GIMBE®
Gruppo Italiano per la Medicina Basata sulle Evidenze
Evidence-Based Medicine Italian Group

Workshop
Decisioni Cliniche e Prove di Efficacia
Seconda Edizione
Riccione, 26-27 marzo 2004

Workshop Clinici Interattivi (3)

Trattamento dell'osteoporosi. E' davvero tutto chiaro? Prove di efficacia e trial comparativi

Marco Grassi

Discussant
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Scenario Clinico (1)

- La signora Noemi è una barista di 57 anni, con storia di ipertensione lieve, trattata con ACE-inibitore (enalapril, 20 mg/die)
- E' alta 154 cm e pesa 47 kg (BMI 19.8), non fuma, né beve alcolici
- Dall'età di 40 anni diagnosi di asma bronchiale, trattata con steroidi inalatori e beta-stimolanti al bisogno. Saltuariamente (3-4 volte l'anno) assume per brevi periodi steroidi per os (prednisone 25 mg/die per 7-10 gg.)
- Menopausa all'età di 50 anni (1997) con sintomatologia vasomotoria severa ed invalidante sul lavoro.

CLINICAL QUESTIONS

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A. Ritieni che il regime di terapia steroidea praticato dalla signora Noemi, incrementi il rischio di osteoporosi?

1. No
2. Sì

Lipworth BJ.

Systemic adverse effects of inhaled corticosteroid therapy. A systematic review and meta-analysis.

Arch Intern Med 1999;159:941-55.

- In patients with asthma, high doses of inhaled corticosteroids:
  - increase the risk for adrenal suppression (particularly with fluticasone)
  - growth reduction (during the short to medium term)
  - posterior subcapsular cataracts, ocular hypertension and glaucoma, and skin bruising.
- Longitudinal studies show no effects on bone mineral density.

Lipworth BJ. Arch Intern Med 1999

Jones A, Fay JK, Burr M, Stone M, Hood K, Roberts G.

Inhaled corticosteroid effects on bone metabolism in asthma and mild chronic obstructive pulmonary disease

The Cochrane Library, Issue 1, 2004.
Chichester, UK: John Wiley & Sons, Ltd.

REVIEWERS' CONCLUSIONS

• In patients with asthma or mild COPD, there is no evidence of an effect of inhaled corticosteroid at conventional doses given for two or three years on BMD or vertebral fracture.

• Higher doses were associated with biochemical markers of increased bone turnover, but data on BMD and fractures at these doses are not available.

• There is a need for further, even longer term prospective studies of conventional and high doses of inhaled corticosteroids.

Jones A, et al. The Cochrane Library 2004

van Staa TP, Leufkens HG, Cooper C.

The epidemiology of corticosteroid-induced osteoporosis A meta-analysis.

Osteoporos Int 2002;13:777-87. Review

• Studies of oral corticosteroid dose and loss of bone mineral density have reported inconsistent results.

• In this meta-analysis, we used information from 66 papers on bone density and 23 papers on fractures to examine the effects of oral corticosteroids on bone mineral density and risk of fracture.

• Strong correlations were found between cumulative dose and loss of bone mineral density and between daily dose and risk of fractures

van Staa TP, et al Osteoporos Int 2002

• The risk of fracture was found to increase rapidly after the start of oral corticosteroid therapy (within 3 to 6 months) and decrease after stopping therapy.

• The risk remained independent of underlying disease, age and gender.

• We conclude that oral corticosteroid treatment using more than 5 mg (of prednisolone or equivalent) daily leads to a reduction in bone mineral density and a rapid increase in the risk of fracture during the treatment period.

van Staa TP, et al Osteoporos Int 2002

Matsumoto H, Ishihara K, Hasegawa T, et al

Effects of inhaled corticosteroid and short courses of oral corticosteroids on bone mineral density in asthmatic patients. A 4-year longitudinal study.

Chest 2001;120:1468-73

BACKGROUND
It is not certain whether inhaled corticosteroid (ICS) therapy reduces bone mineral density (BMD) in asthmatic patients. In addition, the potential risk of osteoporosis associated with the rescue use of short courses of oral corticosteroids (SC-OCS) is unclear.

OBJECTIVE
To evaluate the effect of inhaled beclomethasone dipropionate (BDP) and SC-OCS on BMD in asthmatic patients.

