Complete Summary

GUIDELINE TITLE

The efficacy of antidepressants and various psychotherapies as adjunctive treatments for irritable bowel syndrome (IBS).

BIBLIOGRAPHIC SOURCE(S)

University of Texas, School of Nursing, Family Nurse Practitioner Program. The efficacy of antidepressants and various psychotherapies as adjunctive treatments for irritable bowel syndrome. Austin (TX): University of Texas, School of Nursing; 2006 May. 16 p. [20 references]

GUIDELINE STATUS

This is the current release of the guideline.

** 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.

- May 2, 2007, Antidepressant drugs: Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Irritable bowel syndrome

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Internal Medicine
Nursing
Psychiatry

INTENDED USERS

Advanced Practice Nurses
Nurses
Patients
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians

GUIDELINE OBJECTIVE(S)

- To assist health care providers with a responsible assessment of current management guidelines in using antidepressants and various psychotherapies as adjunctive therapy with other traditional treatments in the adult population with irritable bowel syndrome (IBS)
- To integrate pharmacological and behavioral elements for treatment

TARGET POPULATION

Adults with established diagnosis of irritable bowel syndrome (IBS) without alarm signs

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Symptom-based criteria (Rome II diagnostic criteria)
2. Complete history and physical examination

3. Laboratory studies including stool for ova and parasites, stool for occult blood, comprehensive metabolic panel, complete blood count with erythrocyte sedimentation rate
4. Endoscopic evaluation if indicated

Management/Treatment

1. Establishing effective therapeutic relationship between the patient and health care provider and patient education
2. Antidepressant therapy including tricyclic antidepressants as adjunctive treatment for irritable bowel syndrome (IBS)

   Note: Selective serotonin reuptake inhibitors (SSRIs) were considered but not recommended as routine or first-line therapy.

3. Psychological treatment including referral to a mental health professional, hypnosis, and cognitive-behavioral treatment as adjunctive therapy to traditional treatments for IBS

MAJOR OUTCOMES CONSIDERED

- Quality of life
- Symptomatic improvement
- Safety of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The literature was searched through Medline, PubMed (U.S. National Library of Medicine), the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Cochrane Database beginning in and subsequent to 2001. The search focused on literature containing expert opinion(s), meta-analyses, and/or individual clinical trials, with specific focus on use of antidepressants and cognitive-behavioral therapies in management of irritable bowel syndrome (IBS).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The U.S. Preventive Services Task Force (USPSTF) grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor)

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Informal Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations according to one of five classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms).

A. The USPSTF strongly recommends that clinicians provide the service to eligible patients. The USPSTF found good evidence that the service improves important health outcomes and concludes that benefits substantially outweigh harms.

B. The USPSTF recommends that clinicians provide this service to eligible patients. The USPSTF found at least fair evidence that the service improves important health outcomes and concludes that benefits outweigh harms.

C. The USPSTF makes no recommendation for or against routine provision of the service. The USPSTF found at least fair evidence that the service can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

D. The USPSTF recommends against routinely providing the service to asymptomatic patients. The USPSTF found at least fair evidence that the service is ineffective or that harms outweigh benefits.

I. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing the service. Evidence that the service is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

COST ANALYSIS

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

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A draft of the guideline was developed by a group of family nurse practitioner (FNP) students and submitted for review to the family nurse practitioner faculty. A final review was performed by an external expert, and subsequent changes were made prior to submitting to guidelines committee.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Strength of recommendations (A, B, C, D, I) and quality of evidence (good, fair, poor) are defined at the end of "Major Recommendations field."

