Complete Summary

GUIDELINE TITLE

American Gastroenterological Association medical position statement: diagnosis and treatment of gastroparesis.

BIBLIOGRAPHIC SOURCE(S)

Parkman HP, Hasler WL, Fisher RS. American Gastroenterological Association medical position statement: diagnosis and treatment of gastroparesis. Gastroenterology 2004 Nov;127(5):1589-91. PubMed

GUIDELINE STATUS

This is the current release of the guideline.

According to the guideline developer, the Clinical Practice Committee meets three times a year to review all American Gastroenterological Association Institute (AGAI) guidelines. This review includes new literature searches of electronic databases followed by expert committee review of new evidence that has emerged since the original publication date.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

Drug Withdrawal

- July 27, 2007, Zelnorm (Tegaserod) (Update): U.S. Food and Drug Administration (FDA) announced that it is permitting the restricted use of Zelnorm under a treatment investigational new drug (IND) protocol to treat irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC) in women younger than 55 who meet specific guidelines. See the U.S. Food and Drug Administration (FDA) Web site for more information.
- March 30, 2007, Zelnorm (tegaserod): Voluntary market withdrawal due to serious cardiovascular adverse events, including angina, heart attacks, and stroke. See the U.S. Food and Drug Administration (FDA) Web site for more information.

Additional Notice

- April 6, 2007, Tigan (trimethobenzamide hydrochloride): Product market withdrawal due to lack of evidence of effectiveness -- suppository drug products containing trimethobenzamide hydrochloride only. This action does NOT affect oral capsules and injectable products containing trimethobenzamide that have been approved by FDA.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Gastroparesis

GUIDELINE CATEGORY

Diagnosis
Evaluation
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Internal Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To present evidence for the diagnosis and management of patients with gastroparesis

TARGET POPULATION

Adults with gastroparesis

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. History to evaluate signs and symptoms
2. Physical examination
3. Gastric emptying testing
    - Scintigraphy of a radiolabeled solid meal
    - Breath testing
4. Antroduodenal manometry

Note: Guideline developers discussed but did not recommend additional evaluation techniques, including:

- Upper gastrointestinal barium radiographic, ultrasonography for serial changes in antral area, magnetic resonance imaging to assess for gastric emptying
- Gastric barostat to assess for gastric contractile activity
- Electrogastrography (EGG) to test for gastric myoelectrical activity
- Gastric barostat or satiety test to assess for gastric accommodation

Treatment

1. Dietary manipulation
2. Antiemetic agents
    - Antidopaminergics
    - Antihistamines
    - Anticholinergics
    - Serotonin receptor antagonists
    - Phenothiazine compounds (prochlorperazine, trimethobenzamide, promethazine)

    Note: Guideline developers considered but did not recommend benzodiazepines or cannabinoid drugs for antiemetic agents.

3. Prokinetic agents
    - Metoclopramide
    - Erythromycin
    - Domperidone (not approved in the U.S.)
    - Tegaserod*

    ***Note from the National Guideline Clearinghouse (NGC)**: On March 30, 2007, Zelnorm (tegaserod) was withdrawn from the market due to serious cardiovascular adverse events, including angina, heart attacks, and stroke. See the U.S. Food and Drug Administration (FDA) Web site for more information.

4. **Note**: Guideline developers considered but did not recommend other prokinetic agents, including bethanechol, acetylcholinesterase inhibitors (physostigmine and neostigmine), and cisapride.

