archive ouverte UNIGE

http://archive-ouverte.unige.ch

Article

Osteonecrosis of the jaw after treatment with bisphosphonates: is irreversible, so the focus must be on prevention

LANDIS, Basile Nicolas, et al.

Reference

LANDIS, Basile Nicolas, *et al*. Osteonecrosis of the jaw after treatment with bisphosphonates: is irreversible, so the focus must be on prevention. *BMJ. British medical journal*, 2006, vol. 333, no. 7576, p. 982-3

DOI: 10.1136/bmj.39024.647558.BE

PMID: 17095762

Available at: http://archive-ouverte.unige.ch/unige:36921

Disclaimer: layout of this document may differ from the published version.



top-up treatments may have been too low to produce long term benefits.3 Benefits have been shown to be additive when exercise is delivered with other interventions, such as weight loss strategies.5 If the pharmacy and physiotherapy interventions had been combined instead of being given separately they may have been more effective.

The role of pharmacists in helping patients to manage medication is widely accepted, and prescribing rights have been extended to pharmacists.⁶ Physiotherapy for musculoskeletal conditions has been shown to be beneficial and cost effective in primary care.7 A systematic review has shown that substituting general practitioners (GPs) with appropriately trained nurses can produce comparable health outcomes for patients.8 What was less clear was the impact on doctors' workload and potential cost savings. Another study found that nurse practitioners did not reduce the workload of GPs,9 perhaps because they were being used as supplements rather than substitutes for GP care. The trial by Hay and colleagues did not report effects on GPs' workload, but it did note that during the six month follow-up more people in the control group consulted their GP for knee pain than did those in the other two groups.

Evidence suggests that factors that promote success in changing skill mixes include introducing services or treatments of proved efficacy; appropriate staff education and training; removal of unhelpful boundary demarcations between staff or service sectors, such as lack of integration between health and social care; appropriate pay and reward systems; and good strategic planning and human resource management.¹⁰ The approach described by Hay and colleagues hits the mark on the first two criteria (evidence based treatments and education and training), but implementation of the others would require changes on a much broader scale for implementation across trusts.3

The pharmacy intervention was delivered by a pharmacist in GP surgeries. Could the intervention be delivered in a community pharmacy? Research suggests that the community pharmacy setting is not viewed positively as a site for the delivery of more clinically demanding services.11 Physiotherapy was performed under supervision of community physiotherapists (mean of three consultations), and patients were asked to continue their exercises at home. Supervised exercise sessions are superior to home exercises in the management of knee injury,12 and although one to one supervision is best, group classes can be successful. This approach requires a specific diagnosis (beyond knee pain and stiffness as was used in Hay and colleague's model) as patients are usually grouped according to injury type and prognosis. None the less, group sessions could maximise patient compliance and therapist time in the long term and offer a pragmatic option for primary care management.

Carmel M Hughes professor of primary care pharmacy and Cochrane fellow

(c.hughes@qub.ac.uk)

School of Pharmacy, Queen's University, Belfast BT9 7BL

Chris M Bleakley physiotherapist and research associate

Health and Rehabilitation Sciences Research Institute, University of Ulster, Jordanstown, Newtownabbey BT37 0QB

Competing interests: None declared.

- Victor CR, Ross F, Axford J. Capturing lay perspectives in a randomized
- victor CR, Ross F, Axiord J. Capturing lay perspectives in a randomized controlled trial of a health promotion intervention for people with osteoarthritis of the knee. J Eval Clin Pract 2004;10:63-70.

 Jordan KM, Sawyer S, Coakley P, Smith HE, Cooper C, Arden NK. The use of conventional and complementary treatments for knee osteoarthritis in the community. Rheumatology 2004;43:381-4.