Subjective Assessment

1. Review of past or present symptoms. Alarm symptoms which could suggest an alternative diagnosis of cancer, inflammatory bowel disease (IBS), or infection include:
    - Recurrent fever, weight loss, history of blood in stools, chronic severe diarrhea
2. Complete family history. A family history of colon cancer is considered an alarm factor; inquire specifically about family history of IBS and celiac disease.
3. Psychosocial history, as this may have an important role in the patient's experience of the disease and its outcome

4. Consider screening for depression
5. Social history including recent travel to areas with parasitic diseases.
6. A diagnosis is based on symptoms consistent with the **Rome II Diagnostic Criteria**

At least 12 weeks, which need not be consecutive, in the preceding 12 months of abdominal discomfort or pain that has 2 of 3 features:

1. Relieved with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool

Symptoms that cumulatively support the diagnosis of IBS:

1. Abnormal stool frequency (for research purposes, "abnormal" may be defined as greater than three bowel movements per day and less than three bowel movements per week)
2. Abnormal stool form (lumpy/hard or loose/watery stool)
3. Abnormal stool passage (straining, urgency, or feeling of incomplete evacuation)
4. Passage of mucus
5. Bloating or feeling of abdominal distension

The diagnosis of a functional bowel disorder always presumes the absence of a structural or biochemical explanation for the symptoms.

Physical Exam

A complete physical exam should be performed. Included in the exam are vital signs, abdominal exam, pelvic and bimanual exams (if applicable), and rectal exam. A diagnosis of IBS will be supported by negative physical examination findings. Any abnormal findings suggest an alternative diagnosis and should be followed by more extensive evaluation.

Management

Management of IBS is based upon the severity and nature of symptoms, the degree of functional impairment, and any psychosocial factors affecting the disease course. **The following pharmacologic treatment recommendations are for patients with moderate to severe symptoms who have not had effective symptom control with dietary, herbal and other recommended pharmacologic agents (anticholinergic, antidiarrheal, 5-HT3, 5-HT4 and other agents including antibiotics, probiotics and complementary therapies).**

Antidepressant Treatment of Pain-predominant IBS

1. Tricyclic antidepressants (TCAs) **(Recommendation B, Quality Fair)**
    - Amitriptyline
    - Desipramine
    - Nortriptyline

- Imipramine
- Doxepin

Tricyclic antidepressants in low doses should be considered for patients with pain-predominant IBS or for any patient with moderate to severe symptoms. Secondary amine TCAs (nortriptyline, desipramine) are better tolerated by many patients than parent tertiary amines (amitriptyline, imipramine, doxepin) because of fewer anticholinergic, sedating antihistaminic and alpha-adrenergic adverse effects. Two meta-analyses demonstrated that low-dose tricyclic antidepressants improved pain, global symptoms, and diarrhea. However a systematic review did not support these findings.

2. Selective serotonin reuptake inhibitors (SSRIs) **(Recommendation I, Quality Poor)**
    - Citalopram
    - Escitalopram oxalate
    - Fluoxetine
    - Sertraline
    - Paroxitene

A pilot open-label study suggested that paroxetine is effective in reducing pain and other IBS symptoms. A literature search revealed only one randomized controlled trial (RCT) examining the use of an SSRI (paroxetine) for treatment of IBS. This trial did suggest an improvement in overall well-being in both depressed and non-depressed individuals with IBS. Given the limited evidence, their use is not recommended as routine or first-line therapy except in patients who also have co-morbid depression.

Psychological Treatments

Psychological treatments should be explored in the patient with moderate-severe symptoms, whose symptoms are associated with stressors, or have associated symptoms of anxiety or depression. The primary care provider should educate the patient and family of the importance of involving mental health professionals in a holistic plan of care. There is convincing evidence that psychosocial factors do not cause the disease, but rather contribute to the predisposition, and continuation of IBS symptoms.

The use of hypnotherapy and cognitive-behavioral therapy (CBT) has proven effective in reducing diarrhea and abdominal pain but has not had significant improvement in constipation-predominant symptoms. It should be noted that any patient with moderate-severe IBS related symptoms could show symptom improvement with these listed therapies, regardless of history of anxiety or depression. Patients should be educated that a referral to a mental health professional is not a diagnosis of a psychological disorder. These therapies have proven effectiveness in all groups of patients, regardless of psychological disposition.