Management of Refractory Gastroparesis

1. Switch prokinetic and antiemetic agents
2. Combine prokinetic agents
3. Inject botulinum toxin into the pylorus
4. Use of gastrostomy/jejunostomy tubes
5. Implantation of a gastric electric stimulator
6. Decompressing gastrostomy
7. Feeding jejunostomy tubes
8. Gastric electric stimulation

MAJOR OUTCOMES CONSIDERED

- Sensitivity of diagnostic tests
- Gastric emptying rates, contractile activity, myoelectrical activity, and accommodation
- Symptoms
- Fluid, electrolyte, and nutritional status
- Side effects/complications of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The published peer-reviewed literature on gastroparesis was searched on PubMed using the key words gastroparesis, gastric motility, and gastric dysmotility. Referenced articles from published manuscripts, book chapters, and recent abstracts from national and international meetings were included in this review.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The recommendations are based upon the interpretation and assimilation of scientifically valid research, derived from a comprehensive review of published literature. Ideally, the intent is to provide evidence based upon prospective, randomized placebo-controlled trials; however, when this is not possible the use of experts' consensus may occur.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The American Gastroenterological Association (AGA) Clinical Practice Committee approved this guideline on May 16, 2004. The American Gastroenterological Association Governing Board approved it on September 23, 2004.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Diagnosis of Gastroparesis

The diagnosis of gastroparesis is based on the presence of appropriate symptoms/signs, delayed gastric emptying, and the absence of an obstructing structural lesion in the stomach or small intestine.

Symptoms of Gastric Dysmotility

Clinical symptoms that suggest gastroparesis include nausea, vomiting, and postprandial abdominal fullness. In contrast, dyspepsia refers to a symptom complex of chronic or recurrent upper abdominal pain or discomfort that may have associated symptoms of early satiety, nausea, and postprandial fullness/bloating. There is overlap of the symptoms of gastroparesis and functional dyspepsia. Idiopathic gastroparesis may be one of the causes of functional dyspepsia.

The differential diagnosis of nausea and vomiting is extensive and includes a broad range of pathologic and physiologic conditions affecting the gastrointestinal tract, the central nervous system, and endocrine/metabolic functions. Assessment of the patient begins with a careful history aimed at understanding the patient's symptoms. Vomiting needs to be differentiated from regurgitation, rumination, and even bulimia; the duration, frequency, and severity of symptoms together with a description of their characteristics and the nature of any associated symptoms should be delineated. The physical examination should be directed toward any consequences or complications of vomiting and identification of any signs that may point to the cause of the symptoms.

Evaluation for Gastroparesis

Gastric emptying scintigraphy of a radiolabeled solid meal is the best accepted method to test for delayed gastric emptying. Conventionally, the test is performed for 2 hours after ingestion of a radiolabeled meal. Shorter test durations are inaccurate for determining gastroparesis. For the test meal preparation, the radioisotope needs to be cooked into the solid portion of the meal. Performing the test for a longer duration, up to 4 hours, has been proposed to increase the yield in detecting delayed gastric emptying in symptomatic patients.

Breath testing can be used to measure gastric emptying using the nonradioactive isotope ^{13}C to label octanoate, a medium-chain triglyceride, which can be bound into a solid meal. Studies have also reported labeling the proteinaceous algae (*Spirulina*) with ^{13}C. By measuring ^{13}C in breath samples, gastric emptying can be indirectly determined. The octanoate breath test has been used primarily for clinical research and pharmaceutical studies.

Antroduodenal manometry provides information about coordination of gastric and duodenal motor function in fasting and postprandial periods. Decreased antral contractility and origination of organized fasting migrating motor complexes in the small intestine rather than in the stomach are observed in gastroparesis. With accurate stationary recording, a reduced postprandial distal antral motility index is correlated with impaired gastric emptying of solids. A normal study with a normal transit test result strongly suggests that antral motor dysfunction is not the cause of symptoms. Antroduodenal manometry may differentiate between neuropathic or myopathic motility disorders and may help to diagnose unexpected small bowel obstruction or rumination syndrome.

<u>Treatment of Gastroparesis</u>

Primary treatment of gastroparesis includes dietary manipulation and administration of antiemetic and prokinetic agents.

Dietary recommendations include eating frequent smaller-size meals and replacing solid food with liquids, such as soups. Foods should be low in fat and fiber content.