 Hay EM, Foster NE, Thomas E, Peat G, Phelan M, Yates HE, et al.
- Hay EM, Foster NE, Thomas E, Peat G, Phelan M, Yates HE, et al. Effectiveness of community physiotherapy and enhanced pharmacy review for knee pain in people aged over 55 presenting to primary care: pragmatic randomised trial. *BMJ* 2006 doi: 10.1136/bmj.38977.590752.0B.
- Dumas JE, Lynch AM, Laughlin JE, Phillips Smith E, Prinz RJ. Promoting intervention fidelity. Conceptual issues, methods and preliminary results from the EARLY ALLIANCE prevention trial. Am J Prev Med 2001;20(1S):38-47.
- Bennell K, Hinman R. Exercise as a treatment of osteoarthritis. Curr Opin
- Bennell K, Hinman K. Exercise as a treatment of osteoarum us. Carr Opin Rheumatol 2005;17:634-40. Avery AJ, Pringle M. Extended prescribing by UK nurses and pharmacists. BMJ 2005:331:1154-5. Pinnington MA, Miller J, Stanley I. An evaluation of prompt access to
- physiotherapy in the management of low back pain in primary care. Fam Pract 2004:21:372-80.
- Laurant M, Reeves D, Hermens R, Braspenning J, Gorl R, Sibbald B. Substitution of doctors by nurses in primary care. Cochrane Database Syst Rev 2004;(4):CD001271.
- Laurant MGH, Hermens RPMG, Braspenning JCC, Sibbald B, Grol RPTM. Impact of nurse practitioners on workload of general practitioners: randomised controlled trial. *BMJ* 2004;328:927-32.
 Sibbald B, Shen J, McBride A. Changing the skill-mix of the health care
- workforce. J Health Services Res Policy 2004;9(suppl 1):28-38.

 11 Hughes CM, McCann S. Perceived interprofessional barriers between community pharmacists and general practitioners: a qualitative assessment. Br J Gen Pract 2003;53:600-6.
- 12 Fransen M, McConnell S, Bell M. Exercise for osteoarthritis of the hip or knee. Cochrane Database Syst Rev 2001;(2):CD004376.

doi 10.1136/bmj.39024.417813.BE

Osteonecrosis of the jaw after treatment with bisphosphonates

Is irreversible, so the focus must be on prevention

'ew generation bisphosphonates such as zoledronic acid, pamidronate, and alendronic acid have various indications in medicine. Initially, their use was restricted to patients with metastatic bone malignancy secondary to breast cancer, lung cancer, prostate cancer, or multiple myeloma. Their benefit in these conditions led to wider application for other bone pathologies, such as osteoporosis and Paget's disease.1 Their main effect is to inhibit osteoclast activity;

however, they also seem to have antiangiogenic effects,² and once they are incorporated into the bony matrix, degradation is minimal.3

Reports from several hundred cases over the past three years suggest that long term use of new generation bisphosphonates increases the risk of avascular osteonecrosis of the jaws. 4-6 The mean onset time of osteonecrosis after the treatment is started is one to three years.6 The clinical picture consists of non-

BMJ 2006;333:982-3

healing ulcerated oral lesions and visible necrotic bone, which are sometimes associated with a diffuse jaw or facial pain. Osteonecrotic side effects are relatively rare in patients taking these drugs, and risk is related to the type of drug and the doses given (incidence estimated 1-10%).7 Although rare, these side effects are clinically difficult to manage.6 Such side effects should be considered when new generation bisphosphonates are prescribed for patients without cancer who have better long term survival and thus increased risk of developing delayed osteonecrosis.8

So, is it possible to prevent avascular osteonecrosis? Two recent studies concluded that it cannot be avoided completely.⁶ ⁸ These studies identified (potentially modifiable) risk factors that increased the risk of avascular maxillo-mandibular osteonecrosis, such as poor dental hygiene, periodontal problems, dental extractions, and oral surgery.

Currently, discontinuation of new generation bisphosphonates, treatment with long term antibiotics, and careful surgical debridement may osteonecrosis, but no treatment can totally reverse it. We therefore recommend that patients should be referred for a specialist dental or maxillofacial opinion, so that chronic periodontal problems and foreseeable dental extractions can be considered before treatment is started. The importance of good dental hygiene should be emphasised, and patients should be made fully aware of the benefits and harms so that they can make an informed decision about whether they should start treatment.

Basile Nicolas Landis resident

(Basile.Landis@hcuge.ch)

Michel Richter professor and head of department Ivan Dojcinovic senior resident Max Hugentobler associate professor

Department of Oral and Maxillo-Facial Surgery, University Hospital of Geneva, 1211 Geneva, Switzerland

Competing interests: None declared.

