What is the best diet to prevent recurrent calcium oxalate stones in patients with idiopathic hypercalciuria?

Borghi L, Schianchi T, Meschi T, et al. Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. N Engl J Med 2002; 346:77-84.

■ BACKGROUND About 10% of people in the United States develop at least 1 symptomatic kidney stone during their lives. The recurrence rate after 10 years is at least 50%. Many physicians recommend a low-calcium diet in patients with calcium oxalate stones to prevent recurrence. Recent studies suggest that a low-calcium diet may not be effective and that intake of animal protein and salt may influence renal calcium excretion. This study compares the traditional low-calcium diet with a diet that is low in animal protein and salt.

■ POPULATION STUDIED This study enrolled 120 men with idiopathic hypercalciuria (urinary calcium excretion of more than 300 mg per day on an unrestricted diet) who had been referred to a nephrology clinic in Parma, Italy, and who had had at least 2 episodes of symptomatic renal stones. Reasons for exclusion included previous visits to any "stone disease center" and conditions associated with calcium stones, such as hyperparathyroidism or inflammatory bowel disease.

■ STUDY DESIGN AND VALIDITY The investigators randomly assigned subjects, using concealed allocation, to 1 of 2 diets in this randomized controlled study. The low-calcium diet limited calcium intake to about 400 mg per day. The other diet, which included about 1200 mg per day of calcium, limited sodium chloride to about 3000 mg and animal protein to 93 g (15% of total calories). Both groups were advised to limit intake of high-oxalate foods and encouraged to drink 2 liters of water per day in cold weather and 3 liters in warm weather. Subjects were allowed moderate consumption of beer, wine, coffee, and sodas. (Detailed dietary instructions are available to *New England Journal of Medicine* subscribers in the supplement to the publication at www.nejm.org.) The study followed the patients for 5 years or until they developed clinical or radiologic evidence of a renal stone. Annual x-ray and ultrasound studies identified asymptomatic stone recurrences.

Both groups appeared similar at baseline. Analysis was by intention to treat. The number of withdrawals was similar between groups. Although the subjects could not be masked to their treatment group, the radiologists who confirmed the symptomatic recurrences and diagnosed the asymptomatic recurrences were not aware of the treatment assignments. The authors do not indicate how many of the recurrences were symptomatic.

■ OUTCOMES MEASURED The primary outcome was the time to development of the first recurrence of a renal stone, whether or not it was clinically evident. Other outcomes included changes in calcium and oxalate excretion and calcium oxalate saturation in the urine.

■ RESULTS After 5 years, the low-protein, low-sodium diet led to fewer recurrences (20% compared with 38% in the low-calcium group, relative risk 0.49, number needed to treat with diet for 5 years = 5.5). The risk of recurrence in the low-calcium group was similar to the 35% to 40% expected in the absence of any intervention. The disease-oriented changes in urine characteristics were predictable: urinary calcium decreased in both groups, but oxalate secretion increased in the low-calcium group, causing greater calcium oxalate saturation.

RECOMMENDATIONS FOR CLINICAL PRACTICE

A low-protein, low-sodium, high-calcium diet reduces the risk of recurrent renal stones in men with idiopathic hypercalciuria. This diet seems fairly palatable; compliance in the study was generally good. The traditionally recommended low-calcium diet does not appear to prevent further renal stones.

Andrew R. Lockman, MD
Department of Family Medicine
University of Virginia
Charlottesville
E-mail: alockman@virginia.edu

Each month, the POEMs editorial team reviews more than 90 journals of interest to primary care physicians and identifies articles you need to know about to stay up to date. We call these articles POEMs (Patient-Oriented Evidence that Matters) because they address common primary care problems, report outcomes that matter to patients, and, if valid, require us to change the way we practice. The collected reviews are available online at http://www.jfponline.com.

POEMS

What is the relative cardiovascular benefit of lowering cholesterol, blood pressure, and glucose levels in patients with type 2 diabetes?

Huang ES, Meigs JB, Singer DE. The effect of interventions to prevent cardiovascular disease in patients with type 2 diabetes mellitus. Am J Med 2001; 111:633-42.

