POEMs

Pregabalin Does Not Decrease the Pain of Sciatica

Clinical Question

Is pregabalin (Lyrica) an effective treatment for the pain of acute or chronic sciatica?

Bottom Line

Pregabalin does not relieve pain in patients with sciatica. (Level of Evidence = 1b)

Synopsis

Gabapentin (Neurontin) and its prodrug pregabalin are widely used for the treatment of neuropathic pain, including sciatica. This Australian trial recruited patients with moderate to severe sciatica, defined as pain radiating below the knee and accompanied by evidence of nerve root or spinal nerve involvement such as sensory deficits, diminished reflexes, or weakness. The pain had to have been present for between one week and one year. The average age of the 207 participants was 54 years, 85% had dermatomal pain, 37% had a neurologic deficit, and 30% had a motor deficit. The patients were randomly assigned to receive pregabalin in a dosage of 75 mg twice daily, increasing to a final target dosage of 300 mg twice daily at eight weeks, or matching placebo. The primary outcome was pain on a 10-point scale, with a difference of 1.5 points considered to be the minimal clinically important difference. Patients were followed for up to one year, and a variety of secondary outcomes were measured. Groups were balanced at the start of the study, and analysis was by intention to treat. At eight weeks and at 52 weeks, there was no significant difference in the primary outcome and no difference in secondary outcomes including disability, back pain intensity, global perception of the effect, and quality of life.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Mathieson S, Maher CG, McLachlan AJ, et al. Trial of pregabalin for acute and chronic sciatica.* N Engl J Med. *2017;376(12):1111-1120.*

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Dexamethasone May Reduce Sore Throat Symptoms in Adults at 48 Hours

Clinical Question

Are oral steroids effective in the treatment of acute sore throat in adults?

Bottom Line

A single dose of oral dexamethasone is no more effective than placebo in resolving acute sore throat symptoms at 24 hours in adults who do not receive immediate antibiotic therapy. However, among a multitude of exploratory secondary outcomes, the authors found that, compared with placebo, dexamethasone increased the proportion of patients with symptom resolution at 48 hours (number needed to treat [NNT] = 12; 95% confidence interval [CI], 7 to 146). (Level of Evidence = 1b)

Synopsis

These investigators identified adults, 18 years or older, who presented to primary

care offices in England with acute symptoms of sore throat and odynophagia for which the treating clinician did not prescribe immediate antibiotic therapy. Exclusion criteria included the recent use of inhaled or oral steroids, recent adenotonsillectomy, recent use of antibiotics, or a clear alternative diagnosis such as pneumonia. Eligible participants randomly received (concealed allocation assignment) a single dose of dexamethasone (10 mg) or matching placebo; 11 patients were found ineligible and excluded after participation. Treating clinicians could decide to offer no antibiotics (n = 349) or a delayed antibiotic (n = 227). Patients unaware of group assignment self-assessed outcomes including the primary outcome of complete resolution of sore throat symptoms at 24 hours. Secondary exploratory outcomes included complete resolution of sore throat at 48 hours, duration of moderately bad symptoms, time to onset of pain relief and time to complete resolution of symptoms, consumption of delayed antibiotic prescription, time missed from work or education, attendance at or telephone contact with any heath care facility because of the sore throat, and use of over-the-counter medications and/or other prescription medications in the first seven days. Complete follow-up occurred for 94% of participants at one month.

Using intention-to-treat analysis, no significant difference occurred among the steroid group and the placebo group in achieving complete resolution of symptoms at 24 hours. Results were similar between patients who were and were not offered a delayed antibiotic prescription. At 48 hours, significantly more participants who received dexamethasone reported complete resolution of symptoms compared with those who received the placebo (35.4% vs. 27.1%, respectively; NNT = 12; 95% CI, 7 to 146). Neither severity of sore throat at baseline nor a positive throat culture for *Streptococcus* bacteria on throat swab was related to group differences. No significant differences occurred between the treatment group and the placebo group in other secondary outcomes or serious adverse events.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (primary care)

Reference: *Hayward GN, Hay AD, Moore MV, et al. Effect of oral dexamethasone without immediate antibiotics vs placebo on acute sore throat in adults: a randomized clinical trial.* JAMA. *2017;317(15):1535-1543.*

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No Increased Risk of ASD, ADHD, or SGA with First-Trimester Antidepressant Use

Clinical Question

Does maternal exposure to an antidepressant in the first trimester of pregnancy increase the risk of preterm birth, small for gestational age (SGA), autism spectrum disorder (ASD), or attention-deficit/hyperactivity disorder (ADHD) in offspring?