- Drake WM, Kendler DL, Brown JP. Consensus statement on the modern therapy of Paget's disease of bone from a Western Osteoporosis Alliance symposium. Biannual foothills meeting on osteoporosis, Calgary, Alberta, Canada, September 9-10, 2000. Clin Ther 2001;23:620-6.
- Wood J, Bonjean K, Ruetz S, Bellahcene A, Devy L, Foidart JM, et al. Novel antiangiogenic effects of the bisphosphonate compound zoledronic acid. J Pharmacol Exp Ther 2002;302:1055-61. Lin JH, Russell G, Gertz B. Pharmacokinetics of alendronate: an overview.
- Int J Clin Pract 1999;101(suppl):18-26.

 Marx RE. Pamidronate (Aredia) and zoledronate (Zometa) induced avas-
- cular necrosis of the jaws: a growing epidemic. J Oral Maxillofac Surg 2003:61:1115-7
- Ruggiero SL, Mehrotra B, Rosenberg TJ, Engroff SL. Osteonecrosis of the jaws associated with the use of bisphosphonates: a review of 63 cases
- J Oral Maxillofac Surg 2004;62:527-34.

 Marx RE, Sawatari Y, Fortin M, Broumand V. Bisphosphonate-induced exposed bone (osteonecrosis/osteopetrosis) of the jaws: risk factors, recognition, prevention, and treatment. J Oral Maxillofac Surg 2005;63:1567-
- Moo SB, Hellstein JW, Kalmar JR. Narrative review: bisphosphonates and osteonecrosis of the jaws. *Ann Intern Med* 2006;144:753-61.

 Farrugia MC, Summerlin DJ, Krowiak E, Huntley T, Freeman S, Borrowdale R, et al. Osteonecrosis of the mandible or maxilla associated with the use of new generation biphosphonates. Laryngoscope 2006;116:115-20.

doi 10.1136/bmj.39024.647558.BE

What should we do about climate change?

Health professionals need to act now, collectively and individually

ction on climate change has been likened to teenage sex. Everyone claims to be in on the action, but only a few are, and those not very effectively. Given the scientific consensus that global warming-the underlying cause of climate change-is mainly caused by human beings12 and its effects are likely to be seriously damaging to global health,^{3 4} citizens and governments must take much more effective action. This sense of urgency has been confirmed by the Stern report, commissioned by the UK chancellor, Gordon Brown, and published last week.⁵ It concludes that the cost of doing something to combat climate change is likely to be 1% of global gross domestic product, but the cost of doing nothing will be up to 20% of global gross domestic product. It also concludes that the cost to the environment of each ton of carbon dioxide emitted is £50 (€75; \$95), a figure that gives us a financial yardstick of the damage we are doing by our continued reliance on fossil fuels.

Health professionals have a track record of identifying and helping resolve serious public health issues. We are well placed to have a leadership role. Indeed it is a role that we cannot shirk. So what should we do? The BMJ has set up a carbon council with the objective of harnessing the intelligence and imagination of health professionals to expedite the transition to a low carbon world (see bmj.com for list of council members).

The council's strategy is fourfold. Firstly, to recruit as many health professional as possible to act and act now. Although the global effects of climate change and benefits of resolving these are well known,67 many doctors and other health professionals have not articulated for themselves and others the public health priority of climate change compared, for example, with smoking and inequalities in health. This is alarming, given that climate change related rises in sea level and changing food growing patterns will lead to massive social disruption, with the increased likelihood of resource wars, the spread of many "tropical" diseases, and a greatly increased burden of ill health. The BMJ's contribution will be to present the evidence for the health damaging impacts of climate change, both in the developed and developing world, and the health benefits of moving towards low carbon living.

Secondly, we want to identify the most effective low carbon policies that when implemented will reduce greenhouse gas emissions. The BMf's climate change issue in June of this year offered examples of such policies,8 which must ensure welfare development for the global poor at the same time as controlling carbon emissions. Of several possible approaches, contraction and convergence is our favoured option.9 10 Adoption of this policy would create a global carbon budget, with a phased reduction over the next 30 years (to tackle global warming), and an equal per capita allocation of

BMI 2006;333:983-4