■ BACKGROUND Type 2 diabetes is increasingly recognized as a powerful risk factor for coronary artery disease (CAD) events. In its recommendations for treating cholesterol levels, the Third Adult Treatment Panel of the National Cholesterol Education Program (NCEP) considers diabetes mellitus the equivalent of preexisting CAD.[1] The United Kingdom Prospective Diabetes Study (UKPDS) showed that blood pressure control had a greater overall effect on diabetes-related morbidity and mortality than did intensive glucose control.[2] The study under consideration examines data from the major trials of cardiovascular risk reduction to determine the relative benefit of controlling blood pressure and cholesterol and glucose levels in patients with type 2 diabetes.

■ POPULATION STUDIED Adult patients with diabetes who participated in a variety of studies looking at reduction of risk factors for CAD.

■ STUDY DESIGN AND VALIDITY This meta-analysis combined data from previous studies of intensive coronary risk factor reduction in patients with diabetes. The authors searched MEDLINE from 1966 to 2001 for articles published on the topic in English. Studies were included if they were randomized controlled trials of adults that included some patients with diabetes, compared intensive risk factor reduction with drug therapy versus either placebo or routine care, had at least 1 year of follow-up, and reported the requisite cardiovascular outcomes. The studies were independently reviewed by 2 authors for inclusion in the analysis based on these inclusion criteria; disagreement was resolved by consensus. There was no explicit validity assessment of the articles. Data were abstracted in a structured manner. The results were analyzed for heterogeneity and pooled appropriately.

While the process of conducting the meta-analysis of results was appropriate, it falls short of the ideal of a systematic review because of the lack of a serious attempt to find all existing data on the subject (eg, through searches of other databases and unpublished studies) and because of the lack of validity assessment of the included studies. These are not fatal flaws, as it is not likely that the authors missed any important studies, and the articles included are generally large, well-performed randomized controlled trials.

■ OUTCOMES MEASURED The outcomes measured included "aggregate cardiac events" (CAD death and nonfatal myocardial infarction [MI]), cardiovascular mortality, MI, and stroke. The results are presented in changes in rates over person-years and as person-years needed to treat. This was done to account for the variable lengths of patient follow-up in these large trials; these findings can be interpreted similarly to standard event rates and numbers needed to treat (NNT). One caveat is that to report an outcome for cholesterol lowering and blood pressure control across a time span of only 1 person-year is artificial, given that most changes in outcomes produced by these therapies take several years to manifest themselves.

■ RESULTS Cholesterol lowering (a total of 5 studies of both primary and secondary prevention) reduced aggregate cardiac events (30 vs 41 events per 1000 person-years, NNT for 1 year 106, 95% confidence interval [CI} 62-366). Cholesterol lowering as secondary prevention contributed most to this result (3 trials, 34 vs 44 events per 1000 person-years, NNT for 1 year 120, 95% CI, 61-4856); the results of primary prevention through cholesterol lowering did not reach statistical significance. Blood pressure reduction also reduced aggregate cardiac events (17 vs 23 per 1000 person-years, NNT for 1 year 157, 95% CI, 88-726). Two trials of blood glucose reduction as primary prevention failed to show a significant difference in aggregate cardiac events. The individual cardiac outcomes (cardiovascular mortality and MI each alone) showed results consistent with the aggregate outcomes.

RECOMMENDATIONS FOR CLINICAL PRACTICE

This study reinforces the conclusions of the UKPDS study and the recommendations of the NCEP guidelines that aggressive management of cholesterol and blood pressure in patients with diabetes is essential in preventing CAD. Intensive control of blood sugar levels does not seem to alter CAD events or mortality.

John Epling, MD
Center for Evidence-Based Practice
SUNY–Upstate Medical University
Syracuse, New York
E-mail: Eplingj@upstate.edu

REFERENCES

1. Third report of the National Cholesterol Education Program Expert Panel on detection, evaluation and treatment of high blood cholesterol in adults. Bethesda, Md: US Dept of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute; 2001.
2. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ 1998; 317:703-13.

Which is most effective for osteoarthritis of the knee: rofecoxib, celecoxib, or acetaminophen?

Geba GP, Weaver AL, Polis AB, Dixon ME, Schnitzer TJ, et al. Efficacy of rofecoxib, celecoxib, and acetaminophen in osteoarthritis of the knee. A randomized trial. JAMA 2002; 287:64-71.

