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Chronic Diarrhea: Diagnosis and Management

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Chronic diarrhea is a common problem affecting up to 5% of the population at a given time. Patients vary in their definition of diarrhea, citing loose stool consistency, increased frequency, urgency of bowel movements, or incontinence as key symptoms. Physicians have used increased frequency of defecation or increased stool weight as major criteria and distinguish acute diarrhea, often due to self-limited, acute infections, from chronic diarrhea, which has a broader differential diagnosis, by duration of symptoms; 4 weeks is a frequently used cutoff. Symptom clusters and settings can be used to assess the likelihood of particular causes of diarrhea. Irritable bowel syndrome can be distinguished from some other causes of chronic diarrhea by the presence of pain that peaks before defecation, is relieved by defecation, and is associated with changes in stool form or frequency (Rome criteria).

Patients with chronic diarrhea usually need some evaluation, but history and physical examination may be sufficient to direct therapy in some. For example, diet, medications, and surgery or radiation therapy can be important causes of chronic diarrhea that can be suspected on the basis of history alone. Testing is indicated when alarm features are present, when there is no obvious cause evident, or the differential diagnosis needs further delineation. Testing of blood and stool, endoscopy, imaging studies, histology, and physiological testing all have roles to play but are not all needed in every patient. Categorizing patients after limited testing may allow more directed testing and more rapid diagnosis.

Empiric antidiarrheal therapy can be used to mitigate symptoms in most patients for whom a specific treatment is not available.

Keywords: Diarrhea; Definitions; Classification; Diet; Diagnostic Testing; Therapy.

This clinical perspective addresses the definition, pathogenesis, diagnosis, and treatment of chronic diarrhea, which is based on a systematic review produced for the World Congress of Gastroenterology in 2013[1] and updated by the authors in 2016. Fifteen clinical questions are posed, followed by 24 recommendations pertinent to those questions with supporting evidence. In many instances there is not high-quality evidence to support the recommendations, and that is noted.

A search of PubMed for the years from 1975 to 2015 was conducted by using the following major search terms and subheadings including "diarrhea," "stool analysis," "irritable bowel syndrome," "chronic diarrhea AND diagnosis," "chronic diarrhea AND therapy," and "breath tests." Systematic reviews and meta-analyses were given priority for each topic when available, followed by clinical trial evidence.

The GRADE system was used to evaluate the strength of the recommendations and the overall quality of evidence.[2] A recommendation was graded as "strong" when the desirable effects of an intervention clearly outweigh the undesirable effects and as "conditional" when there is uncertainty about the tradeoffs. The quality of evidence ranged from "high" (implying that further research is unlikely to change the authors' confidence in the conclusion or in the estimate of the effect) to "moderate" (further research is unlikely to have an effect on the conclusion but might have an impact on the estimate of effect) or "low" (further research would be expected to have an important impact on the estimate of the effect or might change the conclusion altogether). For each recommendation, strength is abbreviated as "1" (strong) or "2" (conditional) and quality of evidence as "a" (high), "b" (moderate), or "c" (low).

How Is Chronic Diarrhea Defined?

Recommendations

1. Patients define diarrhea as loose stools, increased stool frequency, or urgency; physicians should note precisely what the patient means. (1b)
2. Chronic diarrhea is defined by a duration of >4 weeks. (2b)

Diarrhea can refer to urgency or high stool frequency, although most patients use the term to describe changes in consistency (loose or watery stools).[3] In fact, frequent defecation with normal consistency is termed *pseudodiarrhea*;

Abbreviations used in this paper: BAM, bile acid malabsorption; CD, celiac disease; CT, computed tomography; EGD, esophagogastroduodenoscopy; GI, gastrointestinal; HIV, human immunodeficiency virus; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; MR, magnetic resonance; SBS, short bowel syndrome; SIBO, small intestinal bacterial overgrowth.

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therefore, abnormal stool form and not frequency should be used to define diarrhea.

Most diarrheal episodes in developed countries are acute and self-limited and are usually due to infections. In immunocompetent patients, acute infectious diarrhea typically resolves within 4 weeks (most commonly within 1 week). Therefore, chronic diarrhea is defined as that lasting longer than 4 weeks. It is estimated that 1%–5% of adults suffer from chronic diarrhea.[4] In immunocompetent patients in developed countries, chronic diarrhea is generally not infectious. The challenge in managing these patients is the fact that the differential diagnosis is vast. However, a careful history and thorough physical examination with judicious use of selected tests often lead to a specific diagnosis and an appropriate treatment plan.

