POEMs

Patient-Oriented Evidence That Matters

Five Days of Antibiotic Therapy Is Comparable with 10 Days in Children with Community-Acquired Pneumonia

Clinical Question

In children with pneumonia who do not need hospitalization, is five days of treatment with high-dose amoxicillin comparable with 10 days of treatment?

Bottom Line

In a limited study, children with community-acquired pneumonia who were treated with five days of high-dose amoxicillin had cure rates comparable with those who were treated for 10 days. (Level of Evidence = 1b)

Synopsis

The study took place before the COVID-19 pandemic in two emergency departments in Hamilton, Ontario, and enrolled children six months to 10 years of age with radiographically confirmed community-acquired pneumonia who were not sick enough to be hospitalized. The researchers randomized the children to receive five days of high-dose amoxicillin (75 mg per kg to 100 mg per kg per day) plus five days of placebo (n = 140) or 10 days of high-dose amoxicillin (n = 141). The dose range was based on Canadian Paediatric Society guidelines that allow for slight dose variation to simplify medication administration and reduce potential dosing errors. After two to three weeks of follow-up, more children who received five days of treatment had a clinical cure (85.7%) than those who received 10 days of treatment (84.1%). The number of days lost in caregiving was lower among those treated for five days (two days vs. three days, respectively), and there was no difference in absenteeism among the children (one day for each group). Approximately 10% of children in each group were lost to follow-up. The study was designed as a noninferiority study and needed 135 participants in each group to be confident that the two interventions were comparable.

Study design: Randomized controlled trial (nonblinded)

Funding source: Foundation

Allocation: Concealed

Setting: Inpatient (any location)

Reference: *Pernica JM, Harman S, Kam AJ, et al. Short-course antimicrobial therapy for pediatric community-acquired pneumonia: the SAFER randomized clinical trial.* JAMA Pediatr. *2021; 175(5):475-482.*

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Antibiotic Therapy Does Not Prevent Death or Acute Exacerbations in Adults with Idiopathic Pulmonary Fibrosis

Clinical Question

Do prophylactic antibiotics improve outcomes in adults with idiopathic pulmonary fibrosis (IPF)?

Bottom Line

The study found an increased number of adverse events without any significant benefit from antimicrobial therapy compared with usual care alone for adults with IPF. The study was terminated earlier than planned because of futility and the possibility of significantly increased harm. (Level of Evidence = 1b)

Synopsis

An increased lung bacterial load is associated with disease progression in adults with IPF. The investigators randomized (concealed allocation assignment) 513 adults, 18 years or older, who met the standard diagnostic criteria for IPF to receive antimicrobial therapy (trimethoprim, 160 mg/sulfamethoxazole, 800 mg twice daily, plus folic acid, 5 mg daily, or doxycycline, 100 mg once or twice daily, depending on body weight) in addition to usual care or to usual care alone (no placebo was provided). Although patients and their clinicians remained aware of their treatment group assignment, the individuals who assessed outcomes were unaware of the assignments. Complete follow-up occurred for more than 97% of participants for a median of 12.7 months. Using intention-to-treat analysis, no differences occurred between the antimicrobial group and the usual care alone group for the primary end point of respiratory event–related

hospitalization or all-cause mortality. No significant treatment group differences occurred in multiple secondary outcomes, including respiratory infections, fatigue, or quality of life. An increased number of adverse events occurred in the antimicrobial groups, including diarrhea, rash, vomiting, and arrhythmias secondary to hyperkalemia.

Study design: Randomized controlled trial (single-blinded)

Funding source: Foundation

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: *Martinez FJ, Yow E, Flaherty KR, et al.; CleanUP-IPF Investigators of the Pulmonary Trials Cooperative. Effect of antimicrobial therapy on respiratory hospitalization or death in adults with idiopathic pulmonary fibrosis: the CleanUP-IPF randomized clinical trial.* JAMA. *2021;325(18):1841-1851.*

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Dual Antiplatelet Therapy Is Superior to Aspirin in Preventing Short-Term Recurrent Stroke at the Cost of More Major Bleeding

Clinical Question

Is dual antiplatelet therapy, started within 24 hours of symptom onset, more effective than aspirin in preventing subsequent cerebrovascular events in patients who have had acute stroke or transient ischemic attack (TIA)?