■ BACKGROUND Traditional nonsteroidal anti-inflammatory drugs (NSAIDs) and the newer cyclooxygenase-2 enzyme (COX-2) selective inhibitors are recommended as second-line agents in patients with osteoarthritis (OA) who fail to respond to acetaminophen. This study compared the effectiveness of rofecoxib (Vioxx), celecoxib (Celebrex), and acetaminophen (Tylenol) in patients with OA of the knee.

■ POPULATION STUDIED This study included 382 patients from 29 US clinical centers with symptomatic OA of the knee for 6 months or longer. All patients had been treated with NSAIDs or acetaminophen for at least 30 days before enrollment, were 40 years of age or older, and retained moderate functional mobility of the knee (American College of Rheumatology functional class I, II, or III). Baseline criteria for OA severity were determined using the Western Ontario McMaster University Osteoarthritis Index (WOMAC) and Investigator Global Assessment of Disease Status scoring. Patients were excluded if they had concurrent medical or arthritic disease or abnormal laboratory results that would have confounded the effectiveness evaluation or increased the risk of complications.

■ STUDY DESIGN AND VALIDITY This research was a randomized double-blind controlled study. Allocation to treatment group (using computer-generated assignment) was concealed from enrolling investigators. After a 3-day to 7-day washout period, patients were randomized to receive 12.5 mg rofecoxib once daily, 25 mg rofecoxib once daily, 200 mg celecoxib once daily, or 1000 mg acetaminophen 4 times daily for 6 weeks. Exact matching placebos were used to maintain double-blind conditions. Response was evaluated using intent-to-treat analyses. Early effectiveness, using the WOMAC Index and Patient's Global Assessment of Response to Therapy (PGART) questionnaires, was defined as occurring within the first 6 days. Later clinical effectiveness was evaluated during office visits using the WOMAC and PGART at weeks 2, 4, and 6.

This was a well-designed study. The WOMAC and PGART are valid OA disease assessments; multiple time evaluations of therapy are clinically relevant markers of effectiveness. However, WOMAC and PGART are best used as a composite score rather than to evaluate individual subcomponents of these scales, as reported in this study. Doses of all agents were appropriate for OA. Still, better responses might have been seen if celecoxib dosage had consisted of either 100 mg twice daily or 200 mg twice daily (a dose not approved for OA). This study lacked the power to detect small differences in response between the 2 doses of rofecoxib. Traditional NSAIDs (eg, ibuprofen, naproxen), which have demonstrated similar effectiveness when compared to rofecoxib in OA, were not evaluated in this study.

■ OUTCOMES MEASURED The primary outcomes measured were pain on walking, night pain, pain at rest, and morning stiffness (WOMAC Index) and global responses to therapy (PGART).

■ RESULTS Seventy-nine percent of patients completed the 6-week follow-up. More patients treated with acetaminophen than patients treated with either rofecoxib or celecoxib discontinued early because of lack of effectiveness (17% vs 8% to 9%; composite number needed to treat for 1 withdrawal because of lack of efficacy = 8). As compared with celecoxib or acetaminophen, WOMAC response over 6 weeks showed that 25 mg rofecoxib once daily provided significantly greater responses in reduction of rest and night pain, composite pain scale, and stiffness scale. Physical function scale results were significantly better with 25 mg rofecoxib once daily than with acetaminophen but were no different from those with celecoxib. PGART response at 6 weeks also showed the best response with 25 mg rofecoxib once daily. Early response results were similar to later response results in showing that the best response was achieved with 25 mg rofecoxib once daily.

RECOMMENDATIONS FOR CLINICAL PRACTICE

In this study, 25 mg rofecoxib once daily was more effective than either celecoxib or acetaminophen in relieving persistent pain and stiffness from knee OA. However, only 1 of 6 patients taking acetaminophen, which is inexpensive and safe, discontinued treatment for lack of efficacy. Therefore, using acetaminophen as first-line therapy is reasonable. Less expensive traditional NSAIDs (eg, ibuprofen or naproxen) have been shown to have similar effectiveness as compared with either rofecoxib or celecoxib in OA. For patients at low risk for serious NSAID-associated gastrointestinal complications, traditional NSAIDs should be the next agents of choice. For patients at high risk, COX-2 selective inhibitors are reasonable second-line agents, since they pose a lower risk of NSAID-associated gastrointestinal complications with long-term use.

