POEMs

Patient-Oriented Evidence That Matters

A Low FODMAP Diet Is Better Than an Oral Spasmolytic for Irritable Bowel Syndrome

Clinical Question

Is using a smartphone application to increase adherence to a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) diet or an oral antispasmodic agent (otilonium bromide [not available in the United States]) more effective for the treatment of irritable bowel syndrome (IBS)?

Bottom Line

The pragmatic trial found a clinically meaningful benefit of a low FODMAP diet, implemented using a smartphone application, compared with an active medication. Because of its safety and low cost, the authors state that a low FODMAP diet should be first-line therapy for patients with IBS. The process includes eliminating FODMAP foods from the diet and reintroducing them one at a time until the offending food or foods are identified. The smartphone application used in the Belgian study was in French and Dutch, but there are many highly rated applications available. (Level of Evidence = 1b–)

Synopsis

Low FODMAP diets and otilonium bromide have been shown in randomized trials to be effective for the treatment of IBS. FODMAPs are short-chain carbohydrates that are poorly absorbed by some people. The trial enrolled primary care patients who were diagnosed with IBS by their physician. Patients with psychiatric comorbidity, who had used a FODMAP diet, or who had taken otilonium bromide were excluded. The dietary intervention consisted of a smartphone application that provided guidance for a low FODMAP diet and provided more than 100 recipes; the patients in the otilonium bromide intervention were given 40 mg three times daily. Groups were similar at baseline, with a mean age of 41 years, and 76% were female. Analysis was by intention to treat. The primary outcome was a clinically significant improvement of 50 points on the 500-point IBS-Symptom Severity Scale. A response was noted by more patients in the FODMAP group than in the otilonium bromide group at four weeks (62% vs. 51%; P = .02; number needed to treat [NNT] = 9) and eight weeks (71% vs. 61%; P = .03; NNT = 10). The average decline in the severity score was significantly higher in the FODMAP group (–97 vs. –77 points; P = .02). There were no differences between groups in overall quality-of-life scales. The authors prespecified a subgroup analysis of the 309 patients (70%) who met the Rome IV criteria for IBS. The benefit was greater in these patients in terms of the percentage of responders (77% vs. 62%; P = .004; NNT = 7). Adherence was higher for the diet than the medication (94% vs. 73%).

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Carbone F, Van den Houte K, Besard L, et al.; Domino Study Collaborators. Diet or medication in primary care patients with IBS: the DOMINO study–a randomised trial supported by the Belgian Health Care Knowledge Centre (KCE Trials Programme) and the Rome Foundation Research Institute.* Gut. *2022;71(11):2226-2232.*

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Letrozole More Effective Than Clomiphene for Infertility Treatment Among Individuals With Polycystic Ovary Syndrome

Clinical Question

Is letrozole superior to clomiphene for infertility treatment among individuals with polycystic ovary syndrome (PCOS)?

Bottom Line

The meta-analysis of randomized controlled trials showed that for individuals with PCOS, treatment of infertility with letrozole compared with clomiphene resulted in a higher rate of ovulation induction, more pregnancies, and more live

births. The conclusions are less than certain due to the high risk of bias in some studies. (Level of Evidence = 1a–)

Synopsis

The authors conducted a meta-analysis of randomized controlled trials (N = 29; 3,952 participants; 7,633 ovulation induction cycles) to compare the effect of letrozole and clomiphene on fertility among individuals with PCOS. They included studies that met the criteria of diagnosis of PCOS based on the 2003 Rotterdam criteria, had timed intercourse or insemination, and reported at least one of the three outcomes of interest. Seven studies were graded as having a high risk of bias to one or more of the following: quasi-randomization (n = 3), lack of fully described allocation concealment (n = 3), lack of masking (n = 6), or differences between groups in duration of infertility (n = 1). Meta-analysis for all primary outcomes favored letrozole: ovulation induction rate (22 studies; 6,862 participants; 67% vs. 59%; relative risk [RR] = 1.14; 95% CI, 1.06 to 1.21; $P < .001$), pregnancy rate (28 studies; 3,936 participants; 35% vs. 23%; RR = 1.48; 95% CI, 1.34 to 1.63; $P < .001$), and live birth rate (eight studies; 1,725 participants; 33% vs. 22%; RR = 1.49; 95% CI, 1.27 to 1.74; $P < .001$). The authors judged the certainty of evidence to be low for ovulation induction rate and moderate for pregnancy and live birth rate.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Self-funded or unfunded

Setting: Various (meta-analysis)

Reference: *Liu Z, Geng Y, Huang Y, et al. Letrozole compared with clomiphene citrate for polycystic ovarian syndrome: a systematic review and meta-analysis.* Obstet Gynecol. *2023;141(3):523-534.*

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Early Invasive Strategy Does Not Reduce Mortality for Moderate to Severe Ischemic Heart Disease After 5.8 Years

Clinical Question

For patients with moderate to severe reversible ischemic heart disease, does adding an initial invasive strategy to optimal medical therapy reduce mortality more than optimal medical therapy alone?

