Therapeutics

Paracetamol as first line for treatment of knee and hip osteoarthritis

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Although several clinical guidelines recommend paracetamol as a first-line agent in the management of knee and hip osteoarthritis, the authors of a recently published Cochrane review called for a review of this recommendation.

Paracetamol is widely used as a first-line treatment for symptom relief in patients with osteoarthritis (OA). It is usually preferred to non-steroidal anti-inflammatory drugs because of its better harms profile, especially in people at risk of gastrointestinal bleeding.

In a recent Cochrane review,[1] the authors compared the effectiveness of paracetamol versus placebo in the management of knee or hip OA. They searched seven scientific databases for relevant studies, including randomised controlled trials of participants with hip or knee OA irrespective of the intensity or duration of symptoms. The main outcomes were pain intensity, physical function, quality of life, adverse events, serious adverse events, withdrawal because of adverse events and liver toxicity. They used minimal clinically important difference (MCID) to compare the effect between paracetamol and placebo—MCIDs are a patient-centred concept that represents the smallest improvement that a patient considers 'meaningful and worthwhile'.[2]

Statistically significant benefit versus clinical importance

The review included 10 trials with 3541 participants and reported that paracetamol did not result in clinically important improvements in pain: MCID 3% (95% CI: 1% to 5%); or physical function: MCID 3% (95% CI: 1% to 5%). There were no data on quality of life and no statistically significant or clinically important differences found in rates of adverse events, serious adverse events, withdrawal because of adverse events and liver toxicity between paracetamol and placebo.

The quality of evidence for most outcomes including pain and physical function was high. The review results were consistent with those of a previous network meta-analysis (NMA)[3] which concluded that there is no role for using paracetamol as monotherapy for treatment of OA. The results also support the conclusions of another NMA, which found paracetamol to be least efficacious agent for OA management.[4]

However, several caveats exist. The MCID used by the authors was based on those of a previous publication,[5] who in turn based their estimates on the median MCID from four other prior publications. To my knowledge there is no evidence that the cut-off point of 0.9 or 1.0 on a 10 point scale (9 or 10 on a 100-point scale) for pain or physical function respectively has been validated for use in OA—a recent study of patients with knee OA concluded that adjustment for confounders could facilitate the generalisation of the results.[6] In addition, the Cochrane review did not report data on the proportion of participants who reported improvement in pain symptoms.

That paracetamol had statistically significant benefits for pain and physical function (despite not achieving MCID thresholds; see the online supplementary table 1), coupled with its good harms profile indicate the drug should not be jettisoned as one of the first-line treatments for managing pain in the management of OA. Indeed, a recent large prospective study of elderly subjects (n=5429) concluded that 'despite polypharmacy and polymorbidity', acetaminophen (paracetamol) remains a first-line analgesic for managing pain.[7]

EBM Verdict

EBM Verdict on: Paracetamol versus placebo for knee and hip osteoarthritis. *Cochrane Database Syst Rev* 2019;2:CD013273.

- Until convincing high-quality evidence demonstrates safety and effectiveness of other agents over paracetamol, it should remain a first-line agent in management of knee or hip osteoarthritis.

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