POEMs

Patient-Oriented Evidence that Matters

Each month, the POEMs editorial team reviews more than 80 journals of interest to primary care physicians, identifying 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 8 most important articles are critically appraised here each month. Occasionally, we include articles that confirm an important practice for which there had been only weak evidence previously (POEs – Patient-Oriented Evidence) or research that is focused on intermediate outcomes (DOEs – Disease-Oriented Evidence). We call attention to the latter so improper changes in currently valid practices are prevented. The collected reviews are available at www.infopoems.com. Additional POEMs and other important evidence-based material are published in a monthly newsletter called *Evidence-Based Practice* (available through subscription — phone: 1-201-782-5726; fax: 1-201-391-2778; Internet: www.infopoems.com).

Beta-Blockers for the Treatment of Congestive Heart Failure

CIBIS-II Investigators and Committees. The cardiac insufficiency bisoprolol study II (CIBIS-II): a randomized trial. Lancet 1999; 353:9-13.

Clinical question **Do beta-blockers reduce mortality in patients with moderate to severe congestive heart failure?**

Background Congestive heart failure (CHF) is a common and serious condition that affects at least 4.8 million people in the United States. It is the leading cause of hospital admissions for patients older than 65 years and has an annual mortality rate of 5% to 30%, depending on the severity of the disease.[1] In recent years, recognition of the sympathetic activation associated with CHF has renewed interest in treatment with beta-blockers. The CIBIS-II trial was designed to study the effect of bisoprolol (a beta-1–selective blocker) on mortality and hospitalization in patients with CHF.

Population studied A total of 2647 people with moderate to severe CHF (New York Heart Association class III or IV), aged 18 to 80 years, with symptoms for at least 3 months, and having a documented ejection fraction of 35% or less were recruited from European hospitals. Patients were taking diuretics and angiotensin-converting enzyme (ACE) inhibitors and had been clinically stable for at least 6 weeks. Patients were excluded if they had recent coronary artery disease events or interventions, resting bradycardia, high-grade atrioventricular block without a pacemaker, renal failure, or reversible obstructive lung disease. Of the patients included, the average age was 61 years; 70% had underlying ischemic heart disease; 50% were taking digoxin; and 15% were taking amiodarone. Thus, the study population seems similar to many patients managed by US family physicians.

Study design and validity This was a well-done randomized double-blind placebo-controlled trial. Dosing was initiated at 1.25 mg and titrated to 10 mg as tolerated by symptoms without any run-in period. A total of 564 patients (42%) reached this goal without limiting side effects, and an additional 328 patients (25%) tolerated up to 7.5 mg. Patients were permanently withdrawn from treatment when they could no longer tolerate the study drug or when the clinical need for a beta-blocker arose. Analysis was by intention to treat. The study was stopped early because of significant improvement in mortality in the treatment arm, resulting in an average length of follow-up of 1.3 years; follow-up was better than 99.7%. Except for concurrent medication use, other components of CHF disease management—including daily weights, sodium restriction, nurse follow-up, and social services—were not described.

Outcomes measured The primary end point measured was all-cause mortality. Secondary end points included all-cause hospital admissions, cardiovascular mortality, cardiovascular admissions, and permanent premature treatment withdrawals.

Important clinical events were reviewed by a blinded committee and classified according to strict criteria. Symptoms, quality of life, functional status, and costs were not described.

Results The experimental and control groups were similar. In the bisoprolol group, 156 patients (11.8%) died compared with 228 (17.3%) in the placebo group (P <.001; number needed to treat [NNT] = 18). Patients in the bisoprolol group also had fewer hospital admissions (33% vs 39%; P = .006; NNT = 17.5) and fewer cardiovascular deaths (9% vs 12%; P = .005; NNT = 31). Permanent treatment withdrawal was equal in both groups (15%). Treatment effects did not differ according to country or etiology of heart failure. Little information was given regarding side effects, but more patients in the bisoprolol group were admitted for bradycardia (14 vs 2) and stroke (31 vs 16), and significantly fewer for ventricular arrhythmias (6 vs 20) and hypotension (3 vs 11).

