POEMs

Patient-Oriented Evidence That Matters

Selective Serotonin Reuptake Inhibitors Are Probably the Best First Option for Patients With Panic Disorder

Clinical Question

Is treatment with medication effective for patients with panic disorder?

Bottom Line

In a body of evidence plagued by poorly designed studies of short duration, selective serotonin reuptake inhibitors (SSRIs) show the best balance of effectiveness vs. risk. The analysis did not give a comparison of medication with psychotherapy, although a meta-analysis of limited research was unable to document a benefit of one over the other. (Level of Evidence = 1a–)

Synopsis

The researchers identified randomized controlled trials that evaluated medications to treat panic disorder (with or without agoraphobia) by searching three databases as well as reference lists of identified studies and meta-analyses. They included 87 studies published in any language that included a total of 12,800 participants and 12 drug classes, with two researchers independently selecting studies for inclusion and abstracting the data. Only one study was at low risk of bias, and all studies were of short duration (12 weeks or less). The other studies had problems with randomization and allocation concealment (which could affect outcomes) or were at risk of selectively reporting outcomes (many studies were conducted before registration of study protocols was a standard practice). The authors used network meta-analysis, a method of comparing different drug treatments when they were not studied in head-to-head trials. Evaluating the effect on remission, which was defined as no panic attacks for at least one week by the end of the study, all drug classes studied were more effective than placebo, with benzodiazepines, tricyclic antidepressants, and SSRIs, in that order, as the three best treatments for remission. All three drug classes were associated with an increased likelihood of adverse effects, with SSRIs having the least likelihood. Among the SSRIs, sertraline (Zoloft) and escitalopram (Lexapro) were associated with high remission and low risk of adverse events.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Self-funded or unfunded

Setting: Outpatient (specialty)

Reference: *Chawla N, Anothaisintawee T, Charoenrungrueangchai K, et al. Drug treatment for panic disorder with or without agoraphobia: systematic review and network meta-analysis of randomised controlled trials.* BMJ. *2022;376:e066084.*

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For Mild to Moderate Acne, Adapalene Plus Benzoyl Peroxide, Clindamycin Plus Benzoyl Peroxide, and Adapalene Alone Are Most Effective

Clinical Question

What is the best topical treatment for patients with mild to moderate acne vulgaris?

Bottom Line

For patients with mild to moderate acne, this network meta-analysis suggests starting with adapalene/benzoyl peroxide (Epiduo), clindamycin plus benzoyl peroxide (Neuac), or adapalene (Differin) alone. Patients who do not tolerate either combination containing benzoyl peroxide are likely to tolerate adapalene alone. (Level of Evidence = 1a)

Synopsis

An interdisciplinary team of U.K. researchers began by asking patients with acne what was most important to them in a study of acne treatments. The patients stated that self-reported improvement was more important than investigator-reported outcomes. Thus, the primary outcomes of this study were the proportion of patients who reported moderate or better improvement, and the proportion who withdrew from the study or stopped using the

medication due to adverse events. This network meta-analysis identified 40 randomized trials evaluating 12 topical agents or topical combinations in 18,089 patients; 79% of the studies were from North America or Europe. Only studies that reported acne severity, and in which fewer than one-half of patients had severe acne, were included. The studies were a mix of an active drug vs. vehicle cream, or an active drug vs. a different active drug. A network meta-analysis reports a meta-analysis of direct comparisons and a meta-analysis of direct and indirect comparisons.

The authors found that adapalene plus benzoyl peroxide was the most effective compared with vehicle cream based on meta-analyses of both direct and indirect comparisons (odds ratio [OR] = 3.65; 95% CI, 2.58 to 5.15), clindamycin plus benzoyl peroxide coming in second (OR = 2.98; 95% CI, 2.22 to 4.01), and adapalene alone, third (OR = 2.44; 95% CI, 1.66 to 3.60). Limiting the analysis to studies that only made a direct comparison with vehicle cream had similar findings (coherence), which gives greater confidence in the overall results. Adapalene plus benzoyl peroxide had the highest rate of withdrawals due to adverse events (OR = 2.93; 95% CI, 1.69 to 5.08), followed by benzoyl peroxide alone (OR = 1.59; 95% CI, 0.98 to 2.57) and clindamycin plus benzoyl peroxide (OR = 1.44; 95% CI, 0.75 to 2.72). Although absolute probabilities and numbers needed to treat or harm are not reported, the researchers state that withdrawals due to adverse events were uncommon.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Government

Setting: Outpatient (any)

Reference: *Stuart B, Maund E, Wilcox C, et al. Topical preparations for the treatment of mild-to-moderate acne vulgaris: systematic review and network meta-analysis.* Br J Dermatol. *2021;185(3):512-525.*

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British Society of Gastroenterology Guidelines for the Management of Irritable Bowel Syndrome

Clinical Question

What is the best way to manage irritable bowel syndrome (IBS)?