Joseph J. Saseen, PharmD
Departments of Pharmacy Practice and Family Medicine
University of Colorado Health Sciences Center
Denver
E-mail: joseph.saseen@uchsc.edu

CONTINUED ON PAGE 311

Which oral antihyperglycemics are most efficacious in reducing hemoglobin A_{1C} in diabetic patients?

Inzucchi SE. Oral antihyperglycemic therapy for type 2 diabetes. JAMA 2002; 287:360-72.

■ BACKGROUND Many new oral medications have been developed to treat diabetes, but uncertainty remains regarding which are best for initial treatment and whether effectiveness rates differ. This review compares the available oral antihyperglycemics.

■ POPULATION STUDIED A total of 63 randomized controlled clinical trials involving oral hypoglycemic drugs for type 2 diabetes was identified by a MEDLINE search and review of the bibliographies of articles found initially. Other inclusion criteria were study duration of at least 3 months, at least 10 subjects at the study's conclusion, and hemoglobin A_{1C} levels reported. Other search details, such as the year and key words of a study, were not mentioned. More than 15,000 subjects have been enrolled in the identified trials, but no information was given regarding important clinical characteristics such as age, ethnicity, body mass index, or medical conditions other than diabetes. Therefore, assessing generalizability of the data to typical patients of family practitioners is difficult.

■ STUDY DESIGN AND VALIDITY The article lists available randomized clinical trials that evaluate sulfonylureas, metformin, α-glucosidase inhibitors (AGIs), thiazolidinediones (TZDs), and nonsulfonylurea secretagogues as monotherapy versus placebo, in head-to-head trials or in combination, and compares their outcomes in terms of hemoglobin A_{1C} reduction. When multiple doses of a drug were tested, the results from the highest dose were used. There was no attempt to synthesize the data provided by the studies into a meta-analysis.

As a traditional review, this article has a number of major limitations as a source of information to primary care providers. The search strategy was not well described and appears to lack thoroughness, in that non-English articles were not addressed and other sources of studies such as experts or non-evidence-based reviews were addressed. Articles were not reviewed blindly and assessed for quality. Important clinical confounding variables such as body mass index, diet, and exercise were not addressed. Side effects were not quantified. The most important outcomes—myocardial infarction, blindness, renal failure, and peripheral vascular disease—were not systematically addressed. Also not addressed was publication bias, which may be particularly important in an area in which pharmaceutical manufacturers fund much of the research.

■ OUTCOMES MEASURED The major outcome measured was percent hemoglobin A_{1C} reduction. Side effects were mentioned but not quantified. Cost, patient satisfaction, and quality of life were not addressed.

■ RESULTS Except for the UKPDS, all available studies of oral hypoglycemics are short term and are limited in focus to hemoglobin A_{1C}. Each class of drugs achieved a similar initial reduction in hemoglobin A_{1C} of 1% to 2% except for the AGIs and nateglinide, which were less effective. The results are remarkably consistent across studies. Head-to-head comparison of specific medications further supports this conclusion. When taken in combination, the effects on hemoglobin A_{1C} are additive.

RECOMMENDATIONS FOR CLINICAL PRACTICE

Despite the claims of pharmaceutical marketing, there is little difference among sulfonylureas, metformin, and thiazolidinediones in reduction of hemoglobin A_{1C}. Each class achieves an average reduction of 1% to 2%. Alpha glucosidase inhibitors and nonsulfonylurea secretogogues are probably somewhat less efficacious; combinations of medications seem to be additive.

Clinicians should keep in mind that diet and exercise remain first-line treatment for type 2 diabetes. Initial drug therapy should be guided, however, by evidence about long-term outcomes, such as reduction in the risk of myocardial infarction, renal failure, and blindness; to date, only metformin and sulfonylureas have been shown to be beneficial in reducing microvascular complications. Only metformin has been shown to reduce macrovascular complications and all-cause mortality in obese patients with type 2 diabetes. Interestingly, this beneficial effect of metformin is totally independent of blood sugar control. Thus, metformin should be the pharmaceutical agent of first choice in the treatment of type 2 diabetes.