Recommendations for clinical practice **The CIBIS-II trial provides excellent evidence that**

bisoprolol reduces mortality when added to standard therapy with diuretics and ACE inhibitors. This is consistent with other published reports.2 There is still uncertainty as to which class of beta-blockers is most beneficial (beta-1–selective blockers, such as bisoprolol and metoprolol, or nonselective blockers, such as carvedilol), but upcoming trials may answer this question and further assess the impact on quality of life. Clinicians should begin to use beta-blockers for select patients with moderate to severe CHF and look for new studies to determine which specific agents are most beneficial.

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1. Steering Committee and Membership of the Advisory Council to Improve Outcomes Nationwide in Heart Failure. Consensus recommendations for the management of chronic heart failure. Am J Cardiol 1999; 83:2A-38A.
2. Packer M, Bristow MR, Cohn IN, et al. Effect of carvedilol on morbidity and mortality in chronic congestive heart failure. N Engl J Med 1996; 334:1349-55.

Intranasal Budesonide or Fluticasone for Allergic Rhinitis

Day J, Carrillo T. Comparison of the efficacy of budesonide and fluticasone propionate aqueous nasal spray for once daily treatment of perennial rhinitis. J Allergy Clin Immunol 1998; 102: 902-8.

Clinical question **Which intranasal steroid, budesonide or fluticasone, is more effective in controlling symptoms of perennial allergic rhinitis?**

Background Allergic rhinitis affects from 10% to 30% of the population of the United States. Intranasal corticosteroids have become more popular in the treatment of allergic rhinitis because of their ability to affect multiple steps of the inflammatory process while maintaining a large margin of safety. A study comparing the efficacy of aqueous formulations of budesonide and fluticasone had not been previously done.

Population studied A total of 375 subjects from Canada and Spain, aged 18 years and older, with at least a 1-year history of allergic perennial rhinitis were enrolled in this study. Participants were required to exhibit at least 2 of 3 symptoms of rhinitis (blocked nose, runny nose, or sneezing) during at least 8 days of an 8- to 14-day baseline period, and to have a positive skin prick response to 1 or more perennial allergens. Approximately 90% were allergic to dust mites. Exclusion criteria included systemic or intranasal corticosteroid treatment within 2 months before enrollment, inhaled steroids for asthma >1000 µg per day, nasal abnormalities that could interfere with efficacy assessment, pregnancy or breastfeeding, and not using effective contraception (for women of childbearing age).

Study design and validity The study was an adequately designed randomized placebo-controlled trial. Groups were given either budesonide (n = 111), fluticasone (n = 109), or placebo (n = 53). Treatment allocation was double-blind for budesonide and single-blind (to the healthcare provider) for fluticasone. During the 6-week treatment period, patients were instructed to administer 2 doses of the study medication to each nostril every morning (64 µg budesonide aqueous spray for a total of 256 µg; 50 µg fluticasone propionate spray for a total of 200 µg; or placebo using the same dosage vehicle as budesonide). Loratidine 10 mg was used as rescue medication throughout the study, when subjects considered symptoms intolerable. A high dropout rate of 27% (102 of the 375 randomized subjects) weakens the study somewhat, especially since explanation was lacking. The manufacturer of budesonide funded the study.

Outcomes measured The principal outcome measure was patient assessment of 3 symptoms: blocked nose, runny nose, and sneezing. Each symptom was self-scored on a 4-point scale, where 0 = no symptom and 3 = severe symptom. Secondary outcomes were patient assessment of overall treatment effectiveness (substantial/total control, minor control, aggravated/no control), nasal examination by rhinoscopy, use of rescue medication, and adverse events.

Results The reduction in the combined nasal symptom score was statistically significant for both budesonide and fluticasone when compared with placebo ($P < .001$ and $P = .001$, respectively). Of the 3 nasal symptoms assessed, nasal blockage was significantly more decreased with budesonide compared with fluticasone (0.75 vs 0.5 points, $P = .009$). Patient assessment of overall treatment efficacy was not statistically different between the 2 medications at 3 and 6 weeks after beginning treatment. Both were effective compared with placebo. The use of rescue medication was reduced in both active treatment groups with no difference between the 2 groups. Bloody nasal discharge was more common in the budesonide group (18%) versus the fluticasone group (7%).

Recommendations for clinical practice **Intranasal budesonide and fluticasone propionate are both effective in relieving symptoms of perennial rhinitis. Although symptom reduction scores were better for budesonide, especially for nasal blockage, patients considered overall symptom control to be substantial or complete for both**