DESIGN
A 4-year longitudinal study

Matsumoto H, et al. Chest 2001

METHOD
• Lumbar BMD was measured twice by dual-energy x-ray absorptiometry at a mean (+/- SD) interval of 4.2 +/- 0.1 years in 35 asthmatic adults (15 men and 20 post-menopausal women), who had been treated with BDP and SC-OCS.

RESULTS
• Changes in BMD and Z scores in patients receiving high doses of BDP were not significantly different from those of patients receiving lower doses
• Patients receiving frequent SC-OCS (> 2.5 courses per year) showed a significantly greater loss in BMD and Z score compared with those receiving sporadic courses (≤ 2.5 courses per year)

Matsumoto H, et al. Chest 2001

CONCLUSIONS
• ICS therapy per se does not affect BMD, whereas frequent SC-OCS may do so

Matsumoto H, et al. Chest 2001

Scenario Clinico (2)

• In seguito alla comparsa della sintomatologia vasomotoria (1997), la signora Noemi inizia terapia sostitutiva ormonale (TOS) - estradiolo 50 mcg/24 h. a cessione programmata - con immediato beneficio sintomatico.

• Dopo 2 anni, nel tentativo di sospendere la TOS, si assiste ad una rapida, ma attenuata ricomparsa, della sintomatologia vasomotoria.

• Nell'autunno del 2002, alla luce dei risultati dello studio WHI, viene rivalutato il profilo rischio/beneficio della TOS e, considerata la notevole riduzione della sintomatologia vasomotoria, la signora Noemi decide di sospendere la TOS

CLINICAL QUESTIONS

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B. Alla luce delle recenti evidenze, ritieni sia ancora ragionevole prescrivere la TOS solo con l'obiettivo di prevenire l'osteoporosi?

1. No
2. Sì

Ministero Della Salute

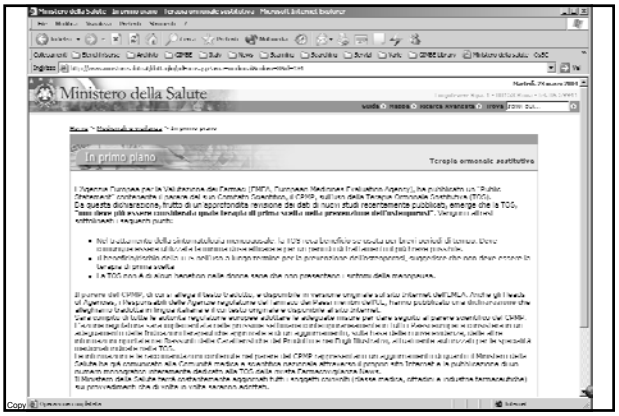
TOS - Terapia Ormonale Sostitutiva

Comunicato del 05 Dicembre 2003

Dichiarazione pubblica dell'EMEA su recenti pubblicazioni riguardanti la terapia ormonale sostitutiva (TOS)

In seguito alla pubblicazione di studi sui rischi correlati alla TOS (WHI, WHI-MS, Million Women Study), alcuni Stati Membri hanno chiesto al Comitato Scientifico dell'EMEA di riesaminare tali dati e di valutare se questi potessero sollevare un problema di Sanità Pubblica in relazione all'uso sicuro ed efficace della TOS.

Ministro della Salute. Comunicato del 5-12-03



- Il rapporto beneficio/rischio della TOS è favorevole nel trattamento dei sintomi della menopausa (climaterio) che influiscono negativamente sulla qualità della vita; deve comunque essere utilizzata la più bassa dose efficace per un tempo di trattamento il più breve possibile.
- Per la prevenzione dell'osteoporosi o delle fratture osteoporotiche, nelle donne con fattori di rischio o con osteoporosi conclamata, il rapporto beneficio/rischio della TOS non è favorevole come trattamento di prima scelta
- Il rapporto beneficio/rischio della TOS è generalmente non favorevole nelle donne sane che non manifestano i sintomi del climaterio.

Ministro della Salute. Comunicato del 5-12-03

- In base a tali considerazioni, il CPMP conclude che c'è un problema di Salute Pubblica relativamente all'uso sicuro ed efficace della TOS.
- L'EMEA ha comunicato i risultati di questa rivalutazione alle Autorità Competenti degli Stati Membri per un'ulteriore valutazione scientifica e l'assunzione di appropriate misure regolatorie.

