

Osteoarthritis

NSAIDs in osteoarthritis: irreplaceable or troublesome guidelines?

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Current treatment of osteoarthritis relies too heavily on pharmacological approaches

In sports medicine, non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for relieving pain and modulating inflammation in acute injuries. They have also been used in osteoarthritis (OA) of the knee, which is one of the most common disorders of modern society. Besides genetic and sex dispositions, previous knee injury in sports is one of several identified risk factors. Half of the 8 million patients with OA in the United Kingdom use NSAIDs regularly, and this contributes to the annual estimated 2000 deaths from NSAID side effects in this country.^{1,2} NSAID safety has been debated widely over the last few months, and the increased risk of cardiovascular infarcts finally led to withdrawal of Vioxx and marketing restrictions for other cyclo-oxygenase-2 inhibitors (coxibs). The high risk of gastrointestinal side effects from non-specific NSAIDs has long been known, whereas coxibs were thought to be safer and equally effective. The NSAID safety controversy seems to have left a gap in OA management. Some doctors and patients with OA have appeared in the media complaining that they miss having coxibs to prescribe/take. The lower risk of gastrointestinal side effects from coxibs compared with unspecific NSAIDs makes this understandable. Some doctors have turned back to non-specific NSAIDs, adding a costly proton pump inhibitor drug. But are NSAIDs and other pharmacological therapies really irreplaceable in OA management?

In the new NHS guidelines (<http://www.prodigy.nhs.uk/guidance.asp?gt=osteoarthritis>), non-pharmacological interventions (exercise and weight loss) receive first line recommendation. However, the NHS guidelines seem to downplay drug treatment in OA of the knee by suggesting limited recommendation: "Pharmacological management of OA of the knee is limited to short-term symptomatic relief of pain and stiffness but does not alter disease progression." One way of interpreting these guidelines is that clinicians may actually treat mild and moderate OA of

the knee without pharmacological interventions.

If we look at the efficacy studies, EULAR guidelines for knee OA management states that the standardised mean effect size (SMD) for oral NSAIDs is in the range 0.47–0.96, which would be rated as "good" or very "good".³ However, these results were only calculated from five of the existing trials in which results were easily accessible for effect size calculations. When we calculated SMD for pain from all 23 randomised, placebo controlled trials of knee OA, the SMD fell to 0.32 (0.24 to 0.39) when half of the trials only included selected responders to NSAIDs. The unbiased SMD fell further to 0.23 (0.15 to 0.31) when only the sample of unselected patients with knee OA were included.⁴ For paracetamol (the first choice drug in EULAR guidelines), other authors have found that the SMD is barely significant at 0.21 (0.02 to 0.41),⁵ and that was before a large scale study found no significant effect from paracetamol in patients with OA of the knee.⁶ The biggest problem is perhaps that too many patients keep on taking NSAIDs unnecessarily for long periods even if they obtain adequate pain relief from other interventions such as exercise.⁷ The effect size of NSAID treatment in OA decreases as time goes by, and there is a lack of hard evidence to support NSAID therapy beyond three months in OA.

We predict that it will be more and more difficult for clinicians to decide which OA treatment to choose. Developing guidelines with recommendations of pharmacological treatments with poor efficacy is a double edged sword. In the near future, we will be swamped with claims that unusual alternative therapies, such as magnetic bracelets,⁸ are just as effective (or ineffective) for OA as the recommended pharmacological interventions. And they are of course right.

Could it be that we have been too focused on pharmacological treatments for OA? The EULAR guidelines were presented with a systematic review of 33

interventions and expert panel opinions before settling on 10 treatment recommendations. It is not often mentioned that the preparation of the EULAR guidelines was sponsored by a pharmaceutical company and that the five members of the American College of Rheumatology panel had between four and nine stated conflicts of industrial interest. The integrity of their treatment recommendations may be questioned when no manual techniques or electrophysical agents are recommended for the management of OA of the knee. In the 20 October 2005 issue of *Nature*, the editor comments on an article uncovering the fact that 35% of guideline developers had conflicts of interests with the industry.⁹ His standpoint is crystal clear: it is unhealthy for prescription guidelines to be written by people with such conflicts of interests.

If we return to alternative therapies, it is true that some of the non-pharmacological interventions such as ultrasound and shortwave lack scientific support in OA management. What about short bouts of other manual and electrophysical therapies? The EULAR systematic review grades the level of evidence for unrecommended treatments such as acupuncture, transcutaneous electrical nerve stimulation (TENS), and laser therapy as class 1B, which is the same evidence level as for coxibs and paracetamol. In fact, although the strength of evidence for these treatments may not yet have reached the same level as oral NSAIDs for OA, their statistical power equals that of several other pharmacological interventions. In addition, these treatments are usually safer, and published trials are more often funded by independent non-industry sources. And these empirical therapies may have potential for improvement as more of their biological mechanisms of actions and dose-response patterns are elucidated.

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COMMENTARY

If the recent controversies surrounding the safety of both traditional and cyclo-oxygenase-2 selective NSAIDs make clinicians improve their focus on non-pharmacological treatments for OA, then this may be a good thing! Most patients use drugs only intermittently (despite how they may be

prescribed), and simple muscle strengthening exercises may have an equal pain reducing efficacy to analgesics. All OA sufferers should understand that their treatment is a combination of a biomechanical approach (for OA of the knee: quadriceps strengthening, weight loss, and appropriate footwear) and drugs. NSAIDs are no doubt a useful adjunct treatment, as are paracetamol and codeine-containing analgesics, and intra-articular steroids are useful as short term pain “circuit breakers” while quadriceps are strengthened. Advances in surgery, especially unicompartmental joint replacements, may also increase options for some patients.

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