Treatting the symptoms of osteoarthritis

Oral treatments

In 2004–2005, 15% of Australians reported having arthritis.¹ Osteoarthritis (OA) is by far the most common form, and is a leading cause of pain and disability among people over 65 years of age.²

Nonsteroidal anti-inflammatory drugs (NSAIDs), while not first line, have long been a mainstay of OA treatment but may be associated with adverse effects, particularly in the elderly. COX-2 inhibitors (C2I) were developed as it was considered theoretically plausible that they wouldn’t cause gastrointestinal side effects such as gastric erosion.³ This was borne out by multiple large randomised controlled trials (Table 1).

Table 1. Key trials: ulcer complications with nonselective NSAIDs vs. selective C2Is

<table>
<thead>
<tr>
<th>Trial</th>
<th>Drugs and doses</th>
<th>Total number of participants</th>
<th>Key results</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUCCESS⁸</td>
<td>Celecoxib 100 mg twice per day, or Celecoxib 200 mg twice per day, or Diclofenac 50 mg twice per day, or Naproxen 500 mg twice per day</td>
<td>13 274</td>
<td>• Odds of ulcer complication &gt;7 times greater in NSAID than celecoxib group</td>
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<td></td>
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<td></td>
<td>• No significant difference if participants also on aspirin</td>
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<td></td>
<td></td>
<td>• Not powered to detect cardiovascular differences</td>
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<td></td>
<td></td>
<td></td>
<td>• Celecoxib 100 mg twice per day and 200 mg twice per day equally efficacious for OA</td>
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<tr>
<td>VIGOR⁹</td>
<td>Rofecoxib (Vioxx) 50 mg/day, or Naproxen 500 mg twice per day</td>
<td>8076</td>
<td>• Relative risk of a complicated gastrointestinal event on rofecoxib compared with naproxen is 0.4</td>
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<td></td>
<td></td>
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<td>• Patients had rheumatoid arthritis</td>
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Table 2. Summary of Cochrane review on tramadol for osteoarthritis¹⁰

- The review included 11 RCTs, in which 1019 adults with OA of hip and/or knee received tramadol or tramadol/paracetamol and 920 received placebo or active control. Average length of follow up was 35 days (range 7–91 days)
- Tramadol rated slightly better than placebo for pain control as measured by a pain scale, but the clinical significance of the measured difference is doubtful
- One trial of 20 participants found paracetamol 1500 mg/day was more effective than 150 mg/day of tramadol for pain control and had fewer side effects
- One trial compared tramadol with an NSAID (diclofenac). The two drugs had similar effects on function with roughly half of participants in both groups reporting at least moderate overall improvement. Over the 2 month follow up period there were significantly more minor adverse events with tramadol than with diclofenac
- Compared with placebo, tramadol increased the likelihood of at least moderate overall improvement with a NNTB of 6. However, people taking tramadol were more than twice as likely as those taking placebo to have a minor adverse event such as vomiting, headache or constipation – NNTH is 5

NNTB = number needed to treat to benefit, NNTH = number needed to treat to harm

This series of articles facilitated by the Australian Cochrane Musculoskeletal Group aims to place the findings of recent Cochrane musculoskeletal reviews in a context immediately relevant to general practitioners. This article looks at treatment options for osteoarthritis.

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In 2004, the COX2 rofecoxib (Vioxx) was withdrawn from the market after it was found that the relative risk of a cardiovascular event compared with placebo after 18 months of therapy was 1.8. \(^4\) Concern was raised about celecoxib’s safety, particularly in higher doses. \(^5\) A recent meta-analysis found the risk of a cardiovascular event to be the same with celecoxib as with placebo. \(^6\) Nonetheless, concern about the safety of NSAIDs as a whole persists, as diclofenac and others have been linked to adverse cardiovascular outcomes. \(^7\)

In this setting, the need for a safe, effective oral treatment for OA is pressing. Two possibilities – apart from paracetamol – include tramadol and glucosamine. The results are summarised in Table 2 and 3 and how these results might affect practice are shown in Table 4.

**Conclusion**

Glucosamine seems safe but it is controversial whether it benefits pain or function. Emerging evidence suggests that it may help both alone and when combined with chondroitin in the group that has moderate to severe knee symptoms. The optimum dose seems to be 1500 mg once daily. Tramadol has marginal effects on OA pain and can bring about functional improvement. It has a higher rate of unpleasant side effects in the short term than diclofenac and placebo, but its long term effects (vs. those associated with NSAIDs) are unknown.

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**Case study**

Mrs Jones, 55 years of age, is a teacher with moderate left knee OA and borderline hypertension. She is increasingly uncomfortable about taking Celebrex. She already takes paracetamol regularly and didn’t tolerate diclofenac or ibuprofen. What can you advise her?

You can advise her that while celecoxib in high dose (800 mg/day and 200 mg twice daily, but not 400 mg once daily) does appear to increase the risk of cardiovascular events, 200 mg once daily has not been linked to heart disease. Her brother has been prescribed tramadol for knee pain. Would it be worth trying that?

You can tell Mrs Jones that tramadol was only very slightly better than a placebo for OA pain, and about the same as diclofenac for its ability to bring about overall improvement. However, in the short term tramadol was much more likely to cause side effects such as vomiting, headache, constipation and dizziness than diclofenac. One in 6 people who take tramadol will get unpleasant minor side effects, and one in 5 will get a sense of at least moderate improvement. There may be specific patients who have trouble with other medication who may benefit from tramadol. She decides not to try tramadol at the moment.

What about the glucosamine she’s noticed in the pharmacy?

You can tell her that while the jury is still out overall, a considerable body of evidence shows that glucosamine sulphate 1500 mg/day is more effective for pain control than ibuprofen, and that studies have found glucosamine to benefit function. Also, glucosamine may slow disease progression and the need for knee replacement and is safe (except in patients with shellfish allergy).

You decide to advise her that taking glucosamine at the recommended dose for at least 2 months is worthwhile. She needs to be aware that because glucosamine is sold as a supplement rather than a therapeutic drug, it is not subject to the same type of quality control measures as celecoxib. That said, Therapeutic Goods Administration data has suggested there is no problem with glucosamine available in Australia.
References


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