COMUNICAZIONE DEI RESPONSABILI DELLE AGENZIE REGOLATORIE DEL FARMACO DEI PAESI MEMBRI DELL'UE SULLA SICUREZZA DELLA TERAPIA ORMONALE SOSTITUTIVA (TOS):

NON PIÙ RACCOMANDATA QUALE TERAPIA DI PRIMA SCELTA PER LA PREVENZIONE DELL'OSTEOPOROSI

Ministro della Salute. Comunicato del 5-12-03

Raccomandazioni per i medici prescrittori

- Nel trattamento della sintomatologia menopausale, la TOS reca beneficio se usata per brevi periodi di tempo.
- Deve comunque essere utilizzata la minima dose efficace e per un periodo di trattamento il più breve possibile.
- Il beneficio/rischio della TOS nell'uso a lungo termine per la prevenzione dell'osteoporosi, suggerisce che non deve essere la terapia di prima scelta
- La TOS non è di alcun beneficio nelle donne sane che non presentano i sintomi della menopausa.

Ministro della Salute. Comunicato del 5-12-03

clinical evidence

Fracture prevention in postmenopausal women

Search date May 2003

Olivier Bruyere, John Lamerds, and Jean-Yves Reginster

BMJ Publishing Group

INTERVENTIONS	
Beneficial	**Likely to be ineffective or harmful**
	Hormone replacement therapy 1317
Likely to be beneficial	
Unknown effectiveness	
Unlikely to be beneficial	

Decisione clinica (1)

• Valutato con parametri clinici, senza esecuzione della densitometria ossea, il rischio di osteoporosi, la paziente inizia trattamento con calcio + vitamina D3 (calcio carbonato 1 gr/die + colecalciferolo 880 U.I./die)

CLINICAL QUESTIONS

?

3. Trattamento dell'osteoporosi. E' davvero tutto chiaro?

C. Ritieni che il rischio osteoporotico della signora Noemi, avrebbe giustificato un trattamento farmacologico per la prevenzione primaria delle fratture?

1. No
2. Sì, un bifosfonato (alendronato, risedronato)
3. Sì, raloxifene

Osteoporosis: why, whom, when and how to treat

• If drugs were 100% efficacious, 100% safe, and cost-free, and patients were 100% compliant, the answer would be to treat everyone and early.

• As this is not the case, the most important factor determining whom and when to treat is an individual's absolute risk of fracture.

• Hence, cost effectiveness is mainly driven by the baseline absolute fracture risk.

Seeman E, et al. Med J Aust 2004

La valutazione del rischio basale di fratture

• Those who have already experienced a fracture are at high risk of a further fracture.
• The next group to target are those with osteoporosis risk who have not yet sustained a fracture (table)

Table 1: Risk factors for osteoporosis (when no history of fracture)

Strongest risk factors	Other significant risk factors
Female sex	Caucasian origin
Age >60 years	Early menopause
Family history of osteoporosis	Low BMI
	Smoking
	Sedentary lifestyle
	Long term (>3 months) corticosteroid use

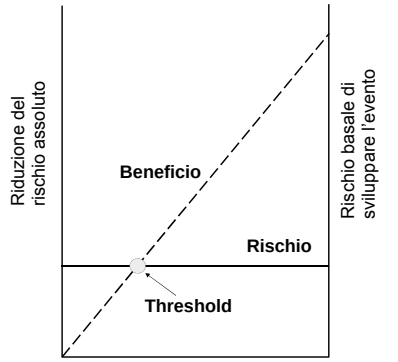
SIGN. July, 2003

Il rischio basale

• Il beneficio che il paziente individuale può ottenere da un intervento terapeutico cresce proporzionalmente al rischio basale di sviluppare un evento sfavorevole.

• Il rischio di eventi avversi conseguenti al trattamento é indipendente dal rischio basale del paziente.

Glasziou P et al. BMJ 1995



Glasziou P, et al. BMJ 1995

Nota 79: alendronato, risedronato, raloxifene

• Per ognuno dei tre farmaci è documentata l' efficacia nel ridurre l' incidenza di fratture post-menopausali

• L' entità di questo effetto, espressa nel numero di donne da trattare per 3 anni, per evitare una frattura vertebrale (NNT) è compreso fra 10 e 20; l' effetto è più modesto per le fratture non vertebrali e per quelle del femore.

