Important New Evidence Service

In Partnership with The Centre for Medicines Optimisation at Keele University

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Pain: meta-analysis finds limited efficacy of non-steroidal anti-inflammatory drugs (NSAIDs) for spinal pain

Spinal pain (neck or low back pain) is the leading cause of disability worldwide and is commonly managed in general practice using prescription medicines. The NICE guideline recommends non-pharmacological therapies first line, highlighting the limited evidence-base for drug treatments. Supporting this recommendation, a new systematic review and meta-analysis found that NSAIDs do not provide a clinically important improvement in spinal pain compared with placebo.

Reference: Machado GC, Maher CG, Ferreira PH *et al.* Non-steroidal anti-inflammatory drugs for spinal pain: a systematic review and meta-analysis. Annals of the Rheumatic Diseases Published Online: 2/2/17. doi: 10.1136/annrheumdis-2016-210597

What do we know already?

- The recently updated NICE guideline on low back pain and sciatica recommends non-drug treatments as first-line therapy, while NSAIDs are now the first-line pharmacological treatment ahead of paracetamol. The guideline development group (GDG) based this recommendation on evidence from short-term placebo-controlled trials (*head-to-head and long-term studies were lacking*), and in consideration of the relatively low cost of NSAIDs (ref: full guideline). The GDG's 'downgrading' of paracetamol is in line a recent Cochrane review that found no difference for paracetamol versus placebo in acute or chronic back pain, and the reduced role of opioids in the guideline reflects the lack of clinically important benefits, but clinically important harms, seen in studies of opioids.
- The limited efficacy of NSAIDs in spinal pain has been noted in several reviews. A 2016 Cochrane Review found low quality evidence that NSAIDs were slightly more effective than placebo in chronic low back pain, but the magnitude of difference was small, and when limited to higher quality studies, the differences were reduced. A 2008 Cochrane review concluded that NSAIDs were also only slightly effective for short-term symptomatic relief in patients with acute non-specific low back pain without sciatica. Regarding the management of neck pain, few trials have specifically tested drug treatments. The NICE Clinical Knowledge Summary on neck pain provides general recommendations, which includes the use of NSAIDs. However, advice is extrapolated from trials in back pain and other musculoskeletal conditions and based on expert advice.

What does this evidence add?

- This article provides a further review of the evidence for NSAIDs in spinal pain. Broadly in agreement with Cochrane reviews and the NICE guideline, main findings were that whilst NSAIDs reduced pain and disability scores, the magnitude of effects were small and, in this analysis, did not meet the threshold for clinical importance. The authors calculated a number needed to treat (NNT) of 6 (i.e. 6 people need to be treated with an NSAID rather than placebo for 1 additional person to achieve a clinically important reduction in pain in the short term). Thus, whilst many may not benefit, NSAIDs may be effective for some patients, reflecting the heterogeneous nature of spinal pain.
- In this analysis, NSAIDs increased the relative risk of gastrointestinal adverse effects 2.5-fold, although as trials were typically of short duration (median 7 days), these findings should be viewed with caution.
- Study limitations included the grouping of a wide range of studies that investigated different NSAID formulations (topical, oral, injectable), doses and types of pain (acute and chronic low back pain, sciatica and neck pain). Contributing studies were of variable quality, and most were of short-term duration (<14 days).

- In practice, clinicians should continue to follow NICE guidance when managing patients with back pain, as treatment choices (which also include interventions such as exercise and psychological therapies) have been made following an assessment of population safety, with an awareness of their possible limited efficacy for individual patients. Patients with an inflammatory component to pain may derive benefit from the use of an NSAID, while others may find them ineffective and require alternative treatments e.g. muscle relaxants, tricyclic antidepressants or a non-pharmacological intervention. When prescribing NSAIDs, NICE state they should be used at the lowest dose for the shortest duration, with consideration given to a patient's risk factors, ongoing monitoring and gastroprotection. The updated NICE guideline also promotes the use of risk stratification (such as STarT Back) to aid decisions about management.

Study details

Study selection and analyses:

- The aim of the systematic review was to investigate the efficacy and safety of NSAIDs compared with placebo in patients with spinal pain, with or without radicular pain.
- The review included 35 randomised placebo-controlled trials (n = 6,065) published in peer-reviewed journals in any language.
- Trials included acute or chronic spinal pain of any intensity reporting patient-relevant outcomes, such as pain intensity, disability status, quality-of-life and adverse effects. Trials evaluating postoperative analgesia were excluded, as were and non-randomised controlled trials, review articles, guidelines and observational studies.
- The quality of the evidence was evaluated using the Grade of Recommendation Assessment Development and Evaluation (GRADE) approach.
- A follow-up period of <2 weeks was defined as 'immediate term' and a follow-up between 2 weeks and 3 months as 'short-term'. No trial reported data beyond these time points.
- Pain and disability scores used in trials were converted to a common 0-point (no pain or disability) to 100-point (worst possible pain or disability) scale to facilitate review and interpretation. Quality of life measures needed no conversion (range: 0-100).
- A difference of 10 points on a 0-100 scale for pain, disability and quality of life was considered the smallest worthwhile effect (as stated in a paper published in 2013).

Key findings:

- The median treatment duration of included trials was 7 days. NSAIDs were mostly administered orally, but 5 trials used intravenous or intramuscular injection and 3 used a topical formulation.
- Pooling of all included trials revealed moderate quality evidence that NSAIDs reduce pain in the immediate-term (Mean Difference [MD] in pain score -9.2, 95% Confidence Interval [CI]: -11.1 to -7.3; NNT = 5; 95% CI 4 to 6), and the short-term (MD -7.7, 95% CI: -11.4 to -4.1; NNT = 6; 95% CI: 4 to 10).
- Effects on disability were slightly smaller than for pain, with effects at immediate-term follow-up being -8.1 (95% CI: -11.6 to -4.6) and at short-term -6.1 (95% CI: -9.5 to -2.8).
- The authors note that the differences in the pain and disability scores with NSAIDs were, however, less than the 10-point threshold for clinical importance.
- Findings on the effects of NSAIDS on the use of rescue medication were mixed, with four trials providing moderate-quality evidence of no difference in use, whilst four trials provided high-quality evidence of a reduction in use (MD in use of rescue tablets per day -0.4, 95% CI −0.5 to −0.3). The authors suggest this difference may not be clinically important.
- 21 trials were included in the safety analysis (n = 5,153), and while no difference was found between NSAIDs and placebo in the rate of all adverse events, a higher number of participants in the NSAID group reported gastrointestinal adverse events compared with placebo (Risk Ratio 2.5, 95%CI: 1.2 to 5.2). No data on safety beyond 14 days was available.

Level of evidence:
Level 1 (good quality patient-oriented evidence) according to the SORT criteria.

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