Antiemetic agents are administered for nausea and vomiting. The principal classes of antiemetic drugs are antidopaminergics, antihistamines, anticholinergics, and more recently serotonin receptor antagonists. The antiemetic action of phenothiazine compounds is primarily due to a central antidopaminergic mechanism in the area postrema of the brain. Commonly used agents include prochlorperazine, trimethobenzamide, and promethazine.

Serotonin (5-HT_3) receptor antagonists are helpful in treating or preventing chemotherapy-induced nausea and vomiting. The sites of action of these compounds include the area postrema as well as peripheral afferent nerves. These agents are frequently used for nausea and vomiting due to other etiologies with little published evidence demonstrating their efficacy. These agents are best used on an as-needed basis.

Current prokinetic agents include metoclopramide and erythromycin, which can be administered orally or intravenously. Domperidone, a dopamine (D_2) receptor antagonist, is not approved in the United States but is available in Canada, Mexico, and Europe. Tegaserod*, a partial 5-HT_4 receptor agonist, enhances gastric emptying; however, no clinical trials have confirmed its efficacy in reducing symptoms in patients with gastroparesis.

> ***Note from the National Guideline Clearinghouse (NGC)**: On March 30, 2007, Zelnorm (tegaserod) was withdrawn from the market due to serious cardiovascular adverse events, including angina, heart attacks, and stroke. See the U.S. Food and Drug Administration (FDA) Web site for more information.

Patients refractory to the initial treatment of gastroparesis can be difficult to manage. Treatment may involve switching prokinetic and antiemetic agents, combining prokinetic agents, injecting botulinum toxin into the pylorus, using gastrostomy/jejunostomy tubes, and implanting a gastric electric stimulator.

A treatment recently reported to be helpful for refractory gastroparesis is endoscopic injection of botulinum toxin into the pyloric sphincter. Botulinum toxin, which reduces the release of acetylcholine from cholinergic nerves, may relax pyloric sphincter resistance, allowing more food to empty from the stomach. In open-label trials, pyloric botulinum toxin has been reported to produce modest temporary symptom improvements in selected patients. To date, no placebo-controlled trials have been reported for this therapy of gastroparesis. Long-term control is not to be expected from this treatment.

Decompressing gastrostomy and feeding jejunostomy tubes are occasionally used when necessary. A jejunostomy tube may provide a route for administering enteral nutrition, hydration, and medications.

Gastric electric stimulation is an emerging therapy for refractory gastroparesis. There are several ways to stimulate the stomach by varying the electrical parameters. With gastric electrical pacing, the goal is to entrain and pace the gastric slow waves at a higher rate than the patient's normal 3-cpm myoelectric frequency. One unblended study in a small number of subjects has shown this to accelerate gastric emptying and improve dyspeptic symptoms. The second method is to use high-frequency stimulation at 4 times the basal rate (12 cpm). High-frequency gastric electric stimulation has been evaluated in several studies, showing an improvement in symptoms with only a modest change in gastric emptying. Studies to better evaluate the efficacy of gastric electric stimulation are ongoing. As this type of treatment evolves, further delineation of the overall effectiveness, the type of patient who will likely respond, optimal electrode placement, and stimulus parameters should be explored.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

General

Accurate diagnosis of gastroparesis and development of an effective treatment plan

Specific Benefits of Treatment

- Correct fluid, electrolyte, and nutritional deficiencies.
- Identify and rectify the underlying cause of gastroparesis if possible.
- Reduce symptoms.