Lara Abrahamson, MD
Warren Newton, MD, MPH
Department of Family Medicine
University of North Carolina
Chapel Hill
E-mail: Warren_Newton@med.unc.edu

CONTINUED ON PAGE 381

Continued from page 311

POEMs

Can a patient information sheet reduce antibiotic use in adult outpatients with acute bronchitis?

Macfarlane J, Holmes W, Gard P, et al. Reducing antibiotic use for acute bronchitis in primary care: blinded, randomised controlled trial of patient information leaflet. BMJ 2002; 324:1-6.

■ BACKGROUND Inappropriate use of antibiotics for acute bronchitis can contribute to the growing incidence of bacterial resistance in the community. Although the majority of acute bronchitis cases are viral, patient expectations that antibiotics are required to treat this illness result in frequent prescribing of these drugs. This study investigates the use of written patient education regarding the role of antibiotics for acute bronchitis in an attempt to decrease antibiotic use.

■ POPULATION STUDIED The researchers recruited 259 patients aged 16 years and older with acute bronchitis from 3 general practices in Nottingham, England. Patients were required to have acute cough and at least 1 other respiratory tract symptom. Patients were excluded with asthma, chronic obstructive pulmonary disease, heart disease, and diabetes. The median age was 44 years; 26% of patients were smokers; and 80% had a clear chest exam.

■ STUDY DESIGN AND VALIDITY The patients' individual physicians used their clinical judgment to divide the patients into 2 groups: those who definitely needed antibiotics and those who did not definitely need antibiotics. Patients in the first group did not participate in the study. Patients in the second group were randomized to receive either a blank sheet of paper or a patient information sheet explaining the natural history of acute bronchitis and discouraging the use of antibiotics (available at http://bmj.com/cgi/content/full/324/7329/91/F1). The physician, who was blinded to randomization, distributed the study sheet in a sealed envelope at the office visit; patients were asked to open the envelope after the visit.

Each patient also received an antibiotic prescription. The patients were counseled by the physician that they were "quite likely not to need" the antibiotic, but to use their judgment and consider taking the antibiotic "if you feel you are getting worse." Blinded investigators contacted the patients at 1 and 2 weeks post visit to determine antibiotic use. Two patients who received information sheets and 5 in the control group were lost to follow-up; these patients were not included in the results analysis.

This study's allocation concealment, randomization, and single-blinding procedures appear adequate. However, the researchers relied primarily on the physicians' clinical judgment to determine which patients to include in the trial. While this method admirably attempts to reflect real-world primary care practice, it may adversely affect the study's external validity, since we aren't sure how the physicians ultimately selected the patients to include in the randomized trial. Also, since the physician verbally counseled each patient in both groups that they probably would not need the antibiotic, the study probably underestimates the true effect of the information sheet.

■ OUTCOMES MEASURED The primary endpoint in this study was whether the patient took the prescribed antibiotic. The secondary endpoint was the number of patients requiring a second office visit within a month for the same illness. Other patient-oriented outcomes such as patient satisfaction, number of sick days, and severity of illness were not directly measured, although the authors state that the rate of patient follow-up is a surrogate measure for these outcomes.

■ RESULTS Of the 259 eligible patients, 212 entered the randomized trial. Forty-nine (47%) patients who received the information sheet took their antibiotics compared with 63 (62%) control patients (relative risk, 0.7; 95% CI, 0.59-0.97; $P = .04$). One additional patient did not take the antibiotic for every 7 patients given the information sheet (number needed to treat = 7). Amoxicillin was the prescribed antibiotic in 96% of both study groups. The number of patients scheduling a follow-up visit within 1 month was similar in both groups (11 patients who received the sheet versus 14 who did not).

RECOMMENDATIONS FOR CLINICAL PRACTICE

In this study, a written patient information sheet along with verbal counseling from the physician stopped 1 additional patient of 7 from filling an antibiotic prescription of questionable necessity. There was no change in other patient outcomes. This intervention can decrease the cost of therapy and, theoretically, may contribute to slowing the spread of antibiotic resistance in the community.

