



THERAPEUTICS INITIATIVE

Evidence Based Drug Therapy

Clinical Pearls from *Prescrire*

The Therapeutics Letter is only one of many independent bulletins in different countries that provide information to physicians, pharmacists and the public about drug treatments. In this Letter we present selected summaries published by a French drug bulletin, *La Revue Prescrire* (*Prescrire*). Like the Therapeutics Initiative, *Prescrire* is a member of the International Society of Independent Drug Bulletins (ISDB).

What is *Prescrire*?

Prescrire is a publication by a non-profit organization in France called Association Mieux Prescrire (AMP) (Association for Better Prescribing). Some articles from the French monthly bulletin, *La Revue Prescrire*, are published in a bi-monthly English version, *Prescrire International*.

AMP believes that health professionals need clear, reliable and independent information on which to base their medical care decisions.

The articles in *Prescrire* are written by health professionals who use standardized methods for literature searches, critical appraisal, and compilation of clinical trial evidence. Before publication each article is also reviewed by subject specialists in order to check the quality and relevance of the information.

Prescrire is financially independent from industry and government. Since 1992, subscriptions provide the sole source of financial support (presently about 30,000 to the French version and 800 to the English version).

The following are direct excerpts or translations from the *Prescrire* articles cited. We support the approach taken by *Prescrire*, but have not validated their conclusions.

Alendronate for secondary prevention of osteoporotic fractures (Dec 1997)



POSSIBLY HELPFUL

In menopausal women who present with a previous collapsed vertebrae (x-ray diagnosis), a large placebo controlled clinical trial showed that alendronate treatment for 3 years moderately reduced the risk of a new symptomatic vertebral collapse (ARR* 2.7%, NNT* 37 for 3 years), hip or wrist fracture. Longer term effects are not



known. Alendronate can lead to esophageal damage and cannot be considered unless the woman is capable of minimizing the risk by taking the drug according to the following regimen: fasting, with a large glass of water and remaining upright for at least 30 minutes.¹

Alendronate for primary prevention of osteoporotic fractures (Jan 2000)

Three trials have shown that alendronate, 5 mg/day slows post-menopausal bone loss. However, this effect disappears on treatment cessation, and mineral bone density is only one risk factor for postmenopausal fractures. A placebo-controlled trial of primary prevention involving more than 4,000 patients showed no reduction in the risk of fracture after 4 years of treatment (alendronate 5 mg/day for 2 years and then 10 mg/day).



NOTHING NEW

The clinical benefit of treatment with alendronate 5 mg/day for primary prevention of postmenopausal fractures has not been demonstrated, whereas this treatment has major constraints.^{2,3}

Risedronate for primary and secondary prevention of osteoporotic fractures (Sep 2001)



NOTHING NEW

There is no evidence that risedronate is any more effective or safer than other available bisphosphonates for preventing fractures linked to osteoporosis in women.^{4,5}



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Alendronate 70 mg tablet (Apr 2003)



POSSIBLY
HELPFUL

For secondary prevention of osteoporotic fractures, postmenopausal women prescribed alendronate can now choose between a weekly dose of 70 mg and a daily dose of 10 mg. This is the only tangible advantage of the new weekly dose strength.^{6,7}

Risedronate 35 mg tablet (Nov 2003)



NOTHING
NEW

For prevention of osteoporotic fractures, it has not been demonstrated in the absence of comparative trials, that a weekly dose of risedronate 35 mg has a better benefit/risk ratio than a weekly dose of alendronate 70 mg.⁸

Osteoporotic fractures in men (Jun 2003)

Osteoporotic fractures also occur in men, but they are only half as frequent as in women. In men, the risk of hip fracture increases markedly after 75 years of age. Falls are the most frequent immediate cause of osteoporotic fracture. Fracture prevention in men with osteoporosis (as in women) is based on fall prevention, adequate calcium and vitamin D intake, and avoidance, when possible, of treatments reducing bone density. Evaluation of drug treatments for osteoporosis in men provides only weak evidence.^{9,10}

Topiramate for migraine prevention: best avoided (May 2006)

The first-line drug for prevention of migraines is propranolol: it is the most thoroughly evaluated treatment, and thus far no other drug has been found to be more effective. Topiramate, an antiepileptic drug, is now also approved for migraine prevention. Only 3 out of 4 double-blind placebo-controlled trials showed that topiramate 100 mg/day was effective: on average, 46% of patients had a reduction of at least 50% in the frequency of migraines, compared to 23% of patients on placebo. Increasing the dose to 200 mg/day did not lead to better efficacy.

A double-blind trial versus propranolol failed to show that topiramate was as effective or better than propranolol.

Topiramate has numerous, frequent and sometimes serious adverse effects, mainly including neurosensory disorders (paraesthesias, language disorders, confusion) and gastrointestinal disturbances.



NOT
ACCEPTABLE

For the prevention of migraine attacks, it remains to be shown whether topiramate is as effective as propranolol. However, topiramate has more frequent and sometimes serious adverse effects. It is better to simply continue using propranolol.^{11,12}

Tiotropium. Just a me-too for COPD (May 2006)



NOTHING
NEW

For patients with chronic obstructive pulmonary disease, tiotropium has more adverse effects than the bronchodilators with which it has been compared, and it has not been shown to be more effective. Ipratropium seems to be the best choice for patients needing inhaled antimuscarinic therapy.^{13,14}

Drug Safety Update from Prescrire

Neuroleptics: Increased mortality in elderly patients (Jun 2005)

The US Food and Drug Administration (FDA) has issued a warning on the use of newer neuroleptics in elderly patients. The FDA warning is more comprehensive than similar warnings issued by the French and European regulatory agencies. Seventeen placebo-controlled trials have tested olanzapine, aripiprazole, risperidone and quetiapine in a total of 5106 elderly patients with dementia and behavioural disturbances.¹⁵

The trials lasted about 10 weeks. Mortality was higher in the neuroleptic groups (4.5%) than in the placebo groups (2.6%). The main causes of death were cardiovascular events (heart failure, sudden death) and infections (pneumonia).¹⁵ The doses used in these trials were not specified.

Other newer neuroleptics have not been tested in this patient population, but the FDA warning nonetheless includes the related neuroleptics clozapine and ziprasidone.

Given the evidence that all neuroleptics have very similar adverse effect profiles, older neuroleptics may also increase mortality in elderly patients.^{16,17}

* ARR = Absolute Risk Reduction
NNT = Number Needed to Treat

References

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The draft of this Therapeutics Letter was submitted for review to 40 experts and primary care physicians in order to correct any inaccuracies and to ensure that the information is concise and relevant to clinicians.