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ACE Inhibitors Decrease Cardiovascular Events in Patients with Diabetes, ARBs Do Not

Clinical Question

In patients with diabetes mellitus, are angiotensin II receptor blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors similarly effective in preventing cardiovascular events?

Bottom Line

In patients with diabetes, ACE inhibitors decrease cardiovascular events and all-cause mortality. ARBs do not. Both drug classes decrease heart failure incidence. Although both drug classes have been available for almost 15 years, there is only one study of 250 patients that directly compared their effectiveness in patients with diabetes. So, we have to rely on this network analysis of studies that compared each drug class with other treatments. (Level of Evidence = 1a)

Synopsis

These researchers in China started their analysis by searching three databases, including the Cochrane Central Register of Controlled Trials, to identify randomized controlled studies comparing ACE inhibitors and ARBs with no treatment, placebo, or active control treatment in patients with diabetes. They also searched a trial registry and meeting abstracts to find unpublished data. They identified 23 studies that evaluated ACE inhibitors and 13 that tested ARBs. Only one study (enrolling just 250 patients) compared an ARB with an ACE inhibitor in this patient population. The quality of these studies is not great, so we have to be concerned about the validity of the data. ACE inhibitors decreased all-cause mortality by 13% (95% confidence interval [CI], 2% to 22%), major cardiovascular events by 14% (95% CI, 5% to 33%), and heart failure by 19% (95% CI, 7% to 29%), and did not decrease stroke risk compared with placebo or other treatments. ARBs did not affect any of these outcomes other than heart failure (30% decrease; 95% CI, 18% to 41%). Ten of the 13 studies of ARBs used a placebo comparison group, which should have inflated their relative benefit.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Government

Setting: Various (meta-analysis)

Reference: *Cheng J, Zhang W, Zhang X, et al. Effect of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers on all-cause mortality, cardiovascular deaths, and cardiovascular events in patients with diabetes mellitus: a meta-analysis.* JAMA Intern Med. *2014;174(5):773-785.*

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Accuracy of Fecal DNA and Fecal Immunochemical Test for Colorectal Cancer Detection

Clinical Question

How accurate are the new fecal DNA and fecal immunochemical tests as screening tests for colorectal cancer?

Bottom Line

Fecal DNA testing is more sensitive but less specific than fecal immunochemical testing (FIT), and as a result, has a higher false-positive rate. It is also more expensive than other noninvasive alternatives such as FIT. We do not know which test will be better at reducing mortality. (Level of Evidence = 2b) ▶

Synopsis

Fecal DNA testing looks for abnormalities characteristic of the DNA in colorectal cancer, whereas FIT is an improved version of the older tests that detect fecal occult blood but requires only a single stool specimen. Adults 50 to 85 years of age at average risk of colorectal cancer who were undergoing screening colonoscopy were invited to participate in the study. A total of 11,016 agreed and underwent the required tests. Of that group, 689 were excluded because of an insufficient specimen for fecal DNA or a specimen that leaked in shipping; 304 others were excluded because of inadequate colonoscopy; and 34 had an insufficient sample for FIT. Of the final group of 9,989 participants, 65 received a diagnosis of cancer.

Fecal DNA testing was 92% sensitive and 87% specific, whereas FIT was 74% sensitive and 95% specific. Although this looks like a clear advantage for fecal DNA (60 of 65 cancers detected compared with 48 of 65 for FIT), it is important to look a bit further. The lower specificity for fecal DNA meant that there were nearly three times as many false-positive results that would have required a follow-up colonoscopy if fecal DNA was the sole screening test (1,231 vs. 472 for FIT). Using fecal DNA, there would have been 22 colonoscopies per cancer detected compared with 11 using FIT. Also, fecal DNA testing requires the entire stool specimen, collected using a small bucket that hangs in the toilet, and costs approximately $400 to $800 (FIT costs approximately $3 to $40). Because colorectal cancer takes several years to progress from adenoma to cancer, FIT could be performed annually at a much lower cost and would likely detect many of the initially missed cancers in subsequent years.