Bottom Line

This study found that maternal antidepressant use during the first trimester of pregnancy is associated with an increased risk of preterm birth, but not SGA, ASD, or ADHD. Another study in the same issue (Brown HK, et al. *JAMA*. 2017;317(15):1544-1552) also reported no increased risk of ASD with in utero exposure to selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors. (Level of Evidence = 2b–)

Synopsis

These investigators analyzed data obtained from multiple registries in Sweden that link first-trimester exposure to any antidepressant medication with the risk of preterm birth, SGA, ASD, or ADHD in offspring. Various registries also provided information related to potential confounding variables, including parity, year of birth, maternal and paternal age at childbirth, level of completed education, history of criminal conviction, and history of severe psychiatric illnesses. Maternal exposure was defined by self-report and pharmacy dispensation records. "First-trimester exposure" was defined as having at least one medication dispensation between 90 days before and 90 days after the estimated date of conception. "Use before pregnancy only" was defined as having at least one medication dispensation between 270 days and 90 days before estimated conception and no dispensations during pregnancy or during the first 180 days after pregnancy. Birth outcomes were assessed using standard international diagnostic criteria. To account for shared genetic and early environmental influences, a sibling comparison model evaluated antidepressant exposure and outcomes within families with siblings born to the same mother.

The final cohort of eligible offspring (N = 1,580,629) included those born between 1996 and 2012. Of these, 1.4% (n = 22,544) of the offspring were exposed to any antidepressant during the first trimester, with 82% (n = 18,470) of those exposed to selective serotonin reuptake inhibitors. Median follow-up time for neurodevelopmental disorders (ASD and ADHD) in offspring was approximately nine years for the unexposed group

and six years for the exposed group. When compared with unexposed offspring, exposed offspring had a higher probability of preterm birth, SGA, ASD, and ADHD overall. However, in the sibling comparison models, although first-trimester exposure was significantly associated with preterm birth, it was not significantly associated with SGA, ASD, or ADHD. Likewise, when comparing maternal antidepressant first-trimester exposure with before-pregnancy exposure only, a significant association occurred with an increased risk of preterm birth, but not for any of the other outcomes, including SGA, ASD, or ADHD. Finally, antidepressant use during the second or third trimester was also not associated with ASD or ADHD.

Study design: Cohort (retrospective)

Funding source: Government

Setting: Population-based

Reference: *Sujan AC, Rickert ME, Oberg AS, et al. Associations of maternal antidepressant use during the first trimester of pregnancy with preterm birth, small for gestational age, autism spectrum disorder, and attention-deficit/hyperactivity disorder in offspring.* JAMA. *2017;317(15):1553-1562.*

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No Added Benefit with Higher Doses of Ketorolac for Treatment of Acute Pain in the Emergency Department

Clinical Question

Are lower doses of ketorolac as effective as standard doses for acute pain control in patients presenting to the emergency department?

Bottom Line

A 10-mg dose of ketorolac is as effective as higher doses for the short-term treatment of acute pain for patients in the emergency department. (Level of Evidence = 1b)

Synopsis

Ketorolac is a nonsteroidal anti-inflammatory drug available in parenteral form for the treatment of acute pain. Although higher doses are often used, ketorolac may have a therapeutic ceiling of 10 mg. To investigate the effectiveness of lower doses of ketorolac, these investigators used a convenience sample of patients presenting to the emergency department on weekdays between 8:00 a.m. and 8:00 p.m. to enroll those with acute flank, abdominal, musculoskeletal, or headache pain rated at least 5 on a 10-point rating scale. The authors excluded patients with unstable vital signs, active peptic ulcer disease or gastrointestinal bleeding, or history of liver or renal disease, and those who were pregnant or breastfeeding. Using concealed allocation, investigators randomized 240 patients to receive a 10-mg, 15-mg, or 30-mg dose of ketorolac. Patients who still required pain medication 30 minutes after administration of the study drug received intravenous morphine at a dose of 0.1 mg per kg.

The three groups were similar at baseline: All groups had a mean age of 40 years, two-thirds of patients were women, and the baseline pain score was between 7 and 8. Analysis was by intention to treat. The primary outcome was a reduction of pain scores at 30 minutes after administration of the study drug. In all three groups, there was a significant decrease in pain scores from baseline to 30 minutes by at least two points. However, there were no significant differences in reduction of pain scores across the three groups at 30 minutes, or at subsequent time points of 60, 90, and 120 minutes. Further, there were no differences in the use of rescue morphine analgesia among the three groups. The most common adverse effects reported were dizziness, nausea, and headache, and they were similar in all three groups.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Emergency department

Reference: *Motov S, Yasavolian M, Likourezos A, et al. Comparison of intravenous ketorolac at three single-dose regimens for treating acute pain in the emergency department: a randomized controlled trial [published online ahead of print December 16, 2016].* Ann Emerg Med. *http://www.sciencedirect.com/science/article/pii/S0196064416312446 [login required]. Accessed June 27, 2017.*

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