Michael DeBisschop, PharmD
Beth Robitaille, MD
University of Wyoming Family Practice Residency Program
Casper
E-mail: medrx@uwyo.edu

POEMS

Is splinting of distal radius torus fractures an acceptable alternative to casting?

Davidson JS, Brown DJ, Barnes SN, Bruce CE. Simple treatment for torus fractures of the distal radius. J Bone Joint Surg [Br] 2001; 83-B:1173-5.

■ BACKGROUND Torus fractures of the distal radius are common; recommendations for management are diverse. The investigators conducted a survey of orthopedic surgeons to determine typical management of these fractures. The authors also conducted a randomized trial to compare treatment with either plaster casting or immobilization splinting.

■ POPULATION STUDIED First, the investigators surveyed 104 pediatric orthopedic surgeons in Great Britain. Second, they conducted a randomized prospective study of 201 children aged 2 to15 years with distal radius torus fractures. A total of 22 patients was lost to follow-up, 4 in the cast group and 18 in the splint group, leaving 179 in the study.

■ STUDY DESIGN AND VALIDITY Three studies were included in this article. The postal questionnaire was sent to 104 pediatric orthopedic surgeons. The questionnaire determined the incidence of torus fractures and the typical method of treatment by the individual practitioners. Clinic verses emergency department (ED) evaluation was considered, as was the prevalence of subsequent visits with and without additional radiologic studies. Only 65 (62.5%) of the questionnaires were returned and analyzed.

After being diagnosed with a distal radius torus fracture in the ED, 201 patients were referred to a fracture clinic, where they were nonrandomly allocated to treatment with either a plaster forearm cast or a forearm Futura splint. Allocation was not concealed. Patients returned to the orthopedic clinic 3 weeks later for clinical examination and radiographic evaluation. The patient and family were questioned about complications. Only 179 of the 201 (89%) patients returned for evaluation.

This paper lacks a detailed description of methods used. Our confidence in the results would have been stronger if random assignment with concealed allocation had been used. Although neither the treating doctor nor the patient was blinded to treatment, the final outcome should not have been affected as long as the patients wore the splints as instructed. Whether the assessor of the final outcome was blinded is not mentioned. Failure to blind could have led to bias in reporting of healing rates.

■ OUTCOMES MEASURED The postal questionnaire measured incidence and treatment approach for torus fractures of the distal radius. The prospective randomized trial measured clinical and radiographic outcomes for plaster casting versus splinting treatment. Additionally, compliance with treatment assignment was assessed. Cost-benefit analysis compared the total costs of plaster casting versus splinting.

■ RESULTS The questionnaire revealed that each orthopedist treated 5.1 (SD ± 4.8) torus fractures each week. For treatment that occurred in the ED, 64 physicians used some form of casting for treatment and 1 used a splint. When treatment took place in the office, however, 60 (92.3%) physicians used some form of casting and 5 (7.7%) used wrist splints. The fractures were immobilized for a mean of 2.9 (SD ± 0.64) (1 to 4) weeks. Eleven (16.9%) consultants routinely x-rayed the site at the end of treatment.

Of the 201 consecutive patients, 85 were randomized to a plaster cast and 116 to a Futura splint. The imbalance in randomization probably occurred because patients were assigned depending on the day they presented to the clinic. Compliance was good except for 2 very young participants who tried to remove the splints initially. All fractures united clinically and radiographically with no loss of position.

The cost analysis showed that treatment in a cast, which involved a radiograph in the ED, a temporary splint, evaluation in the orthopedic clinic, application of the cast, and return for removal of the cast, was about twice the cost of splinting.

RECOMMENDATIONS FOR CLINICAL PRACTICE

This study showed that treating torus fractures of the distal radius with casting versus splinting has no clinical difference in outcome. Some cost saving seems to occur when torus fractures are treated with splinting rather than casting, since splinting obviates a follow-up visit for cast removal. After reading this study, we agree that Futura splinting of distal radial torus fracture for 3 weeks appears to be a reasonable alternative to casting. The absence of complications in both groups suggests that a follow-up visit and confirmatory radiologic imaging may not be necessary.