• L' utilità di questi farmaci per la prevenzione di fratture in donne con osteoporosi, ma senza fratture pregresse, è fortemente limitata dalla minore frequenza di fratture (NNT 100) e dalle riserve sull' accuratezza della densitometria come singolo indicatore del rischio di fratture.

Nota 79: alendronato, risedronato, raloxifene

• Profilassi secondaria di fratture osteoporotiche in donne in post-menopausa con pregresse fratture vertebrali o del femore non dovute a traumi efficienti.
Ac. alendronico, ac. risedronico (5 mg), ralossifene

• Profilassi secondaria di fratture osteoporotiche in uomini con pregresse fratture vertebrali o del femore non dovute a traumi efficienti;
Ac. alendronico

• Profilassi secondaria di fratture osteoporotiche in donne o uomini in trattamento da almeno 3 mesi con dosi >5 mg/die di prednisone o dosi equivalenti di altri corticosteroidi, con pregresse fratture vertebrali o del femore non dovute a traumi efficienti
Ac. alendronico, ac. risedronico (5 mg)

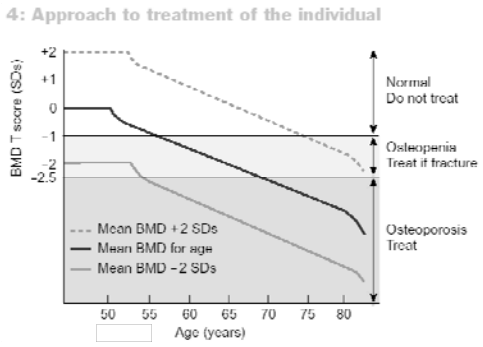
• Profilassi primaria di fratture osteoporotiche in donne in menopausa o uomini di età >50 aa in trattamento da almeno 3 mesi con dosi >5 mg/die di prednisone o dosi equivalenti di altri corticosteroidi.
Ac. alendronico, ac. risedronico (5 mg).

Nota 79: alendronato, risedronato, raloxifene

• In tutte le indicazioni è raccomandata la somministrazione associata di calcio e vitamina D.

• Va, inoltre, sottolineata la necessità di effettuare un adeguato esercizio fisico e di modificare le condizioni ambientali e individuali favorenti i traumi per la prevenzione delle fratture.

• I tre principi attivi non sono privi di effetti collaterali anche gravi, dei quali bisogna tenere conto nella valutazione complessiva della terapia.



Seeman E, et al. Med J Aust 2004

Cranney A, Waldegger L, Graham ID, et al.

Systematic assessment of the quality of osteoporosis guidelines

BMC Musculoskeletal Disorders 2002;3:20

BACKGROUND

• The study objective was to conduct a systematic assessment of the quality of osteoporosis guidelines produced since 1998

METHODS

• Guidelines were identified by searching MEDLINE (1998+), the world wide web, known guideline developer websites, bibliographies of retrieved guidelines, and through consultation with content experts.

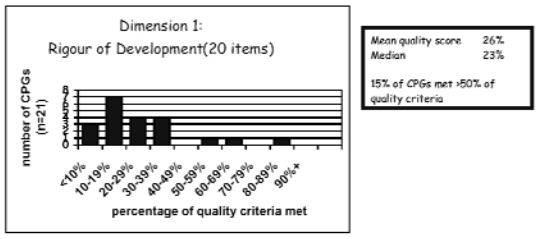
• Each guideline was then assessed by three independent appraisers using the "Appraisal Instrument for Clinical Guidelines".

Cranney A, et al. BMC Musculoskeletal Disorders 2002;3:20

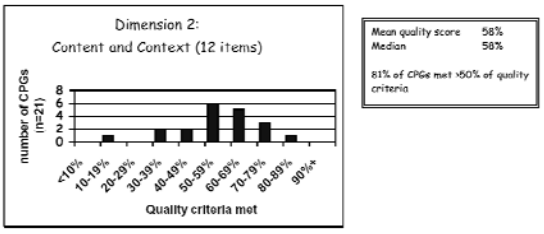
RESULTS

• We identified 26 unique guidelines from 1998–2001 and 21 met our inclusion criteria.

