POEMs

Patient-Oriented Evidence That Matters

Five Days of Penicillin for Strep Throat Is Equal to 10 Days

Clinical Question

Can strep throat in children and adults be treated with five days of oral penicillin?

Bottom Line

Five days of 800-mg penicillin four times a day produced noninferior results to 10 days of 1,000-mg penicillin three times a day, with shorter symptom duration. This is not the first study to show similar benefits with a shorter duration of oral antibiotics. (Level of Evidence = 2b)

Synopsis

The investigators enrolled 317 adults and 105 children (six years and older) from 17 primary care centers in Sweden. Eligible patients had to have at least three Centor criteria and a positive rapid antigen test result for group A streptococcus. Using concealed allocation, patients were randomly assigned to receive either 800-mg penicillin four times a day for five days or 1,000-mg penicillin three times a day for 10 days. This was an open-label trial, meaning that patients and clinicians were aware of the treatment the patient received. The researchers who analyzed the data were masked to treatment until the results were assembled. Clinical cure, defined as complete recovery without major residual symptoms or clinical findings, was assessed five to seven days after the completion of treatment; that is, on day 10 to day 12 in the five-day treatment group and on day 15 to day 17 in the 10-day treatment group. This timing of assessment could possibly favor better results with longer treatment. In the per-protocol analysis (patients who completed treatment), cure rates at five to seven days post treatment were 89.6% in the five-day group and 93.3% in the 10-day group. Results were similar when using intention-to-treat analysis. Patients receiving the higher daily dose/shorter duration had quicker symptom resolution. Bacterial cure rates were higher with 10 days of treatment but there was no difference in complication rates or new episodes of tonsillitis at the three-month follow-up. Adverse events such as diarrhea, nausea, or vaginitis were more likely and lasted longer in the 10-day group. The study had a power of 85% to detect a greater than 10% difference between treatments if one existed.

Study design: Randomized controlled trial (single-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (primary care)

Reference: *Skoog Ståhlgren G, Tyrstrup M, Edlund C, et al. Penicillin V four times daily for five days versus three times daily for 10 days in patients with pharyngotonsillitis caused by group A streptococci: randomised controlled, open label, non-inferiority study.* BMJ. *2019;367:l5337.*

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Bedtime Instead of Morning Ingestion of Hypertension Medication Equals a Significantly Higher Reduction in Cardiovascular Disease Risk

Clinical Question

Does bedtime ingestion instead of morning ingestion of hypertension medications produce better cardiovascular disease risk reduction in adults with hypertension?

Bottom Line

This study found a significant reduction in mortality and morbidity among patients who took their once-daily antihypertensive medications at bedtime instead of in the morning. No significant difference occurred in compliance rates between bedtime and morning ingestion times. Individual experiences may differ in clinical practice. (Level of Evidence = 1b–)

Synopsis

The investigators identified 19,168 adults, 18 years or older, who met standard criteria for hypertension that required prescription treatment to lower blood pressure (BP). The study participants randomly received (uncertain

concealment) assignment to the intervention group or to the control group. The intervention group was told to ingest the entire daily dose of one or more prescribed BP-lowering medications at bedtime. The control group was told to ingest the entire daily dose upon waking. Clinicians provided care without restriction of choice of BP-lowering medication approved for once-daily dosing (e.g., angiotensin receptor blocker, angiotensin-converting enzyme inhibitor, calcium channel blocker, beta blocker, diuretic). Statins, aspirin, and diabetes mellitus medications were also prescribed as needed and ingested as recommended. Individuals masked to treatment group assignment assessed outcomes, including the primary composite outcome of myocardial infarction, coronary revascularization, heart failure, stroke, and cardiovascular disease death. Complete follow-up occurred for more than 99% of participants at a median of 6.3 years.

Using intention-to-treat analysis, significantly fewer patients in the bedtime group experienced the primary cardiovascular disease outcome (n = 1,752 total) compared with the morning group (adjusted hazard ratio = 0.55; 95% CI, 0.50 to 0.61; number needed to treat = 20.3; 95% CI, 17.4 to 24.3). Adverse events occurred similarly in both groups. Poor adherence was similarly reported at any visit during follow-up in both groups (approximately 3%).

Study design: Randomized controlled trial (single-blinded)

Funding source: Government

Allocation: Uncertain

Setting: Outpatient (primary care)

Reference: *Hermida RC, Crespo JJ, Domínguez-Sardiña M, et al.; Hygia Project Investigators. Bedtime hypertension treatment improves cardiovascular risk reduction: the Hygia Chronotherapy Trial [published online October 22, 2019].* Eur Heart J. *https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehz754/5602478*

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Results of Fecal Immunochemical Tests for Colorectal Cancer Screening Not Affected by NSAIDs, Aspirin, or Anticoagulants

Clinical Question

Are the modern fecal immunochemical tests (FIT) for occult blood in the stool less accurate in patients who are taking aspirin, an anticoagulant, or a nonsteroidal anti-inflammatory drug (NSAID)?

