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Paracetamol Is Ineffective for Spinal Pain and Knee and Hip Osteoarthritis

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Context

While paracetamol continues to be recommended as an initial pharmacological treatment for osteoarthritis and to a lesser extent for back pain, increasingly trials and meta-analyses have suggested that its efficacy is minimal and some epidemiological evidence suggests that at high doses, paracetamol may be dangerous. Machado and colleagues carried out the most comprehensive meta-analysis yet of the efficacy and safety of paracetamol versus placebo for back pain, neck pain and knee and hip osteoarthritis pain.

Methods

The authors carried out a comprehensive search for randomised trials comparing efficacy and safety of paracetamol versus placebo for the aforementioned conditions. They registered their meta-analysis following PRISMA guidelines. Articles had to report pain and/or functional outcomes. Risk of bias and publication bias were assessed. For each treatment arm in each trial, the authors converted pain and function outcomes to a 0–100 visual analogue-type scale and then computed the difference between these treatments on this scale.

Findings

The authors found 3 spinal pain trials and 10 trials of knee and/or hip osteoarthritis. For each of these disorders there was little heterogeneity across trial findings and the evidence was rated formally as of moderate to high quality. Paracetamol dosages in these trials were consistently over 3 g a day.

The authors found no effect of paracetamol on spinal pain in the immediate (<2 weeks) or short term (>2 weeks but <3 months) with placebo patients actually doing marginally better in terms of pain than acetaminophen patients (1.4 on a 0–100 scale (95% CI −1.3 to 4.1)). Effects were the same for function. For osteoarthritis there was a modest effect of paracetamol with little heterogeneity across trials. In the immediate term, the paracetamol patients on average had an improvement compared to placebo of 3.3 on a 0–100 scale with the 95% confidence bound not extending up to the minimal clinically important difference for pain of 9 per 100. For short term, the effect was almost identical with the upper bound of the effect not reaching the minimal clinically important difference. Paracetamol-treated patients had no increase in adverse events other than an increase in liver function tests of unclear clinical significance.

Commentary

This meta-analysis is the most comprehensive yet to evaluate the efficacy of paracetamol at a high dose and is consistent with earlier study findings. One systematic review (osteoarthritis) reported that the effect size for paracetamol versus placebo was <0.2 SDs versus placebo on a scale where 0.2–0.5 is characterised as a small therapeutic effect.[1] Non-steroidal anti-inflammatory drugs at therapeutic doses have effect sizes of 0.3–0.5 using the same approach.[2] This meta-analysis of short-term trial data did not include a comprehensive examination of toxicity which is better addressed in long-term observational studies.

Some data suggests that paracetamol at a high dose may inhibit cyclooxygenase, especially COX-2. Long-term observational cohort studies have reported that people who take paracetamol daily may be at an increased risk of incident hypertension, deterioration in renal function and even myocardial infarction. It should be noted that no such risks have been reported for people who use paracetamol intermittently or at a lower dose.[3] Also, paracetamol at a high dose[4] may cause a drop in haemoglobin level, suggesting that this cyclooxygenase inhibitor may cause gastrointestinal bleeding.

It is clear that high-dose paracetamol ultimately not only offers little in terms of efficacy but, at least at high dose, may have an unfavourable therapeutic to toxic index—this does not take into account the potential liver toxicity that might attend at higher dose use.

Implications for Practice

While intermittent paracetamol to relieve occasional pain is safe and may be marginally effective, high-dose paracetamol should probably be avoided given its limited efficacy and risk of toxicity. If occasional paracetamol is not effective, intermittent non-steroidal anti-inflammatory drugs or other pharmacological treatments should be considered. Furthermore, for osteoarthritis, exercise treatment, has been shown to be efficacious, is safe and is underutilised.

References

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