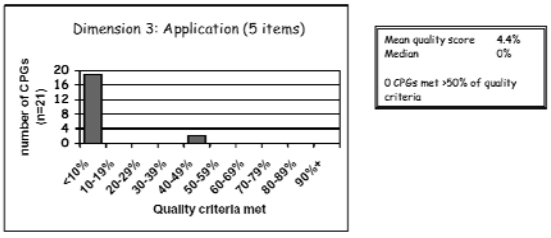
Cranney A, et al. BMC Musculoskeletal Disorders 2002;3:20



Cranney A, et al. BMC Musculoskeletal Disorders 2002;3:20



Cranney A, et al. BMC Musculoskeletal Disorders 2002;3:20



Cranney A, et al. BMC Musculoskeletal Disorders 2002;3:20

CONCLUSION

• The methodological quality of current osteoporosis guidelines is low, although their scores for clinical content were higher.

• Few guidelines were judged as acceptable for use in their current format.

Cranney A, et al. BMC Musculoskeletal Disorders 2002;3:20

AGREE

www.agreecollaboration.org

AGREE
Appraisal of Guidelines for Research & Evaluation

- Strumento per la valutazione di qualità delle LG
- Elaborata da un gruppo internazionale
- Finanziamento della Comunità Europea
- Disponibile in versione italiana

- 23 item in 6 dimensioni
  - obiettivi della LG
  - coinvolgimento delle parti in causa
  - rigore metodologico
  - chiarezza espositiva
  - applicabilità
  - indipendenza editoriale

Guidelines for rating the overall assessment:

Strongly Recommend	the guideline rates high (3 or 4) on the majority of items and most domain scores are above 60%. This indicates that the guideline has a high overall quality and that it could be considered for use in practice without provisos or alterations
Recommend (with provisos or alterations)	the guideline rates high (3 or 4) or low (1 or 2) on a similar number of items and most domain scores are between 30 and 60%. This indicates that the guideline has a moderate overall quality. This could also be due to insufficient or lacking information in the guideline for some of the items. If provisos or alterations are made – and sufficient information is provided on the guideline development method - the guideline could still be considered for use in practice, in particular when no other guidelines on the same clinical topic are available.
Would not recommend	the guideline rated low (1 or 2) on the majority of items and most domain scores are below 30%. This indicates that the guideline has a low overall quality and serious shortcomings. Therefore it should not be recommended for use in practice.

Scottish Intercollegiate Guidelines Network

71 Management of osteoporosis
A national clinical guideline

Score AGREE totale 86%

clinical evidence

BMJ Publishing Group

Fracture prevention in postmenopausal women

Search date May 2003

Olivier Bruyere, John Edwards, and Jean-Yves Reginster

Scenario Clinico (3)

• La signora Noemi, dopo circa un anno, richiede una visita domiciliare per la comparsa di dorsalgia severa, resistente al trattamento con FANS.

• Il dolore era insorto da alcuni giorni quando, in seguito a maldestra manovra di estrazione del cestello della lavastoviglie, la signora aveva perso l'equilibrio e riportato un trauma diretto sulla regione costale.

• La paziente aveva praticato (autoprescrizione) diclofenac 100 mg (1-2 supposte/die) per 7 giorni, con scarso beneficio sul dolore.

Scenario Clinico (3)

• Accentuandosi la sintomatologia algica fino alla impotenza funzionale, la signora Noemi richiede una visita domiciliare.

• La paziente lamenta, a livello del tratto dorso-lombare della colonna, un dolore intenso che si irradia anteriormente all'emitorace destro e si accentua in posizione eretta.

• Obiettivamente: dolorabilità alla digitopressione sia sull'apofisi spinosa delle prime vertebre lombari, sia all'emitorace dx.

Scenario Clinico (3)

• Nel sospetto di una frattura costale richiedo una rx del torace in 2 proiezioni, che evidenzia osteopenia diffusa e schiacciamento della prima vertebra lombare (L1).

• La paziente si rivolge ad un ortopedico che prescrive:
- busto ortopedico per 40 giorni
- alendronato, 10 mg/die

• Viene, inoltre, consigliato, di eseguire
- una densitometria ossea basale ed, a sei mesi, per valutare l'efficacia del trattamento con alendronato.
- controllo trimestrale dei markers di metabolismo osseo (test di Nordin)

CLINICAL QUESTIONS

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D. Ritieni appropriata la prescrizione di alendronato? In caso contrario, quale farmaco avresti prescritto alla signora Noemi?