POTENTIAL HARMS

- Side effects from phenothiazines are common and include sedation and extrapyramidal effects.
- The side effects from metoclopramide result from antidopaminergic actions in the central nervous system (CNS) and may restrict its use in up to 30% of patients. Acute dystonic reactions such as facial spasm, oculogyric crisis, trismus, and torticollis occur in 0.2-6% of patients; when this occurs, it is often observed within 48 hours of initiating therapy. Drowsiness, fatigue, and lassitude are reported by 10% of patients. Metoclopramide can aggravate

underlying depression. Other side effects may include restlessness, agitation, irritability, and akathisia. Increased prolactin release may result in breast engorgement, lactation, and menstrual irregularity. Prolonged treatment with metoclopramide can produce Parkinsonian-like symptoms. Parkinsonian symptoms usually subside within 2-3 months following discontinuation of metoclopramide. Because of this effect, patients with Parkinson's disease should be given metoclopramide cautiously, if at all. Tardive dyskinesia, characterized by involuntary movements of the face, tongue, or extremities, may occur with prolonged use and may not reverse after stopping the medication. The prevalence of tardive dyskinesia ranges from 1% to 15% when taking metoclopramide for at least 3 months, and the complication has been reported to occur with short-term use. Metoclopramide-evoked tardive dyskinesia is 3-fold more common in women than men.
- Side effects of erythromycin at higher doses include nausea, vomiting, and abdominal pain.
- The most common side effects of domperidone relate to induction of hyperprolactinemia, with induction of menstrual irregularities, breast engorgement, and galactorrhea. An intravenous formulation of domperidone was removed in the 1980s due to generation of cardiac arrhythmias.
- The main complication of the implantable neurostimulator has been infection, which has necessitated device removal in approximately 5-10% of cases.
- Complications of jejunostomy tubes include infection, tube dysfunction, and tube dislodgment.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The Medical Position Statements (MPS), developed under the aegis of the American Gastroenterological Association (AGA) and its Clinical Practice Committee (CPC), were approved by the AGA Governing Board. The data used to formulate these recommendations are derived from the data available at the time of their creation and may be supplemented and updated as new information is assimilated. These recommendations are intended for adult patients, with the intent of suggesting preferred approaches to specific medical issues or problems. They are based upon the interpretation and assimilation of scientifically valid research, derived from a comprehensive review of published literature. Ideally, the intent is to provide evidence based upon prospective, randomized placebo-controlled trials; however, when this is not possible the use of experts' consensus may occur. The recommendations are intended to apply to healthcare providers of all specialties. It is important to stress that these recommendations should not be construed as a standard of care. The American Gastroenterological Association stresses that the final decision regarding the care of the patient should be made by the physician with a focus on all aspects of the patient's current medical situation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Parkman HP, Hasler WL, Fisher RS. American Gastroenterological Association medical position statement: diagnosis and treatment of gastroparesis. Gastroenterology 2004 Nov;127(5):1589-91. PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Nov

GUIDELINE DEVELOPER(S)

American Gastroenterological Association Institute - Medical Specialty Society

SOURCE(S) OF FUNDING

American Gastroenterological Association Institute

GUIDELINE COMMITTEE

American Gastroenterological Association Clinical Practice Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

According to the guideline developer, the Clinical Practice Committee meets three times a year to review all American Gastroenterological Association Institute (AGAI) guidelines. This review includes new literature searches of electronic databases followed by expert committee review of new evidence that has emerged since the original publication date.

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Gastroenterological Association Institute (AGAI) *Gastroenterology* journal Web site.

Print copies: Available from the American Gastroenterological Association Institute, 4930 Del Ray Avenue, Bethesda, MD 20814.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Parkman HP, Hasler WL, Fisher RS. American Gastroenterological Association technical review on the diagnosis and treatment of gastroparesis. Gastroenterology. 2004 Nov; 127(5):1592-1622

Electronic copies: Available from the American Gastroenterological Association Institute (AGAI) *Gastroenterology* journal Web site.

Print copies: Available from the American Gastroenterological Association Institute, 4930 Del Ray Avenue, Bethesda, MD 20814.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on January 10, 2005. The information was verified by the guideline developer on January 26, 2005. This summary was updated by ECRI Institute on April 20, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Tigan (trimethobenzamide hydrochloride). This summary was updated by ECRI Institute on August 7, 2007 following the U.S. Food and Drug Administration (FDA) updated advisory on Zelnorm (tegaserod maleate).

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