Bottom Line

If the authors have found all the relevant studies, administering dual antiplatelet therapy within 24 hours of a mild to moderate stroke or TIA is more effective than aspirin at decreasing recurrent stroke over the subsequent 90 days. There is a low overall risk of major bleeding, but it is significantly higher with dual antiplatelet therapy than with aspirin. (Level of Evidence = 1a–)

Synopsis

The authors searched several databases and a trial registry to identify randomized trials that included adult patients with acute stroke or TIA who were randomized to receive antiplatelet therapy within 24 hours of symptom onset. The included studies compared the safety and efficacy of dual antiplatelet therapy (aspirin plus a P2Y12 inhibitor such as clopidogrel [Plavix], ticagrelor [Brilinta], or prasugrel [Effient]) with aspirin alone. The authors excluded patients with presumed cardioembolic strokes and patients who were not already using anticoagulation. The authors do not describe a formal assessment of study quality. They included four studies with a total of 21,459 patients: three studies evaluated clopidogrel and one evaluated ticagrelor. Although all the trials enrolled patients with mild to moderate stroke (National Institutes of Health Stroke Scale score 0 to 5) or TIA, the distribution of patients with TIA varied from 2.6% to 43.2%. Therapy duration ranged from 21 to 90 days, and the longest follow-up period was 90 days. The rate of recurrent stroke was lower in patients treated with dual antiplatelet therapy (5.8% vs. 7.7%; number needed to treat = 53; 95% CI, 40 to 83), but the rate of major bleeding was also higher in those receiving dual antiplatelet therapy (0.66% vs. 0.27%; number needed to harm = 256; 95% CI, 172 to 476). There was no difference between groups in all-cause mortality. There were variable degrees of heterogeneity among the data.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Unknown/not stated

Setting: Various (meta-analysis)

Reference: *Bhatia K, Jain V, Aggarwal D, et al. Dual antiplatelet therapy versus aspirin in patients with stroke or transient ischemic attack: meta-analysis of randomized controlled trials.* Stroke. *2021;52(6):e217-e223.*

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Anticonvulsants, SNRIs, and Rubefacients Are Best Initial Choices for Chronic Pain Caused by Diabetic Neuropathy or Postherpetic Neuralgia

Clinical Question

Which treatments for chronic neuropathic pain can provide clinically meaningful improvement?

Bottom Line

Given the balance of benefits and harms, there is moderately good evidence for anticonvulsants (pregabalin [Lyrica] and gabapentin [Neurontin] were similarly effective and well tolerated) and serotonin-norepinephrine reuptake inhibitors (SNRIs; with duloxetine [Cymbalta] and venlafaxine being similarly effective and well tolerated) for treating diabetic neuropathy and postherpetic neuralgia. Rubefacients (usually salicylates) appear to be effective but are less well studied with low-quality evidence. Acupuncture, opioids, and tricyclic antidepressants cannot be recommended based on current evidence. (Level of Evidence = 1a–)

Synopsis

This report describes findings from a series of meta-analyses of placebo-controlled randomized trials of at least three months' duration on the effectiveness of drug and nondrug treatments for chronic neuropathic pain, with a focus on diabetic neuropathy, postherpetic neuralgia, and trigeminal neuralgia. Only studies that provided results as

the presence or absence of a clinically meaningful response, defined as at least a 30% improvement on a scale of pain and/or function, were included. Studies in pregnant patients, of acute pain, and those with an active comparator were excluded. The authors found no qualifying studies for trigeminal neuralgia, or for topical lidocaine or exercise as interventions. The authors identified 40 randomized controlled trials with moderate certainty of evidence for anticonvulsants; the bulk of the evidence was for pregabalin and gabapentin, and both were effective (number needed to treat [NNT] = 7 for one patient to respond; number need to harm [NNH] = 17 to 22 for withdrawal due to adverse events). Rubefacients (topical drugs that cause irritation and redness of skin) were studied in 10 randomized controlled trials with low certainty of evidence; low-dose patches or creams and high-potency patches were similarly effective (NNT = 7) and were generally well tolerated (NNH = 25 for withdrawal). The SNRIs duloxetine, venlafaxine, and desvenlafaxine (Pristiq) were studied in eight moderate-certainty studies, with an NNT of 7 for response and NNH of 13 for withdrawal. Opioids were studied in six low-certainty studies, with an NNT of 8 for one patient to respond but a similar NNH of 12 for withdrawal due to adverse events. Acupuncture was only studied in three trials with very low certainty; no significant benefit was detected, although the confidence interval is wide (relative risk = 1.81; 95% CI, 0.55 to 6.0). Tricyclic antidepressants were studied in only two small, low-certainty studies and no significant benefit was seen in the appropriate random effects meta-analysis. Results are summarized in *the accompanying table*.

SUMMARY TABLE

Intervention	Studies (participants)	Number needed to treat (95% CI)	Number needed to harm	Quality
Anticonvulsants	40 (9,575)	7	17 to 22	Moderate
Serotonin-norepinephrine reuptake inhibitors	8 (2,746)	7	13	Moderate
Rubefacients	10 (2,344)	7	25	Low
Opioids	6 (1,149)	8	12	Low

Study design: Meta-analysis (randomized controlled trials)

Funding source: Self-funded or unfunded

Setting: Various (meta-analysis)

Reference: *Falk J, Thomas B, Kirkwood J, et al. PEER systematic review of randomized controlled trials: management of chronic neuropathic pain in primary care.* Can Fam Physician. *2021;67(5): e130-e140.*

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