1. Sì
2. No, Risedronato
3. No, Etidronato
4. No, Raloxifene
5. No, Calcitonina

Osteoporosis: why, whom, when and how to treat

• Comparator trials are unavailable, so whether one drug is more efficacious than another is not known.

• Claims of superiority based on mean differences in relative fracture risk reduction cannot be sustained.

• If the aim is to reduce vertebral fractures, then any one of the agents alendronate, risedronate or raloxifene is suitable

• The choice of drug may also be influenced by the route of administration, by the need for extraskeletal effects, by reimbursement policies

Seeman E, et al. Med J Aust 2004

clinical evidence — BMJ Publishing Group

INTERVENTIONS

Beneficial
Alendronate 1307
Risedronate 1307

Likely to be beneficial
Calcitonin 1311
Calcium plus vitamin D 1309
Etidronate 1307
Hip protectors 1314
Pamidronate 1307

Unknown effectiveness
Environmental manipulation . . 1312
Exercise 1313

Unlikely to be beneficial
Calcium alone 1309
Vitamin D alone 1309

Likely to be ineffective or harmful
Hormone replacement therapy 1317

To be covered in future updates
Effects of dietary intervention
Effects of helmets
Effects of joint and limb pads
Prevention of pathological fractures
Raloxifene

See glossary, p 1319

• **Alendronate**. Two systematic reviews in postmenopausal women have found that alendronate reduces vertebral and non-vertebral fractures compared with placebo.

• **Risedronate**. One systematic review in postmenopausal women has found that risedronate reduces vertebral and non-vertebral fractures compared with placebo.

• **Etidronate.** One systematic review in postmenopausal women found that etidronate reduced vertebral fractures over 2 years compared with control, but found no significant difference in non-vertebral fractures.

• **Calcitonin**. One systematic review in postmenopausal women found that calcitonin reduced vertebral fractures compared with placebo, but found no significant difference between calcitonin and placebo in non-vertebral fractures.

• **Raloxifene**. Will be covered in the next issues

Clinical Evidence. March 2004

Postmenopausal women who have suffered at least one vertebral fracture and who have had osteoporosis confirmed by DXA scanning should be considered for one of the following options:

A **To reduce fracture risk at all sites: treatment with oral alendronate (10 mg daily or 70 mg once weekly + calcium ± vitamin D).**

Although not tested specifically in this scenario in clinical trials, it is likely that risedronate would have equal efficacy to alendronate

A **To reduce vertebral fracture risk: treatment with oral raloxifene (60 mg daily + calcium ± vitamin D).**

B **To reduce vertebral fracture risk: treatment with intranasal calcitonin (200 IU daily + calcium ± vitamin D).**

SIGN. July, 2003

Combination of treatments

• In clinical trials bisphosphonates (alendronate, etidronate, or risedronate), raloxifene and calcitonin have usually been assessed in conjunction with calcium +/- vitamin D.

• Doses of calcium have varied from 500 to 1,000 mg and vitamin D from 6.25 to 20 mg (250 to 800 IU) per day.

• Where calcium intake is suboptimal, daily doses of up to 1000 mg calcium carbonate plus 20 mg (800 IU) vitamin D are appropriate for use in association with these drugs (in the absence of conditions associated with hypercalcaemia).

SIGN. July, 2003

Combination of treatments

• Several clinical trials have reported that the addition of bisphosphonate to HRT or of bisphosphonate to raloxifene confers additional benefit regarding BMD compared with monotherapy.

• Further studies are required to elucidate whether such combinations achieve greater reductions in fracture incidence.

• Until data are available, combinations of HRT or raloxifene with bisphosphonates are not recommended.

SIGN. July, 2003

CLINICAL QUESTIONS

?

3. Trattamento dell'osteoporosi. E' davvero tutto chiaro?

E. Ritieni appropriato monitorare il trattamento farmacologico con la densitometria ossea?

1. No
2. Sì, ogni sei mesi
3. Sì, ogni anno
4. Sì, ogni due anni

Monitoring treatment effects with DXA

• There is evidence of a relationship between therapy associated increases in BMD and the extent of fracture risk reduction.

• The efficacy of monitoring BMD responses by DXA has not been evaluated by clinical trial, although it has been a key end point in most clinical trials relating to osteoporosis management.

