POEMs

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

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Gluten Is Not the Culprit in Many Patients' Symptoms

Clinical Question

Can patients with nonceliac gluten sensitivity tell when they are exposed to gluten?

Bottom Line

Gluten may not be the cause of gastrointestinal symptoms in many patients with nonceliac gluten sensitivity. Only one-third of patients on a gluten-free diet experienced symptoms and correctly identified when they were given gluten-containing flour. Almost one-half (49%) of patients experienced symptoms even though they were given gluten-free flour. (Level of Evidence = 1b–)

Synopsis

Although the incidence of celiac disease—with resulting gluten sensitivity—is approximately 0.4%, many persons who do not have antibodies to gluten identify symptoms when they eat gluten-containing foods. The researchers enrolled 35 patients (86% female) from a celiac disease clinic who did not have celiac disease, but were using a gluten-free diet because of self-identified gluten-related symptoms. These patients had been using a gluten-free diet for at least six months and reported being asymptomatic or mildly symptomatic. The participants were randomized, using a crossover design, to receive gluten-containing flour or gluten-free flour for 10 days, followed by a two-week washout period, and then another 10 days of the other type of flour.

Only 34% (n = 12) of the participants correctly identified when they were given gluten-containing flour. These patients also had a significant increase in symptoms following the gluten challenge using the Gastrointestinal Symptoms Rating Scale. Seventeen participants (49%) believed the gluten-free flour contained gluten, and they had increased symptoms during the gluten-free period. Despite the small number of patients in this study, the crossover design (in which each participant serves as his or her own control) greatly increases the statistical power. However, this group may represent a specific subtype of patient; many patients approached to participate did not do so, because of no interest in the study, fear of symptom recurrence, or an uncertain diagnosis.

Study design: Crossover trial (randomized)

Funding source: Self-funded or unfunded

Setting: Outpatient (specialty)

Reference: *Zanini B, Baschè R, Ferraresi A, et al. Randomised clinical study: gluten challenge induces symptom recurrence in only a minority of patients who meet clinical criteria for non-coeliac gluten sensitivity.* Aliment Pharmacol Ther. *2015;42(8):968-976.*

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Tamsulosin Effective as Expulsion Therapy for 5- to 10-mm Distal Ureteric Stones

Clinical Question

Is tamsulosin (Flomax) effective in the management of distal ureteric stones?

Bottom Line

Tamsulosin promotes stone passage of ureteric stones that are 5 to 10 mm. Five patients would need to be treated with tamsulosin to cause the expulsion of one such stone. Stones smaller than 5 mm have a high rate of spontaneous passage without any intervention. (Level of Evidence = 1b–)

Synopsis

These authors recruited adult patients who presented to the emergency department with symptoms and imaging consistent with distal ureteric stones. Patients with fever, hypotension, stones larger than 10 mm, or kidney disease were excluded. Using concealed allocation, the investigators randomized the patients to receive tamsulosin,

0.4 mg daily, or matching placebo for 28 days or until stone passage. The two groups had similar baseline characteristics and analysis was by intention to treat. The primary outcome was stone expulsion as confirmed by computed tomography, and time to stone expulsion was defined by self-reported passage of stone or 48-hour pain-free period. Compliance with the study medications was poor in both groups, and almost one-fifth of the patients did not have follow-up imaging. Of the approximately 80% of patients in each group who underwent follow-up computed tomography, there was no difference in the percentage of patients with passed stones (87% in the tamsulosin group vs. 82% in the placebo group; $P = .22$). In the subset of patients with larger stones (5 to 10 mm), the tamsulosin group had a significantly higher rate of stone passage than the placebo group (83% vs. 61%; $P = .03$). There were no significant differences detected in time to stone passage, pain, analgesia requirements, need for urologic intervention, or adverse events.

Study design: Randomized controlled trial (double-blinded)

Funding source: Foundation

Allocation: Concealed

Setting: Outpatient (primary care)

Reference: *Furyk JS, Chu K, Banks C, et al. Distal ureteric stones and tamsulosin: a double-blind, placebo-controlled, randomized, multicenter trial.* Ann Emerg Med. *2016;67(1):86-95.*

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Delayed Prescription for Respiratory Infections Produces Similar Results and Satisfaction as Immediate Treatment

Clinical Question

In patients with respiratory tract infections (bronchitis, sinusitis, pharyngitis), is a delayed prescription strategy as effective as immediate treatment and as accepted by patients?

