FPIN's Help Desk Answers

Acetaminophen for Pain Relief in Osteoarthritis

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Clinical Question

Is acetaminophen effective for relief of hip or knee pain due to osteoarthritis?

Evidence-Based Answer

Acetaminophen is no better than placebo for relief of hip or knee pain due to osteoarthritis. Although acetaminophen does provide some pain relief, the effect is small and not clinically significant. (Strength of Recommendation [SOR]: A, based on systematic reviews and meta-analyses.) Higher daily dosages or extended-release formulations also are not effective for relieving hip or knee pain due to osteoarthritis. (SOR: A, based on a meta-analysis and a large randomized controlled trial [RCT].)

Evidence Summary

A 2019 systematic review analyzed available literature published through October 2017 to assess the benefits and harms of acetaminophen in the treatment of pain related to hip or knee osteoarthritis.[1] The review included 10 RCTs with a total of 3,541 patients (mean age range = 55.3 to 70 years) who had hip or knee osteoarthritis diagnosed by imaging or clinical criteria. The acetaminophen dosage was 3,000 to 4,000 mg per day, given as three or four doses, except for one arm of one RCT that used a daily dosage of 1,950 mg. Primary outcomes included functional scores on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC; seven RCTs; n = 3,153) and pain scores on the WOMAC (four RCTs; n = 1,294) or visual analog scale (VAS; four RCTs; n = 1,919). WOMAC pain and function scores were converted to a 0 to 100–point scale to correlate with VAS scores; a difference of 9 points or more was considered clinically significant. All of the RCTs had a low or unclear risk of bias except for two with a high risk of attrition bias. Pooled results after two to 12 weeks of follow-up showed a non–clinically significant reduction in pain scores (–26.2 points with acetaminophen vs. –23 points with placebo; seven RCTs; n = 2,355; mean difference [MD] = –3.2 points; 95% CI, –1 to –5.4). Improvement in functional scores was also not clinically significant (–14.9 points with acetaminophen vs. –12 points with placebo; seven RCTs; n = 2,354; MD = –2.9 points; 95% CI, –1 to –4.9). Adverse event rates were similar between the treatment and placebo groups (six RCTs; n = 3,252; relative risk [RR] = 1.0; 95% CI, 0.9 to 1.1). Liver function abnormalities were more common with acetaminophen compared with placebo (three RCTs; n = 1,237; RR = 3.8; 95% CI, 1.9 to 7.4). The authors concluded that acetaminophen offers minimal improvements in pain and function in patients with hip or knee osteoarthritis.

A 2017 network meta-analysis compared the effectiveness of acetaminophen vs. anti-inflammatory drugs for pain relief in patients

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with hip or knee osteoarthritis (N = 3,209; 71% females; mean age range = 62 to 70 years).[2] Six of the included RCTs (all of which were included in the 2019 systematic review discussed previously) compared daily acetaminophen dosages of less than 2,000 mg, 3,000 mg, or 3,900 to 4,000 mg. The effect size for a clinically significant reduction in pain was −0.37 based on prior studies, which corresponded to a 9-mm difference on a 100-mm VAS. Pooled results yielded an estimated −0.18 overall effect size for acetaminophen; the effect sizes of various dosages were −0.7 (95% CI, −0.42 to −0.27), −0.18 (95% CI, −0.68 to −0.32), and −0.16 (95% CI, −0.27 to −0.06) for less than 2,000 mg, 3,000 mg, and 3,900 to 4,000 mg, respectively. The authors concluded that acetaminophen monotherapy does not have a role in the treatment of pain due to hip or knee osteoarthritis.

A 2018 industry-funded, multicenter, double-blind, double-dummy RCT evaluated the effectiveness and safety of sustained-release and extended-release acetaminophen vs. placebo in adults with hip or knee osteoarthritis.[3] Of the 676 enrolled patients, more than 90% had knee osteoarthritis, 62% were female, 74% identified as Caucasian, and the mean age was 60.5 years. Patients were randomized to sustained-release acetaminophen, 2,000 mg twice daily (n = 235), extended-release acetaminophen, 1,330 mg three times daily (n = 236), or placebo (n = 237) for 12 weeks. The primary outcome was a time-weighted mean change in WOMAC pain scores from baseline, which were converted to VAS scores (0 to 100 mm). All three interventions reduced pain scores from baseline, but there was no difference in pain reduction with sustained-release acetaminophen vs. placebo (–28.2 vs. –25.7 mm, respectively; MD = –2.5 mm; 95% CI, −6.0 to 1.0 mm) or with extended-release acetaminophen vs. placebo (–25.9 vs. –25.7 mm, respectively; MD = −0.2 mm; 95% CI, –3.7 to 3.4).

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