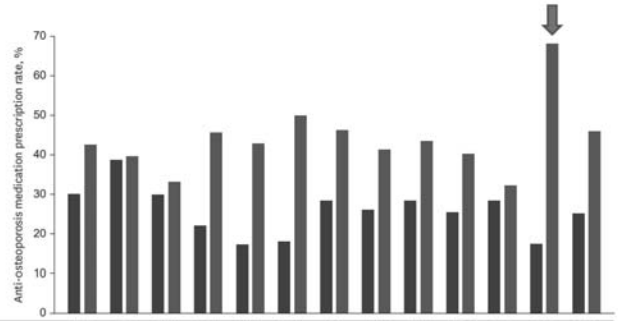
Impact of Bone Mineral Density on the Incidence of Age-Related Vertebral Fragility Fracture

Jeongik Lee,[1] Geunwu Chang,[1] Hyun Kang,[2] Dae-Woong Ham,[1] Jae-Sung Lee,[1] Hyoung Seok Jung,[1] and Kwang-Sup Song[1]

✓VFF might be asymptomatic and often occurs in patients without osteoporosis.



✓Considerable VFFs occurred in the younger age groups without osteoporosis
✓Age itself was another important predictor of VFF especially in older age groups.



	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total
Before fragility vertebral fracture	30.00	38.61	29.84	21.93	17.27	17.97	28.34	25.99	28.28	25.40	28.29	17.42	25.08
After fragility vertebral fracture	42.50	39.60	33.06	45.61	42.73	50.00	46.15	41.24	43.43	40.21	32.24	68.06	45.96

✓ In May 2015, a new National Health Insurance guideline came into effect specifying that patients with osteoporotic fractures with or without osteoporosis (T-score ≤ −2.5) would be treated by anti-osteoporosis medication for 3 years.

MEMO

Take Home messages

- 골다공증(취약성) 척추 골절을 의심할 만한 가장 중요한 증상은 자세를 바꿀 때 심한 통증(motion pain) 이다. 이 소견은 방사선 소견보다 더 신뢰할 수 있다.

"누워서 바로 못 일어나고 옆으로 일어난다"

" 앉았다 일어날 때 칼로 쑤시듯이 아프다. 서 있거나 앉아 있을 때는 안 아프다."

- 초기 단순 방사선 사진으로 골다공증 골절을 진단하기 어렵다. 특히 폐경기 여성에서 2주 이상 motion pain을 호소하는 경우, 척추골절의 가능성을 고지한다.

Take Home messages

- 골다공증(취약성) 척추 골절의 치료는 보존적 치료(보조기, 행동제한 등)으로 대부분 잘 치료된다. 하지만 2-4 주 정도 보존적 치료에도 호전이 없는 경우, 통증 조절목적으로 척추체성형술(VP or KP)을 시행할 수 있다.

- 보존적 치료 중 가장 중요한 점은 골절된 척추체내 불안정성을 줄여 골유합을 유도하는 것이며 후만변형의 발생을 최소화하기 위해 굴곡자세를 제한한다.

Take Home messages

- 골다공증(취약성) 척추 골절의 치료는 3개월정도 수동적 능동적 행동제한이 필요하며 골절이 후 재골절 예방을 위해 약물치료, 신전운동 교육이 필요하다.

- 골다공증 척추골절내 불안정성이 심하거나 너무 심한 통증, 신경증상 발생시 수술적 치료를 시행할 수 있다.