Bottom Line

The use of aspirin, NSAIDs, and oral anticoagulants has no clinically important effects on the positive predictive value of FIT in a screening population. (Level of Evidence = 1a)

Synopsis

Previous research has shown that approximately 6.2% of screening FIT results are positive, with a positive predictive value of 35% to 55%. The authors wondered whether the use of something that can make you bleed would reduce the positive predictive value by making benign lesions more likely to bleed (leading to more false-positive results), or whether it would increase the positive predictive value by making precancerous and malignant lesions more likely to bleed. They did a search of the literature and identified eight studies with 2,022 patients that compared the accuracy of FIT in a screening population of patients taking an oral anticoagulant or an NSAID with those not taking either drug. Of the eight studies, all but one were done in Europe (the eighth was in Hong Kong), and most used a FIT cutoff of 15 to 20 mcg hemoglobin per g. Six studies included aspirin users, four included oral anticoagulant users, and one included NSAID users (three of the studies included more than one medication). The authors found no consistent effect on positive predictive value among users and nonusers of oral anticoagulants and NSAIDs, and in general the differences were small. For example, the pooled positive predictive value for advanced neoplasia was 38.2% in aspirin and NSAID users and 39.4% in nonusers. The positive predictive values for colorectal cancer in oral anticoagulant users and nonusers were 5.7% and 6.2%, respectively. The positive predictive values for advanced neoplasia in oral anticoagulant users and nonusers were 37.6% and 40.3%, respectively.

Study design: Systematic review

Funding source: Self-funded or unfunded

Setting: Various (meta-analysis)

Reference: *Nieuwenburg SA, Vuik FE, Kruip MJ, et al. Effect of anticoagulants and NSAIDs on accuracy of faecal immunochemical tests (FITs) in colorectal cancer screening: a systematic review and meta-analysis.* Gut. *2019;68(5):866-872.*

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No Benefit to Routine Antipsychotic Use for Treatment or Prevention of Delirium in Hospitalized Patients

Clinical Question

Should antipsychotics be used to treat or prevent delirium in hospitalized patients?

Bottom Line

Evidence does not support the routine use of haloperidol or second-generation antipsychotics for the treatment or prevention of delirium in hospitalized patients. Although second-generation antipsychotics may reduce the incidence

of delirium in the postoperative setting, more research is needed to confirm this. The use of second-generation antipsychotics can also lead to QT prolongation, so patients receiving these medications should be closely monitored. (Level of Evidence = 1a–)

Synopsis

The investigators searched multiple databases including PubMed, Embase, and the Cochrane Central Register of Controlled Trials, as well as hand-searched reference lists of included articles, to find randomized controlled trials (RCTs) that compared antipsychotics with either placebo or each other for the prevention of delirium. Two reviewers independently selected articles for inclusion and assessed the risk of bias. Out of the 14 included RCTs (n = 4,281), nine had a low risk of bias (n = 3,407). All were conducted in the inpatient setting, seven in the intensive care unit. There was heterogeneity among the studies in patient populations, settings, antipsychotic medication dosing and administration, and assessment of outcomes. Haloperidol does not affect delirium incidence, delirium duration, mortality, or hospital length of stay. There is insufficient evidence to make conclusions on the effect of haloperidol on delirium severity or sedation. Although there is some evidence that second-generation antipsychotics can reduce delirium incidence in the postoperative setting (relative risk [RR] = 0.36; 95% CI, 0.26 to 0.50), these drugs have no effect on hospital length of stay or mortality and there is insufficient evidence to determine effect on delirium severity, delirium duration, or sedation. This review found no statistically significant differences between haloperidol or second-generation antipsychotics, compared with placebo, in rate of arrhythmias, QTc prolongation, or neurologic events.

In a similarly conducted systematic review evaluating the use of antipsychotics for the treatment of delirium in hospitalized patients, 16 RCTs and 10 observational studies (n = 5,607) were included. Haloperidol or second-generation antipsychotics, compared with placebo, did not affect delirium duration, mortality, sedation status, or hospital length of stay. Second-generation antipsychotic use did, however, result in more harmful cardiac effects, specifically QT prolongation compared with placebo (RR = 1.95; 95% CI, 1.03 to 3.71).

Study design: Systematic review

Funding source: Government

Allocation: Uncertain

Setting: Inpatient (any location)

Reference: *Oh ES, Needham DM, Nikooie R, et al. Antipsychotics for preventing delirium in hospitalized adults: a systematic review.* Ann Intern Med. *2019;171(7):474-484, and Nikooie R, Neufeld KJ, Oh ES, et al. Antipsychotics for treating delirium in hospitalized adults: a systematic review.* Ann Intern Med. *2019;171(7):485-495.*

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Editor's Note: Dr. Ebell is deputy editor for Evidence-Based Medicine for *AFP* and cofounder and editor-in-chief of Essential Evidence Plus, published by Wiley-Blackwell. Dr. Shaughnessy is an assistant medical editor for *AFP*. ■