•Application of repeat DXA to individual patients requires consideration of the following:

SIGN. July, 2003

Monitoring treatment effects with DXA

• Application of repeat DXA to individual patients requires the following considerations:

- The lumbar spine trabecular bony site is the preferred site for follow up DXA.
- Increases of BMD of at least 3-4% are required as the least significant difference that is likely to exceed the error of the measurement.
- Follow-up should normally be undertaken only after at least two years of therapy.

SIGN. July, 2003

CLINICAL QUESTIONS

?

3. Trattamento dell'osteoporosi. E' davvero tutto chiaro?

F. Ritieni appropriato monitorare l'efficacia del trattamento farmacologico con markers di metabolismo osseo?

1. No
2. Sì, sempre
3. Sì, solo in particolari circostanze

Formation markers		Resorption markers			
Osteocalcin		Hydroxyproline	Hyp	Pyridinoline	PYD
Osteocalcin (or bone gla-protein)	OC	Hydroxylysine	Hyl		
Undercarboxylated osteocalcin	OC			Deoxypyridinoline	DPD
Total osteocalcin	total OC	Galactosyl hydroxylysine	Gal-Hyl		
		Glucosyl galactosyl hydroxylysine	Glu-Gal-Hyl	*Type I collagen telopeptides*	
Intact osteocalcin	OC [1–49]			N-terminal crosslinking telopeptide of type I collagen	NTX-I
N-mid fragment of osteocalcin	OC [1–43]				
Alkaline phosphatase				C-terminal crosslinking telopeptide of type I collagen	CTX-I
Total alkaline phosphatase	total ALP				
Bone alkaline phosphatase	bone ALP				
				C-terminal crosslinking telopeptide of type I collagen generated by MMPs	CTX-MMP
Type I collagen propeptides					
Procollagen type I N propeptide	PINP				
Monomer of Procollagen type I N propeptide	mon PINP			Bone sialoprotein	BSP
Intact procollagen type I N propeptide	intact PINP			Acid phosphatase	ACP
Total procollagen type I N propeptide	total PINP			Tartrate-resistant acid phosphatase	TRACP
Procollagen type I C propeptide	PICP				

Delmas PD, et al. Osteoporosis Int, 2000

ICSI
INSTITUTE FOR CLINICAL SYSTEMS IMPROVEMENT

Institute for Clinical Systems Improvement (ICSI)

Biochemical markers for bone turnover in osteoporosis

February, 2001

- The assessment of serum and urine biochemical markers of bone turnover is safe and minimally invasive.
- It is not possible to predict an individual's fracture risk from biochemical marker measurements. A combination of bone mineral density and biochemical marker measurements may be of greater value but the data are inconclusive.
- Biochemical markers do not have adequate sensitivity and specificity to predict osteoporosis in individual, untreated patients.

ICSI, 2001

- There is no conclusive evidence that biochemical markers may be used to assist in selecting the type of therapy or to predict the amplitude of the BMD response for an individual patient.
- Although biochemical markers have the potential to be used to motivate individuals to maintain a therapy program, there are no studies of the use of biochemical markers for this purpose.

ICSI, 2001

Position Statement

Management of postmenopausal osteoporosis:
position statement of The North American Menopause Society

- Biochemical markers of bone turnover have been studied as a means of assessment that could be used earlier in the course of therapy to show therapeutic response.
- Bone turnover changes can provide evidence of osteoporosis therapy efficacy much earlier than BMD changes (sometimes within weeks).
- The value of such markers in routine clinical practice, however, has not been established.

NAMS, 2002

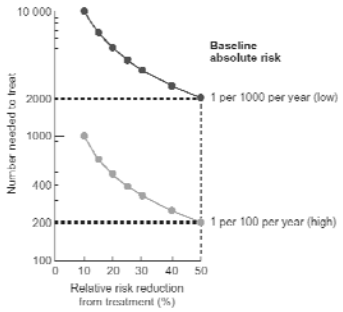
71 Management of osteoporosis
A national clinical guideline

RECOMMENDATION
Biochemical markers of bone turnover should have no role in the diagnosis of osteoporosis or in the selection of patients for BMD measurement (Grade A, Level 1++)

RECOMMENDATION FOR RESEARCH
Identification of the most appropriate biochemical markers for monitoring the effectiveness of treatment, and the preferred strategy for their use.

SIGN, June 2003

3: Number needed to treat to prevent one event at different levels of absolute risk



Seeman E, et al. Med J Aust 2004