J. Kendall Walker, MD
Kevin Y. Kane, MD, MSPH
Department of Family and Community Medicine
University of Missouri–Columbia
E-mail: KaneK@health.missouri.edu

CONTINUED ON PAGE 384

POEMS

Is lansoprazole (Prevacid) or omeprazole (Prilosec) more effective in treating erosive esophagitis?

Richter JE, Kahrilas PJ, Sontag SJ, et al. Comparing lansoprazole and omeprazole in onset of heartburn relief: results of a randomized, controlled trial in erosive esophagitis patients. Am J Gastroenterol 2001; 96:3089-98.

■ BACKGROUND While the superiority of proton pump inhibitors (PPIs) over histamine-2 receptor antagonists in symptom control of gastroesophageal reflux disease (GERD) has been well established, limited work has been done comparing the efficacy of different PPIs. Theoretically, differences in pharmacokinetic properties, such as increased bioavailability of lansoprazole, could play a role in efficacy of symptom control. The purpose of this study was to demonstrate a difference between PPIs in GERD symptom control.

■ POPULATION STUDIED The patient population for this study consisted of 3510 individuals over age 18 years with endoscopically confirmed erosive esophagitis of grade 2 severity or higher who were gathered through a large multicenter clinical trial. To enter the study, patients had to have experienced at least 1 episode of moderate to very severe heartburn within 3 days before their screening visit. Comparison of treatment groups showed the only significant demographic difference was increased reported tobacco use in the omeprazole group (28%) versus the lansoprazole group (25%).

■ STUDY DESIGN AND VALIDITY This study was a double-blind multicenter clinical trial in which participants were randomized to receive either 30 mg lansoprazole or 20 mg omeprazole once daily for 8 weeks. Allocation concealment was not mentioned. Follow-up visits were conducted at the end of weeks 1, 2, and 8 of treatment. Analysis was by intention to treat.

This study was well designed overall. The sample size was large enough to detect small differences between lansoprazole and omeprazole.

■ OUTCOMES MEASURED This study looked primarily at onset and duration of symptom relief and severity as recorded by patients in a diary. Specifically, daytime and nighttime heartburn symptoms were analyzed with regard to percentage of complete heartburn relief as well as average heartburn severity at days 1 to 3 and the end of weeks 1, 2, and 8 of treatment.

■ RESULTS The group treated with lansoprazole showed a statistically significant advantage in symptom relief throughout the treatment period. On day 1 of treatment, the lansoprazole group was found to be 33% heartburn free as compared with 25% in the omeprazole group ($P < .0001$). The number needed to treat (NNT) to see this statistically significant difference was 12.5. Patients receiving lansoprazole versus omeprazole had small but statistically significant decreases in numbers of heartburn-free days (56% vs 49% in first 3 days of treatment, NNT = 14) and nights (NNT = 14) as well as daytime heartburn severity and nighttime severity. The lansoprazole-treated group also showed increased sustained resolution of symptoms over the omeprazole-treated group during the 8-week study period. Overall, however, these differences were extremely small and narrowed as the study progressed to 8 weeks.

RECOMMENDATIONS FOR CLINICAL PRACTICE

Lansoprazole provided a small but sustained advantage over omeprazole in the treatment of heartburn. However, although statistically significant, these differences in efficacy are minor and diminished over the 8-week course of treatment. In deciding to use one PPI over another, clinicians should consider other factors, primarily cost or availability.

Jeffrey D. Kim, MD
University of Washington Family Practice Residency Program
Seattle
E-mail: jeffkim@u.washington.edu

CONTINUED ON PAGE 386

Do intranasal corticosteroids aid treatment of acute sinusitis in patients with a history of recurrent sinus symptoms?

Dolor RJ, Witsell DL, Hellkamp AS, et al. Comparison of cefuroxime with or without intranasal fluticasone for the treatment of rhinosinusitis. The CAFFS trial: a randomized controlled trial. JAMA 2001; 286:3097-105.

■ BACKGROUND The combination of antibiotics and inhaled intranasal corticosteroids for the treatment of chronic persistent sinusitis is a common clinical practice. Theoretically, nasally inhaled steroids should decrease mucosal inflammation and hasten recovery from an acute sinusitis. Previous small studies show a trend toward improvement with this regimen. This study measures the benefit of the addition of fluticasone to cefuroxime in patients with confirmed acute sinusitis and a documented history of chronic or recurrent sinusitis.

