

POEMs

Patient-Oriented Evidence that Matters

This selection of POEMs provides high-level evidence that tricyclic anti-depressants are better than opioids for treating post-herpetic neuralgia, that the Ottawa rule is highly effective for predicting which patients need an ankle x-ray and that the combination of an inhaled steroid and a beta-agonist is better than monotherapy in the treatment of patients who have COPD.

Clinical question

Which is more effective for the treatment of postherpetic neuralgia: opioids or tricyclic antidepressants?

Setting

Outpatient (any)

Study design

Cross-over trial (randomised)

Synopsis

Adults with neuropathic pain for at least three months after lesions had resolved were recruited through physician referral and advertisements. They had to have pain of at least four on a scale of 10 to be included. Of 103 patients who were screened, 76 were randomised and 71 started the study, but only 44 completed all three study periods. This was a crossover trial with patients receiving an opioid, a tricyclic antidepressant (TCA), or a placebo for each of three eight-week study periods, with a one-week washout period between phases. The order in which they received the drugs was randomly assigned using concealed allocation. Outcomes were assessed twice a week via telephone, and at a clinic visit at the end of each study period. The opioid was sustained release morphine (titrated to a maximum of 240mg per day), and was compared

with nortriptyline (titrated up to 160mg per day) or placebo in two or three divided doses per day. Patients who did not tolerate morphine could be switched to methadone, and those who didn't tolerate nortriptyline could be switched to desipramine. Patients who took at least one dose of a medication and gave a rating of pain were included for that study period. The primary outcomes were pain intensity (0 to 10), pain relief (0% to 100%), and cognitive function (using the Wechsler Adult Intelligence Scale and other validated measures).

The mean daily doses were 91mg for sustained-release morphine and 89mg for nortriptyline. Opioids and TCAs were both more effective at reducing pain intensity than placebo (1.9 vs 1.4 vs 0.2 points on the 10-point scale; $P < .01$). This is a clinically meaningful difference, but barely. The percentage pain relief was also similar between opioids and TCAs, and both were again better than placebo (38% vs 32% vs 11%; $P < .001$). TCAs slightly reduced some cognitive measures; opioids and placebo did not. Significantly more pa-

tients preferred opioids to TCAs (54% vs 30%). Constipation, nausea, and drowsiness were common in the opioid group, and dizziness was common in the TCA group. Most important, patients voted with their feet in the opioid group: they were more likely to drop out during or after the opioid phase ($n=20$) than during the TCA ($n=6$) or placebo ($n=1$) phases.

Bottom line

Opioids and TCAs provide similar pain relief for patients with postherpetic neuralgia, but TCAs are generally better tolerated.

Level of evidence

(<http://www.infopoems.com/levelsofevidence.cfm>)

1b

Reviewed by

ME

Reference

Raja SN, Haythornthwaite JA, Pappagallo M, et al. Opioids versus antidepressants in postherpetic neuralgia: a randomized, placebo-controlled trial. *Neurology* 2002; 59:1015-21.

Clinical question

Can the Ottawa ankle rule be used to exclude fractures of the ankle?

Setting

Emergency department

Study design

Meta-analysis (randomised controlled trials)

Synopsis

The Ottawa ankle rule has been used, by those who can remember it, to determine whether an acute ankle sprain warrants an x-ray. This review identified 27 studies, enrolling 15 581 patients, that have evaluated the usefulness and accuracy of these rules in children and adults. The authors did a good job of scouring the literature, using multiple databases, reference lists of identified articles, and contacting authors and experts. The rules were

designed to be 100% sensitive (i.e. not miss any ankle fractures) and, overall, came pretty close to the mark. When ankles were evaluated within 48 hours of injury, the overall sensitivity of the rules was 99.6% (negative likelihood ratio=0.08). In other words, only 0.4% of fractures were missed. The false-negative rate in children was higher: 1.22% (negative likelihood ratio=0.07). The specificity, accordingly, was lower, 10% to 79%, depending on the prevalence of fracture.

Here is the rule: An x-ray is not necessary if the patient can walk at least four steps immediately after the injury or in the emergency department, and there is no localised tenderness of the posterior edge or tip of either malleolus.

Bottom line

The Ottawa ankle rule is highly accurate in identifying patients with ankle sprains who do not need an x-ray, and used properly may reduce the number of unnecessary x-rays by 30% to 40%.

Level of evidence

(<http://www.infopoems.com/levelsofevidence.cfm>)

1a

Reviewed by

AS

Reference

Bachmann LM, Kolb E, Koller MT, Steurer J, ter Riet G. Accuracy of Ottawa ankle rules to exclude fractures of the ankle and mid-foot: systematic review. *BMJ* 2003; 3226:417-9.

Clinical question

Are combined steroids and beta-agonists effective in the chronic management of chronic obstructive pulmonary disease?

Setting

Outpatient (any)

Study design

Randomised controlled trial (double-blinded)

Synopsis

In this large multicenter study, the researchers randomly assigned patients with chronic obstructive pulmonary disease (COPD) to receive 50mcg salmeterol twice daily (n=372), 500mcg fluticasone twice daily (n=374), 50mcg salmeterol and 500mcg fluticasone twice daily (n=358), or placebo (n=361) for 12 months. All the patients had a history of at least 10 pack-years of smoking, of chronic bronchitis, at least one episode of acute COPD symptom exacerbation per year in the previous three years, and at least one exacerbation in the year immediately before trial entry that required treatment with oral corticosteroids, antibiotics, or both. Additionally, they had a baseline FEV₁

before bronchodilation that was 25% to 70% of that predicted, an increase of less than 10% of predicted FEV₁ 30 minutes after inhaling 400µg salbutamol (albuterol), and a prebronchodilator FEV₁/FVC ratio of 70% or less. Although the main outcome of interest was change in FEV₁, the authors also assessed use of rescue medications, night-time awakenings, and other symptoms. The group receiving combined treatment had significantly fewer drop-outs compared with the other groups (89 compared with 119, 108, and 140, respectively). This group also had more improvement in FEV₁. All treatment groups experienced fewer exacerbations (1.04, 1.05, 0.97 per year, respectively) than those given placebo (1.3 per year). Compared with treatment with beta-agonists, you would need to treat 25 patients per year with combined therapy to prevent one exacerbation. Additionally, compared with using steroids alone, you would need to treat 13 with combined therapy. Finally, while all active treatments im-

proved symptoms, combined therapy also improved overall health status.

Bottom line

In this well-designed study, patients with COPD treated with a combination of fluticasone and salmeterol have modest improvements in function, symptoms, and spirometry compared with monotherapy. They also experienced fewer exacerbations. This study doesn't report other important outcomes, like hospitalisations and mortality.

Level of evidence

(<http://www.infopoems.com/levelsofevidence.cfm>)

1b

Reviewed by

HB

Reference

Calverley P, Pauwels R, Vestbo J, et al. Combined salmeterol and fluticasone in the treatment of chronic obstructive pulmonary disease: a randomised controlled trial. *Lancet* 2003; 361:449-56.