1. Hypnotherapy **(Recommendation B, Quality Fair)**

Most widely studied and used psychological therapy for diarrhea and pain-predominant symptoms. Improvements have been seen in all symptom measures,

quality of life and overall well-being. Of the controlled, randomized studies in the last five years, all studies noted improvement with "gut-directed hypnotherapy" versus placebo in reducing diarrhea-predominant and pain-predominant symptoms. Twenty years after hypnotherapy was introduced as an effective treatment for IBS, the mechanisms behind the results are still unclear.

2. Cognitive-Behavioral Therapy **(Recommendation B, Quality Fair)**

Studies on CBT in patients with moderate to severe symptoms show improvement in total somatic symptoms, abdominal pain and bowel dysfunction up to 15 months post therapy. Few studies on the effects of CBT have been conducted in the last five years but evidence from earlier studies show significant improvement with CBT versus symptom monitoring or medical therapy alone. Due to the generally high placebo response rate with functional bowel disorders and the well established psychopathology in IBS, updated high quality studies are needed. Based on the expansive literature from the past twenty years on the use of CBT in bowel disorders, this therapy would be recommended as adjunctive therapy in patients with moderate to severe IBS symptoms who have not responded to medical treatment alone.

Definitions:

Strength of Recommendations (based on U.S. Preventive Services Task Force [USPSTF] ratings)

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B. The USPSTF recommends that clinicians provide this service to eligible patients. The USPSTF found at least fair evidence that the service improves important health outcomes and concludes that benefits outweigh harms.

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I. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing the service. Evidence that the service is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

Quality of Evidence (based on USPSTF rating)

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

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CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for the Management of Irritable Bowel Syndrome (IBS).

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

These recommendations were based primarily on sources such as national guidelines, meta-analysis review, and evidenced-based, randomized, controlled research studies. Guidelines and statements are synthesized to make them applicable to the treatment of IBS.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved treatment and management of patients with irritable bowel syndrome (IBS)
- Improved quality of life for patients with IBS
- Decrease in IBS symptoms, improvement in global assessment criteria

POTENTIAL HARMS

Adverse Effects of Medications

Tricyclic antidepressants (TCAs)

Low-dose: Side effects include sedation/drowsiness, dizziness, constipation, dry mouth/eyes, weight gain, rare sexual dysfunction, urinary retention, restlessness, and insomnia

High-dose: Side effects include sedation, hypotension, and constipation (particularly for amitriptyline, doxepin, and imipramine, over desipramine or nortriptyline), dry mouth/eyes, arrhythmias, weight gain, and sexual dysfunction, syncope, worsening depression and suicidality. With higher doses, there is a greater need for dosage adjustments and a greater risk for overdose. If used in higher doses, providers should be aware of these risks and monitor their patient accordingly.

Selective Serotonin Reuptake Inhibitors (SSRIs)

Side effects include insomnia, agitation, diarrhea, night sweats, weight loss, sexual dysfunction, possibly worsening depression and suicidality.

CONTRAINDICATIONS

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Prescribing *paroxetine* during pregnancy should be avoided because of the risk of teratogenicity in the first trimester, and neonatal withdrawal and/or neonatal serotonin syndrome in the third trimester.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

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

DATE RELEASED

2006 May

GUIDELINE DEVELOPER(S)

University of Texas at Austin School of Nursing, Family Nurse Practitioner Program - Academic Institution

SOURCE(S) OF FUNDING

University of Texas at Austin, School of Nursing, Family Nurse Practitioner Program

GUIDELINE COMMITTEE

Practice Guidelines 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.

GUIDELINE AVAILABILITY

Electronic copies: None available.

Print copies: Available from the University of Texas at Austin, School of Nursing. 1700 Red River, Austin, Texas, 78701-1499

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 25, 2006. The information was verified by the guideline developer on November 14, 2006. This summary was updated by ECRI Institute on November 9, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs.

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