■ POPULATION STUDIED Patients presenting with acute sinonasal symptoms and a history of previously diagnosed recurrent or chronic sinusitis requiring antibiotic treatment were enrolled from 22 sites (12 primary care and 10 otolaryngology clinics). Patients were aged 30 to 55 years; 68% were female and 88% were Caucasian. All patients were required to have evidence of sinus infection on either plain films (Waters view) or nasal endoscopy. Subjects were screened for major sinus symptoms with an instrument developed by the American Academy of Otolaryngology–Head and Neck Surgery. Exclusion criteria included previous sinus surgery, nasal polyposis, intranasal corticosteroid use within the previous 2 weeks, and prior antibiotic use within 7 days of enrollment in the study.

■ STUDY DESIGN AND VALIDITY Ninety-five patients were randomly assigned in a double-blind fashion (concealed allocation assignment) to receive 2 puffs (200 µg/day) of fluticasone propionate (Flonase) or identical placebo nasal spray in each nostril once daily for 21 days. All patients also received 250 mg cefuroxime (Ceftin) twice daily for 10 days and 2 puffs of xylometazoline hydrochloride in each nostril twice daily for 3 days. Follow-up was complete in 93% of patients at 10, 21, and 56 days via telephone interview. Interviewers were blind to treatment group assignment.

■ OUTCOMES MEASURED The primary outcome was the proportion of patients in each treatment arm who experienced clinical success at 10, 21, or 56 days. Clinical success was defined as a patient report of "cured" or "much improved." Secondary outcomes included differences over time in the scores for sinusitis and general health quality of life as measured by the Sinonasal Outcome Test-20 (SNOT-20) and Short Form-12 (SF-12). All measures were taken during telephone interviews at 10, 21, and 56 days post enrollment.

■ RESULTS Using intention-to-treat analysis, a higher proportion of patients in the fluticasone group achieved clinical success (93.5% vs 73.9%; $P = .009$; number needed to treat [NNT] = 6). No significant differences in treatment success rates were found between patients enrolled from otolaryngology vs primary care sites ($P = .21$). Patients in the fluticasone group also improved more rapidly (median of 6.0 days vs 9.5 days, $P = .01$). Differences in symptom scores between treatment groups were not significant, however, as measured by SNOT-20 (day 10, $P = .8$; day 21, $P = .88$; day 56, $P = .54$) and SF-12 (PCS-12, $P = .39$; MCS-12, $P = .21$). Reports of adverse effects were not significantly different between the groups ($P = .07$).

RECOMMENDATIONS FOR CLINICAL PRACTICE

Intranasal corticosteroids increase patient-reported clinical success when used in addition to antibiotics for the treatment of acute sinusitis in patients with a history of recurrent sinusitis (NNT = 6). Although the primary outcome of patient-reported clinical success was improved in the treatment group, the symptom scores also reported by the patients were not significantly different between groups. The current study did not adequately define "recurrent," but a previous study found a similar benefit of intranasal steroids plus antibiotics for patients reporting at least 2 sinus infections requiring antibiotic treatment per year for at least the previous 2 years.[1] There is no evidence that steroids provide additional benefit to the treatment of simple acute sinusitis. In addition, children who are given intranasal steroids for upper respiratory infections are more likely to develop ear infections.[2]

Robert J. Winn, MD
Department of Family Medicine
Thomas Jefferson University
Philadelphia, Pennsylvania
E-mail: robert.winn@mail.tju.edu

REFERENCES

1. Meltzer EO, Charous BL, Busse WW, Zinreich SJ, Lorber RR, Danzig MR. Added relief in the treatment of acute recurrent sinusitis with adjunctive mometasone furoate nasal spray. J Allergy Clin Immunol 2000; 106:630-7.
2. Ruohola A, Heikkinen T, Waris M, Puhakka T, Ruuskanen O. Intranasal fluticasone propionate does not prevent acute otitis media during viral upper respiratory infection in children. J Allergy Clin Immunol 2000; 106:467-71.