Study design: Diagnostic test evaluation

Funding source: Industry

Setting: Outpatient (any)

Reference: *Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening.* N Engl J Med. *2014;370(14):1287-1297.*

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Aspirin in Low Doses Decreases Preeclampsia Risk

Clinical Question

Is low-dose aspirin effective in decreasing the likelihood of preeclampsia?

Bottom Line

Low-dose aspirin—ranging from 60 to 100 mg per day—beginning as early as the second trimester decreases the risk of preeclampsia, preterm birth, and intrauterine growth retardation in women who are at high risk of preeclampsia. No harms to the mother or newborn were identified in the studies. (Level of Evidence = 1a)

Synopsis

To perform this systematic review, these authors searched four databases, including the Cochrane Central Register of Controlled Trials, to identify 15 English-language randomized controlled trials that evaluated the ability of low-dose aspirin to decrease the risk of preeclampsia, preterm birth, and intrauterine growth restriction. They also evaluated two additional observational studies to assess harms. Two investigators independently selected articles for inclusion, and two investigators evaluated study quality, which was generally high. The studies enrolled almost 12,000 patients, with two studies contributing 76% of the total. Low-dose aspirin reduced preeclampsia by 2 to 5 percentage points, depending on baseline risk. Intrauterine growth retardation was also reduced by 1 to 5 percentage points, as was preterm birth (2 to 4 percentage points). No harms were identified. There was no significant heterogeneity for these outcomes.

Study design: Systematic review

Funding source: Government

Setting: Outpatient (any)

Reference: *Henderson JT, Whitlock EP, O'Connor E, Senger CA, Thompson JH, Rowland MG. Low-dose aspirin for prevention of morbidity and mortality from preeclampsia: a systematic evidence review for the U.S. Preventive Services Task Force.* Ann Intern Med. *2014;160(10):695-703.*

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Cold Symptoms Unaffected by Regular Analgesic Dosing or Use of Steam

Clinical Question

Is advice to use an analgesic "only as needed," regular dosing of an analgesic, steam inhalation, or any combination effective in treating cold symptoms?

Bottom Line

Advice regarding the use of steam inhalation, ibuprofen alone or with acetaminophen, acetaminophen alone, and regular vs. as-needed use of analgesics did not show any improved effectiveness in treating symptoms of acute respiratory tract infections. Ibuprofen may be beneficial in patients with chest symptoms and in children. However, ibuprofen advice was associated with a slight increase in the number of patients seeking a second visit for the same illness. (Level of Evidence = 1a)

Synopsis

These investigators enrolled 889 patients at least three years of age who presented to one of 25 primary care practices with a respiratory tract infection of any sort. The authors needed a lot of patients because they were assigned, using concealed allocation, to one of 12 groups. The patients were given advice to treat symptoms: take acetaminophen (paracetamol), ibuprofen, or alternate both analgesics; use regular dosing or as-needed dosing; and use steam (inhaled via a bathroom shower for five minutes three times per day) or no steam.

This was an "advice study"—the patients received advice and not the actual drugs. As a result, the drug dosing was similar between the regular dosing and as-needed use, and was below the maximal doses of either medication (e.g., fewer than three doses of acetaminophen per day and two doses of ibuprofen per day, on average). Steam was used, on average, only twice per day.

Respiratory symptoms were rated by patients on a seven-point scale from "no problem" to "as bad as it could be" two to four days after the visit. Neither advice on analgesic dosing nor on steam inhalation was significantly associated with changes in outcomes. The study had sufficient power to find a difference in these outcomes, if one existed. In specific subgroups, there was no difference between ibuprofen and acetaminophen in patients with otalgia, fever, or severe symptoms. Ibuprofen seemed to be more effective in patients with chest infections, and it also improved symptom scores in children. Patients receiving ibuprofen or the analgesic combination were slightly more likely to return to the office for unresolved symptoms.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (primary care)

Reference: *Little P, Moore M, Kelly J, et al.; PIPS Investigators. Ibuprofen, paracetamol, and steam for patients with respiratory tract infections in primary care: pragmatic randomised factorial trial.* BMJ. *2013;347:f6041.*

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