How Can Symptom Clusters and Settings Focus the Differential Diagnosis?

Recommendation

3. Consider comorbid symptoms and epidemiologic clues when constructing a differential diagnosis. (2c)

The main distinction in patients with chronic diarrhea is between functional and organic etiologies. The functional category includes irritable bowel syndrome (IBS), when abdominal pain accompanies the diarrhea, and functional diarrhea, when abdominal pain is absent.[3] IBS can be prospectively characterized by symptoms such as those defined by the Rome IV criteria (recurrent abdominal pain at least 3 days per month in the last 3 months, associated with a change in stool frequency or form, and improvement with defecation).[3] Functional diarrhea is defined as similar stool changes without prominent pain.[3] However, many patients with organic causes of chronic diarrhea such as microscopic colitis often fulfill these criteria.[5] Therefore, these criteria are not sufficiently specific to rule out organic etiologies. However, for patients with relatively mild symptoms and no alarm features such as gastrointestinal (GI) bleeding, fevers, or significant weight loss, those meeting the Rome IV criteria for IBS or functional diarrhea can be managed with empiric therapy. If empiric therapy fails, then further diagnostic testing may be considered.

Other symptom clusters can also be helpful in suggesting a specific diagnosis. Significant abdominal pain, fever, or GI bleeding suggests an inflammatory cause for diarrhea. Gas and bloating suggest carbohydrate malabsorption. Substantial weight loss suggests malabsorption, maldigestion, or a malignancy (particularly in an older person). Fatigue and night sweats suggest lymphoma, whereas anemia or change in stool caliber suggests colorectal malignancy. The positive predictive values of these symptoms for the underlying problems causing chronic diarrhea are unknown but likely are low. Physical findings can indicate the impact of diarrhea on nutrition and sometimes suggest a specific diagnosis (Supplementary Table 1).

The characteristics of the stool also help. Small, frequent bowel movements with tenesmus and bleeding suggest proctitis, whereas larger volume, less frequent stools suggest a small bowel source of diarrhea. Steatorrhea indicates either fat maldigestion or malabsorption.

Epidemiologic associations and patient characteristics also help limit the differential diagnosis[6] (Supplementary Table 2). Immunosuppressed patients with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome are at increased risk for common and uncommon, opportunistic infections. Recent travelers and migrants from endemic areas with chronic diarrhea should be tested for protozoa, atypical infections, *Strongyloides*, and tropical sprue. In patients with a history of constipation, the possibility of overflow diarrhea due to obstipation should be considered, especially if diarrhea worsens despite antidiarrheal therapy. Patients with diabetes or those attempting to lose weight should be questioned about consumption of diet foods containing poorly absorbed sugar alcohols.

How Can Clinicians Distinguish Irritable Bowel Syndrome From Other Causes of Chronic Diarrhea?

Recommendations

4. The Rome criteria provide a framework for the diagnosis of IBS and emphasize pain. Other etiologies should be sought when these criteria are not met. (1a)

5. Patients without alarm features who meet criteria for IBS should be treated without further testing. Those who do not respond should be evaluated further. (2b)

Criteria have been proposed to distinguish IBS from organic diseases; however, the utility of these criteria is only partially understood at present.[3] The Rome criteria emphasize chronic abdominal pain that is relieved by defecation, associated with a change in stool frequency or consistency.[3] IBS with diarrhea is diagnosed in patients who meet these criteria and have loose stools more than 25% of the time and hard stools less than 25% of the time. The specificity of symptom-based criteria for the diagnosis of IBS versus other colonic pathology is only moderate (~75%),[7–9] but the incorporation of alarm features can improve specificity to ~90%.[9] However, the predictive value of symptoms in identifying organic disease is less than 10%.[10] The performance of symptom-based criteria was highly variable and might not be able to reliably distinguish IBS from other diseases.[8] Thus, symptoms may be more useful in identifying patients requiring additional evaluation than in identifying patients with organic illnesses.[11]