Bottom Line

This high-quality evidence-based guideline provides sound advice for the evaluation and management of IBS in primary care. (Level of Evidence = 1a)

Synopsis

The guidelines from the British Society of Gastroenterology were created by a multidisciplinary panel that included primary care physicians, psychologists, dietitians, and gastroenterologists. Treatment recommendations were based on systematic reviews, and other recommendations were based on a comprehensive review of the literature. There are dozens of recommendations; this POEM outlines the highlights. The guidelines advocate a pragmatic definition of IBS as at least six months of abdominal pain or discomfort with altered bowel habits, and the absence of alarm signs or symptoms. Initial evaluation in primary care should include a complete blood count, C-reactive protein or sedimentation rate, and serology for celiac disease. For patients younger than 45 years who present with diarrhea, order a fecal calprotectin test to rule out inflammatory bowel disease.

Screen for colorectal cancer in accordance with national guidelines; colonoscopy is only recommended for patients with alarm signs and symptoms or who are at increased risk of microscopic colitis (women; patients 50 years and older; those with comorbid autoimmune disease, weight loss, diarrhea for less than 12 months, or nocturnal or severe, watery diarrhea). Consider testing for bile acid diarrhea in patients with nocturnal diarrhea or prior cholecystectomy. The guidelines recommend against testing for pancreatic insufficiency, small intestinal bacterial overgrowth, or carbohydrate intolerance if the symptoms are typical for IBS.

First-line treatment recommendations include exercise and gradually increasing doses of soluble fiber (e.g., ispaghula) but not insoluble fiber (e.g., wheat bran). Probiotics can be considered, although the guideline does not recommend a specific species or dose. Consider loperamide (Imodium) for diarrheal symptoms; antispasmodics and peppermint oil (a recent POEM reported that a well-designed trial found no benefit with peppermint oil) for global symptoms and abdominal pain and cramping; and polyethylene glycol (Miralax) for constipation. Second-line medications in primary care include

tricyclic antidepressants and selective serotonin reuptake inhibitors. Other drug classes, such as medications targeting 5-HT3 and 5-HT4 receptors, should be prescribed after evaluation by a gastroenterologist.

Study design: Practice guideline

Funding source: Foundation

Setting: Outpatient (any)

Reference: *Vasant DH, Paine PA, Black CJ, et al. British Society of Gastroenterology guidelines on the management of irritable bowel syndrome.* Gut. *2021;70(7):1214-1240.*

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No Improved Patient-Oriented Outcomes With Sacubitril/Valsartan in Adults With Heart Failure and Preserved Ejection Fraction

Clinical Question

Is sacubitril/valsartan (Entresto) safe and effective for improving patient-oriented outcomes in adults with heart failure and preserved ejection fraction?

Bottom Line

The addition of sacubitril/valsartan to the treatment regimen of adults with heart failure and preserved ejection fraction significantly decreased plasma N-terminal pro–brain natriuretic peptide (NT-proBNP) levels compared with standard renin-angiotensin system (RAS) inhibitor treatment or placebo. However, no patient-oriented outcomes were significantly improved, including the six-minute walk distance, quality-of-life scores, or New York Heart Association (NYHA) class. (Level of Evidence = 1b)

Synopsis

The investigators identified adults, 45 years and older, with symptomatic heart failure, elevated NT-proBNP levels, NYHA class II through IV, a left ventricular ejection fraction of greater than 40%, and an impaired health-related quality of life as measured by a standard scoring tool. Patients taking an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) at baseline were required to have a history of hypertension. Eligible participants (N = 2,566) were initially assigned to one of three strata based on medication prescribed by their treating clinician: ACE inhibitor (n = 1,066), ARB (n = 1,174), or no RAS inhibitor (n = 326). Within each stratum, patients randomly received (concealed allocation assignment) sacubitril/valsartan or the background medication (i.e., ACE inhibitor, ARB, or placebo/no RAS inhibitor). Clinicians were instructed to up-titrate within four weeks to the maximally tolerated doses. Patients, clinicians, and individuals assessing outcomes remained masked to treatment group assignment. Complete follow-up occurred for more than 99% of patients at 24 weeks.

Using intention-to-treat analysis, patients in the sacubitril/valsartan group had a significantly greater reduction in NT-proBNP levels than the combined comparator group (i.e., ACE inhibitor, ARB, or placebo/no RAS inhibitor). However, at 24 weeks, no group differences occurred in median change from baseline in the six-minute walk distance, quality-of-life scores, or improvement in NYHA class. Adverse events, including hypotension, albuminuria, and hyperkalemia, occurred more often in the sacubitril/valsartan group.

Study design: Randomized controlled trial (double-blinded)

Funding source: Industry

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: *Pieske B, Wachter R, Shah SJ, et al.; PARALLAX Investigators and Committee Members. Effect of sacubitril/valsartan vs standard medical therapies on plasma NT-proBNP concentration and submaximal exercise capacity in patients with heart failure and preserved ejection fraction: The PARALLAX randomized clinical trial.* JAMA. *2021;326(19):1919-1929.*

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