Bottom Line

In almost 400 Spanish primary care patients with mild to moderate symptoms of respiratory infection of less than one week's duration, both a "take-and-hold" prescription and a "come back and pick up, if necessary" prescription produced a similar clinical response—and similar patient satisfaction score—as immediate antibiotic treatment, while decreasing overall antibiotic use. Other studies of this patient population have shown that patients prefer the security of a prescription, delayed or not, over withholding antibiotic treatment. The effect of legitimizing an illness by awarding a prescription should not be underestimated. (Level of Evidence = 1b)

Synopsis

These researchers evaluated 398 adults with acute, uncomplicated respiratory infections from 23 primary care centers in Spain. The patients had acute pharyngitis (46%), acute bronchitis (32%),

rhinosinusitis (20%), or exacerbation of mild to moderate chronic obstructive pulmonary disease (2%). The physicians had "reasonable doubt as to whether to treat with an antibiotic." Patients were, on average, on the younger side (mid-40s), one-half were smokers or former smokers, almost no patients (less than 2%) were febrile, and they reported mild to moderate symptoms for an average of six days. Patients were randomized, using concealed allocation, to one of four potential prescription strategies. One group was given an antibiotic to begin at once; two groups were given a delayed prescription, either a "take and hold" prescription or a "come back and pick up, if necessary" prescription; and the final group was not given any prescription. The average duration of symptoms was significantly longer in patients not given a prescription compared with patients given an immediate antibiotic, with the duration of symptoms in patients given delayed prescriptions somewhere in between but not significantly different from the immediate prescription. The duration of moderate or severe symptoms was lessened significantly with immediate treatment compared with delayed prescriptions, but the average difference in duration was 0.5 to 1.0 day. Patients in the delayed prescription groups experienced fewer days absent from work or unable to do their daily activities. Patient satisfaction was similar across all groups. Prescription use was decreased by two-thirds with the delayed prescription approaches.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (primary care)

Reference: *de la Poza Abad M, Mas Dalmau G, Moreno Bakedano M, et al.; Delayed Antibiotic Prescription (DAP) Group. Prescription strategies in acute uncomplicated respiratory infections: a randomized clinical trial.* JAMA Intern Med. *2016;176(1):21-29.*

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Long-Acting Nitrates No Good for Heart Failure with Preserved Ejection Fraction

Clinical Question

Should nitrates be prescribed for patients who have heart failure with preserved ejection fraction?

Bottom Line

Patients who have heart failure with preserved ejection fraction had decreased levels of activity and more adverse events when they were receiving isosorbide mononitrate than when they were taking a placebo. Moreover, activity levels decreased with increases in the dose of the drug, suggesting a strong correlation. However, almost 90% of the patients in this study were white, which may limit its generalizability. (Level of Evidence = 1b)

Synopsis

Previous studies note that up to 50% of patients who have heart failure with preserved ejection fraction receive nitrates, but the effectiveness of this therapy has not been extensively studied in this population. In the current trial, investigators enrolled patients with a diagnosis of heart failure with preserved ejection fraction who had limited activity levels because of the symptoms of heart failure (dyspnea, chest pain, or fatigue). The patients (N = 110) were randomized to receive 30 mg of isosorbide mononitrate tablets or matching placebo tablets for six weeks, followed by the other therapy (crossover) for another six weeks. For each six-week period, patients took no study drug for the first two weeks, one tablet for the third week, two tablets for the fourth week, and four tablets for the remaining weeks.

All patients wore accelerometers to measure their movement. One accelerometer unit indicates a cumulative 15 minutes of activity. The patients in the study had a mean age of 69 years and a New York Heart Association functional class of II or III; 90% were white. Analysis was by intention to treat. When comparing the group receiving 120 mg of isosorbide mononitrate with the matching placebo group, there was a trend toward decreased daily activity in the treatment group (−381 accelerometer units; 95% confidence interval, −780 to 17; $P = .06$), as well as a statistically significant decrease in hours of daily activity (−0.30 hours; 95% confidence interval, −0.55 to −0.05; $P = .02$). Furthermore, there was a dose-dependent decrease in daily activity in the patients receiving the active drug. No significant differences were detected in exercise capacity (as measured by the six-minute walk test) or quality-of-life scores, but more patients experienced adverse events (including worsening heart failure and syncope) during the isosorbide mononitrate phase of the trial than during the placebo phase.

Study design: Crossover trial (randomized)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (primary care)

Reference: *Redfield MM, Anstrom KJ, Levine JA, et al.; NHLBI Heart Failure Clinical Research Network. Isosorbide mononitrate in heart failure with preserved ejection fraction.* N Engl J Med. *2015;373(24):2314-2324.*

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