

POEMs (patient-oriented evidence that matters) are provided by Essential Evidence Plus, a point-of-care clinical decision support system published by Wiley-Blackwell. For more information, see <http://www.essentialevidenceplus.com>. Copyright Wiley-Blackwell. Used with permission.

For definitions of levels of evidence used in POEMs, see http://www.essentialevidenceplus.com/product/ebm_loe.cfm?show=oxford.

To subscribe to a free podcast of these and other POEMs that appear in *AFP*, search in iTunes for "POEM of the Week" or go to <http://goo.gl/3niWXb>.

This series is coordinated by Sumi Sexton, MD, Associate Deputy Editor.

A collection of POEMs published in *AFP* is available at <http://www.aafp.org/afp/poems>.

In Patients with Type 2 Diabetes and CV Disease, Empagliflozin Reduces CV and All-Cause Mortality

Clinical Question

In patients with type 2 diabetes mellitus and cardiovascular (CV) disease, does the addition of empagliflozin (Jardiance) improve outcomes?

Bottom Line

In patients with established CV disease and type 2 diabetes, the addition of empagliflozin to standard therapy reduces all-cause mortality and CV mortality. This is notable because empagliflozin is the only drug other than metformin to demonstrate a mortality benefit, albeit for a fairly narrow group of patients. A dose of 10 mg appears to provide a similar benefit to the 25-mg dose, but with half the risk of genital infections. It is not appropriate to extend these conclusions to all patients with type 2 diabetes, because they are at lower risk of bad outcomes and are unlikely to benefit to the same degree. (Level of Evidence = 1b)

Synopsis

Empagliflozin decreases reabsorption of glucose in the kidneys, leading to greater urinary excretion. In this industry-sponsored trial, adults with type 2 diabetes and known CV disease were randomized to receive empagliflozin, 10 mg; empagliflozin, 25 mg; or placebo. The 7,028 patients were recruited

from 590 sites in 42 countries. The mean age of participants was 63 years, 71% were men, and 5% were black. This was a very high-risk group: 75% had coronary artery disease, 23% had a previous stroke, 20% had peripheral arterial disease, and 25% had a coronary artery bypass graft. The other hypoglycemic medications used by patients included metformin (75%), insulin (53%), or a sulfonylurea (43%). Outcomes were adjudicated by a committee masked to treatment assignment, and analysis was by modified intention to treat for all patients who received at least one dose of the study drug.

The primary outcome was a composite of myocardial infarction, stroke, or CV death. Patients were followed for a median of 3.1 years. Results for the two empagliflozin doses were pooled and compared with placebo. The patients in the intervention groups had lower all-cause mortality (5.7% vs. 8.3%; $P < .001$; number needed to treat [NNT] = 38 over 3.3 years), CV mortality (3.7% vs. 5.9%; $P < .001$; NNT = 45 over 3.3 years), and hospitalization for heart failure (2.7% vs. 4.1%; $P = .002$; NNT = 71 over 3.3 years). There were no differences in other outcomes, including myocardial infarction, stroke, coronary revascularizations, or transient ischemic attacks. The pooled dropout rate due to adverse events was 11.5% for the study drug and 13.0% for placebo. There were more episodes of urosepsis or pyelonephritis in the empagliflozin groups (0.8% vs. 0.5%), and far more genital infections (5.0% vs. 1.5% in men; 10.0% vs. 2.6% in women).

Study design: Randomized controlled trial (double-blinded)

Funding source: Industry

Allocation: Concealed

Setting: Outpatient (any)

Reference: Zinman B, Wanner C, Lachin JM, et al.; EMPA-REG OUTCOME Investigators. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med*. 2015;373(22):2117-2128.

MARK H. EBELL, MD, MS
Professor
University of Georgia, Athens, Ga.

No Difference Between Oxycodone/Acetaminophen and Hydrocodone/Acetaminophen for Acute Extremity Pain

Clinical Question

How effective is oxycodone/acetaminophen compared with hydrocodone/acetaminophen in the management of acute extremity pain in adults, including sprains/strains and fractures?

Bottom Line

This study found no significant difference in the management of acute musculoskeletal extremity pain, including fractures, with oxycodone/acetaminophen vs. hydrocodone/acetaminophen. Adverse events, including nausea and dizziness, occurred significantly more often with oxycodone/acetaminophen (number needed to treat to harm = 10). (Level of Evidence = 1b)

Synopsis

It is commonly believed that oxycodone/acetaminophen provides better pain relief than hydrocodone/acetaminophen for adults with acute pain. These investigators identified adults (N = 240), 21 to 64 years of age, who presented to an urban emergency department with acute musculoskeletal extremity pain of less than seven days' duration. Extremity was defined as distal to and including the shoulder and hip joint. Exclusion criteria included a history of chronic pain, previous narcotic abuse, or current use of opioid pain medications. Eligible consenting patients randomly received (concealed allocation assignment) a three-day course of oxycodone/acetaminophen (5 mg/325 mg) or identically appearing hydrocodone/acetaminophen (5 mg/325 mg), one dose every

four hours as needed for pain. Individuals masked to treatment group assignment assessed outcomes using a standard validated pain scoring tool two hours after the study medication was given and approximately 24 hours after emergency department discharge. Complete follow-up occurred for 92% of patients at 24 hours.

The final diagnosis of the acute musculoskeletal extremity pain included approximately 65% fractures, 40% sprains and strains, and 5% other. Using intention-to-treat analyses, no significant group differences occurred in mean pain score reduction between baseline and follow-up. Approximately 60% of patients in both groups reported at least a 50% decrease in pain. All patients were also equally satisfied with their analgesic management. Adverse reactions, including nausea and dizziness, occurred significantly more often in patients who received oxycodone/acetaminophen than in patients who received hydrocodone/acetaminophen (number needed to treat to harm = 10). The study was 80% powered to detect a predetermined clinically significant difference in pain scores between the two treatment groups.

Study design: Randomized controlled trial (double-blinded)

Funding source: Foundation

Allocation: Concealed

Setting: Emergency department

Reference: Chang AK, Bijur PE, Holden L, Gallagher EJ. Comparative analgesic efficacy of oxycodone/acetaminophen versus hydrocodone/acetaminophen for short-term pain management in adults following ED discharge. *Acad Emerg Medicine*. 2015;22(11):1254-1260.

DAVID SLAWSON, MD

Director of Information Sciences

University of Virginia Health System, Charlottesville, Va. ■