

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Clarifying the Parameters of Nonacid Reflux

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G&H What is meant by the term “nonacid reflux”?

PK The way nonacid reflux is presently interpreted is that it is gastroesophageal reflux such that the pH in the refluxed fluid is greater than 4; therefore, the distinction between acid reflux and nonacid reflux is simply a matter of the pH, with a pH of 4 as the dividing point. Having said that, the distinction is chemically incorrect because anything that has a pH between 4 and 7 is still acidic, albeit weakly acidic. To be precise, nonacid reflux should really be referred to as “weakly acidic” under these circumstances.

G&H Is nonacid reflux more prevalent in any groups of patients, such as those with acid reflux, Barrett esophagus, or gastric dysmotility?

PK This is where it becomes quite confusing, because everyone has nonacid reflux. Nonacid reflux is caused by a reduction of acidity in the stomach, most commonly resulting from food intake. When a reflux monitoring study is performed postprandially, it shows that everyone has a lot of nonacid reflux, regardless of whether or not they have reflux disease. The other circumstance in which nonacid reflux is seen and which is commonly referred to in the literature is nonacid reflux in association with people taking proton pump inhibitors—another reason why these patients do not have a lot of acid in their stomachs. After all, they are taking a drug that prevents acid secretion. Although this situation is frequently referred to as nonacid reflux, it is clearly a consequence of taking a proton pump inhibitor.

G&H Are there any symptoms associated with nonacid reflux?

PK The most obvious symptom is regurgitation, and in most of the symptom studies that have been performed, the main symptoms linked with nonacid reflux are either regurgitation or cough. Theoretically, nonacid reflux can cause many symptoms; however, most commonly, it causes no symptoms.

G&H If there are usually no symptoms associated with nonacid reflux, how can it be detected and/or monitored? How accurate are these techniques?

PK Multichannel intraluminal impedance is the only technique that reliably detects nonacid reflux because it does not rely on the acidity of the refluxed material in order to detect it, whereas pH monitoring does. pH monitoring is the main alternative to multichannel intraluminal impedance. Multichannel intraluminal impedance has defined this whole area of nonacid reflux and transformed it into an issue of much discussion. We do not have any way of assessing the accuracy of multichannel intraluminal impedance because it has become the reference standard for reflux detection. There is no reason to think that it is not accurate, but on the other hand, there is nothing to compare it to, other than techniques that are less perfect. Thus, this technique is assumed to be reasonably accurate.

The main limitation of multichannel intraluminal impedance is that we do not know how to interpret the data with any certainty because, as discussed above, there are usually no symptoms associated with nonacid reflux. What we are attempting to do is take patients with persistent problems that are thought to be reflux-related and use this technology to try to establish whether or not that relationship is real. Therefore, the strategy for reflux-symptom association is the main issue that continues to require validation and probably requires the most future study.

G&H Is there any role for pH monitoring in this area?

PK It is important to emphasize that reflux disease can still be diagnosed with pH monitoring. However, if pH monitoring is performed in patients who are taking proton pump inhibitors, the result will not be affected; thus, under these circumstances, I think that the test has relatively limited value. Nevertheless, it still is appropriate to perform 24-hour pH monitoring in patients who are not taking proton pump inhibitors because this is still the best way to define reflux disease, with what is currently known. Nonacid reflux remains a little murky to clinicians because it is not easy to define the disease limits.

G&H What are the targeted therapy treatment options for nonacid reflux?

PK The existing therapies are relatively few because clinicians are faced with patients who have already been treated with acid inhibitors. Acid inhibitors prevent reflux to some degree, as they decrease the volume of reflux in the stomach, but not to a great extent. These acid inhibitors mainly convert acid reflux into nonacid reflux. This action is usually sufficient for most patients, as far as controlling the symptoms of concern.

However, there is a subset of patients in which more needs to be done. In this subset, patients either experience regurgitation or cough, or sometimes chest pain or heartburn that is thought to be related to nonacid reflux. In these circumstances, patients will not respond to further treatment with proton pump inhibitors because everything that can be achieved with this method has been. Some method of reflux inhibition is required. Antireflux surgery is the primary currently available option. As for what is on the horizon, clinicians are anticipating the development of drugs that actually inhibit reflux through the modulation of transient lower esophageal sphincter relaxation. There are several drugs currently in development for this indication, with none presently approved. Baclofen is a drug that is currently available that has been shown to modulate transient lower esophageal sphincter relaxation, but it is heavily burdened with side effects and is not very practical in the experience of most people. Some of the drugs under development are GABA_B agonists, modeled after Baclofen.

G&H Is nonacid reflux thought to cause any gastric and/or esophageal injury?

PK True nonacid reflux would not be very injurious. That idea comes from the historic use of the term “non-acid reflux” to encompass bile reflux, which is not what is currently intended by the term “nonacid reflux.” Nonacid reflux is rarely bile. As discussed above, it is much more accurate to think of nonacid reflux as weakly acidic reflux. The old terminology of bile reflux actually reflects the idea that the pH of reflux was above 7; it is very rare for reflux to have a pH above 7.

G&H Why has there been increased interest in nonacid reflux recently?

PK Reasons for the recent interest in nonacid reflux are hard to pinpoint exactly. It is primarily due to the recognition of the phenomenon with the availability of a technology (impedance monitoring) that is capable of detecting it. This technology has led to much enthusiasm, both by its developers and by clinicians trying to understand why patients are still symptomatic despite acid suppression.

G&H What areas of nonacid reflux require further research?

PK The main missing piece is therapy. The fact that nonacid reflux exists has been established. The symptoms that are associated with nonacid reflux need to be more firmly defined as well. Symptom association is difficult to establish with an event that occurs so frequently that chance association is quite possible.

Suggested Reading

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