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Q/What medical therapies work for gastroparesis?

EVIDENCE-BASED ANSWER

A/ IT'S UNCLEAR IF THERE ARE ANY highly effective medications for gastroparesis (TABLE¹⁻¹⁰). Metoclopramide improves the sense of fullness by about 40% for as long as 3 weeks, may improve nausea, and doesn't affect vomiting or anorexia (strength of recommendation [SOR]: **B**, small randomized controlled trial [RCT]).

Whether or not erythromycin has an effect on symptoms is unclear (SOR: **C**, conflicting trials and expert opinion).

Domperidone may improve quality of life (by 2%) for as long as a year, but its effect on symptoms is also unclear (SOR: **C**, small RCTs).

Cisapride may not be effective for symptom relief (SOR: **C**, small conflicting RCTs), and levosulpiride is likely similar to cisapride (SOR: **C**, single small crossover trial).

Nortriptyline (SOR: **B**, single RCT) and intrapyloric botulinum toxin A (SOR: **B**, small RCT and crossover trial) aren't effective for symptom relief.

Evidence summary

Metoclopramide. One systematic review that looked at the efficacy of metoclopramide for gastroparesis identified one small RCT and 3 smaller placebo-controlled crossover trials.¹ The RCT (using 10 mg of metoclopramide after meals and at bedtime) found consistent improvement in the sense of fullness over 3 weeks of therapy, with reduction of nausea at one and 3 weeks, but not at 2 weeks. Vomiting, anorexia, and early satiety didn't improve. The crossover trials had inconsistent results. The largest one, with only 16 patients, didn't find an improvement in symptoms.

■ **Erythromycin.** Two systematic reviews looked at the efficacy of erythromycin, primarily identifying studies 20- to 30-years old. The first systematic review identified only one small (single-blind) RCT in which erythromycin treatment didn't change symptoms.¹ A second review identified 3 trials described as "open label," all with fewer than 14 subjects and all lasting a month or less.² Erythromycin improved patient symptoms in only 1 of the 3, and this trial (like the others) had significant methodologic flaws. The authors of the

second review concluded that "the true efficacy of erythromycin in relieving symptoms ... remains to be determined."

■ **Domperidone.** A systematic review and one subsequent RCT evaluated domperidone. The systematic review identified 11 randomized, placebo-controlled trials (469 patients).³ Six studies found no impact on patient symptoms, while 5 reported a positive effect. The review also identified 6 trials that evaluated domperidone treatment on hospitalization rates. Open-label (single-arm, unblinded) trials tended to find a reduction in hospitalizations with domperidone, an effect not seen in the one double-arm study that evaluated this outcome.

The review authors noted that given the small size and low methodologic quality of most studies "it is not surprising ... that there continues to be controversy about the efficacy of this drug" for symptoms of gastroparesis.

One subsequent RCT, using domperidone 20 mg 4 times daily for 4 weeks, found a 2% improvement over placebo in the physical component of a multifaceted quality-of-life measure.⁴ The improvement was statistically

TABLE

Gastroparesis medication studies: What they found

Medication	Study design (number of patients)	Outcome(s)	Results
Metoclopramide	1 RCT ¹ (44)	Symptom improvement	Reduced sense of fullness (65% vs 22%; $P < .05$) and nausea (77% vs 31%; $P < .05$) at 3 wk
	3 placebo crossover ¹ (39)	Multiple	NS in 1 trial Improvement in 1 trial with no statistics given 17% reduction in a total symptom score ($P < .01$) in 1 trial
Erythromycin	1 RCT ¹ (13)	Symptom improvement	NS
	3 open-label ² (38)	Symptom improvement	NS in 2 trials In 1 trial, 10 of 12 patients "reported improved symptoms from baseline" (no comparison group or statistics)
Domperidone	11 RCTs ³ (469)	Symptom improvement	NS in 6 of 11 studies 4 of 5 studies showing improvement were methodologically flawed
	5 open-label (126) and 1 double-arm ³ (55)	Hospital admission rate	NS in the double-arm study Open-label trials found 73% combined reduction in admissions (no statistics given)
	1 RCT ⁴ (208)	Quality of life (PCS score)*	Mean change=0.65 domperidone vs -1.77 placebo ($P < .05$)
Cisapride	4 RCTs ¹ (53)	Symptom improvement	NS
	1 RCT ⁵ (29)	Symptom improvement	NS
	1 RCT ⁶ (19)	Reduction in dyspepsia score [†]	17% cisapride vs 5% placebo (P not given)
Levosulpiride	1 cisapride crossover ⁷ (30)	Total symptom score	NS between comparators
Nortriptyline ⁸	1 RCT ⁸ (130)	Symptom improvement	NS
Intrapyloric botulinum toxin A	1 RCT ⁹ (32)	Symptom improvement	NS
	1 placebo crossover ¹⁰ (23)	Symptom improvement	NS

NS, not significant; RCT, randomized controlled trial.

*PCS = Physical Component Score of Medical Outcomes Study Short Form-36; scale 0-100.

[†]Dyspepsia score = 0-3 points for fullness/early satiety, nausea, vomiting, anorexia, upper abdominal discomfort/distention (range 0-18, with lower scores indicating fewer symptoms).

significant, but of unclear clinical importance.

■ **Cisapride.** One systematic review and 2 subsequent RCTs evaluated the clinical effects of cisapride. The systematic review included 4 small RCTs (53 patients) that didn't individually find changes in patient symptoms.

In one subsequent RCT, comparing 10 mg cisapride 3 times daily to placebo for 2 weeks, cisapride yielded no significant change in symptoms.⁵ The other RCT compared oral cisapride 10 mg 3 times daily to placebo for one year. Cisapride treatment produced a

➤ **Metoclopramide improves the sense of fullness for up to 3 weeks, may improve nausea, and doesn't affect vomiting or anorexia.**

17% reduction in symptoms ($P < .002$ vs baseline), and placebo produced a 5% reduction ($P = \text{NS}$ vs baseline). The study didn't state if the difference between the 2 outcomes was statistically significant.⁶

■ **Levosulpiride.** One crossover study compared 25 mg levosulpiride with 10 mg cisapride (both given orally 3 times a day) on gastroparesis symptoms and gastric emptying. Each medication was given for one month (washout duration not given). The study found similar efficacy between levosulpiride and cisapride in terms of improvement in gastric emptying rates and total symptom scores.⁷ No studies compare levosulpiride to placebo.

■ **Nortriptyline.** A multicenter, parallel-group, double-blind RCT comparing 75 mg/d nortriptyline for 15 weeks with placebo in adult patients with moderate to severe symptoms of idiopathic gastroparesis for at least 6 months found that nortriptyline didn't improve symptoms.⁸

■ **Botulinum toxin A.** An RCT comparing a single injection of 200 units intrapyloric botulinum toxin A with placebo in adult patients with severe gastroparesis symptoms found that botulinum toxin A didn't result in symptomatic improvement.⁹ A crossover trial comparing 100 units monthly intrapyloric botulinum toxin A for 3 months with placebo in patients with gastroparesis found that neither symptoms nor rate of gastric emptying changed with the toxin.¹⁰

Recommendations

The 2013 guidelines from the American College of Gastroenterology list metoclopramide as the first-line agent for gastroparesis requiring medical therapy, followed by domperidone and then erythromycin (all based on “moderate quality evidence”). Antiemetic agents are also recommended for symptom control.¹¹ **JFP**

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