Bottom Line

An early invasive strategy for patients with moderate to severe ischemic heart disease does not reduce mortality; at best, it shifts mortality from cardiovascular to noncardiovascular causes for those with multivessel disease. (Level of Evidence = 1b)

Synopsis

The ISCHEMIA trial randomized 5,179 patients with moderate to severe reversible ischemic coronary artery disease to receive initial therapy with angiography plus revascularization (75% percutaneous coronary intervention, 25% bypass surgery) and optimal medical therapy or optimal medical therapy alone. Patients with left main stenosis, an ejection fraction of less than 35%, recent acute coronary syndrome, or angina that could not be treated medically were excluded.

Groups were balanced at the start of the trial and analysis was by intention to treat. Approximately 80% of patients in the early intervention group were revascularized, whereas only 23% of patients were ultimately revascularized because of ineffective medical therapy. The original report found no difference in mortality between groups after 3.2 years. The current report extended the follow-up to a median of 5.7 years. All-cause mortality was identical between groups (hazard ratio [HR] = 1.0; 95% CI, 0.85 to 1.18). Although cardiovascular death was less likely for those in the initial invasive group (HR = 0.78; 95% CI, 0.63 to 0.96), noncardiovascular mortality was more likely (HR = 1.44; 95% CI, 1.08 to 1.91). These mortality numbers were driven by patients with at least 70% obstruction of two or more vessels. For the 48% of patients who did not have multivessel disease, there was no difference in all-cause, cardiovascular, or noncardiovascular mortality between groups.

Study design: Randomized controlled trial (single-blinded)

Funding source: Industry and government

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: *Hochman JS, Anthopolos R, Reynolds HR, et al.; ISCHEMIA-EXTEND Research Group. Survival after invasive or conservative management of stable coronary disease.* Circulation. *2023;147(1):8-19.*

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Limited Benefit for Routine Cervical Cancer Screening With Cotesting vs. HPV Testing Alone

Clinical Question

Is the detection of high-grade cervical neoplasia superior with primary human papillomavirus (HPV) testing alone or with cytology cotesting?

Bottom Line

The results of this population-based retrospective Swedish cohort support HPV testing alone as a routine screening approach for cervical cancer. Among individuals confirmed to have cervical intraepithelial neoplasia grade 2, grade 3, or cancer (CIN2+) by biopsy, cytology was positive in less than

0.02% of individuals with negative HPV results. The results did not hold for testing based on clinical or unknown indications; 3.8% of individuals with CIN2+ would have been missed without cytology in addition to HPV testing. (Level of Evidence = 2b)

Synopsis

The study is a large, retrospective, population-based cohort study (N = 208,701) that used Swedish registry data to assess cervical cancer screening outcomes with HPV testing alone vs. HPV testing with cytology. The authors included individuals 40 to 42 years of age in 2019 who had cervical cancer testing (n = 18,674), 10,643 of which were the population of interest (10,664 tests) and were part of the Swedish cervical screening program. The remainder of testing was for clinical (n = 4,529) or unknown (n = 3,481) indications. In most cases, cotesting was on the same day (99.6%). Cotests outside of the 14-day window were excluded. There were 197 individuals who had a biopsy within six months of cotesting with positive results for CIN2+. Of these, 189 had both positive cytology and HPV tests, six had negative cytology with a positive HPV test, and two (less than 0.02%) had positive cytology with a negative HPV test. CIN2+ with positive results from cytology and a negative HPV test was more common among individuals who were tested for clinical or unknown indications (11 out of 290 participants; 3.8%). The prevalence of HPV vaccination in the population studied was not provided.

Study design: Cohort (retrospective)

Funding source: Government

Setting: Population-based

Reference: *Kleppe SN, Andersson H, Elfsröm KM, et al. Evaluation of co-testing with cytology and human papillomavirus testing in cervical screening.* Prev Med. *2023;166:107364.*

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Answers to This Issue's CME Quiz

Q1. D	Q4. A	Q7. D	Q10. D	Q13. D
Q2. D	Q5. B	Q8. D	Q11. A	Q14. A
Q3. A	Q6. A	Q9. D	Q12. C	Q15. A