

Significant Temporal Association of Esophageal Air Events (Supragastric Belches, Air Swallows, and Gastric Belches) With Hiccups: A Case Study in an Adolescent

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Abstract: We previously reported our ability to objectively assess the strength of temporal relationships between gastroesophageal reflux (GER) disease-like symptoms with esophageal air events (EAEs) (air swallows, gastric belching, and supragastric belching) using impedance-pH monitoring. Recently, we similarly evaluated an adolescent female who presented to our clinic with symptoms of recurrent hiccups and with what appeared to be numerous EAEs. Hiccups were associated with GER (symptom association probability [SAP] = 100%), air swallows (SAP = 99.7%), supragastric belches (SAP = 100%), and gastric belches (SAP = 100%), with almost twice as many of the supragastric belches preceding a hiccup than any of the other 3 esophageal disturbance types (EDs) ($P < 0.00001$). Our data showing a significant temporal association between EAEs and hiccups support a previous report in which belching was suspected of being associated with hiccups in an adult male. Reports such as this underscore the importance of considering the assessment of temporal relationships between extra-esophageal symptoms and EDs that include not only GER, but also EAEs, such as air swallows, gastric belches and supragastric belches, when devising strategies for clinical management of patients with hiccups.

Key Words: hiccups, impedance, supragastric belch, gastric belch, sensory-motor activation, vagal reflex, supraesophageal symptoms

INTRODUCTION

Hiccups are a common phenomenon in both children and adults (1). While the pathophysiology of hiccups is unclear, it has been suggested that hiccups may be related to gastroesophageal reflux (GER), and it has also been suggested that belches may be involved (2).

Using 24-hour impedance-pH monitoring (I-pHM), Hopman et al (2) found that supragastric belches (SGBs) were frequent and a sequence of gastric belches (GBs) immediately preceded esophageal contractions in a 74-year-old man who suffered from chronic hiccups for >18 months.

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The authors report no conflicts of interest.

Informed consent was obtained from the now adult patient for publication of the details of this case.

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Recently, we reported that a novel application of I-pHM could be used to objectively assess the strength of temporal relationships between esophageal air events (EAEs) (e.g., SGB's, air swallows [ASs], and GB's) and symptoms that have historically been thought to be associated with GER (3). The aim of this report was to apply our novel application of I-pHM to objectively evaluate the involvement of EAEs with hiccups in an adolescent female.

CASE STUDY

A 17-year-old female presented with symptoms that included hiccups, belching, and regurgitation. Review of the patient's chart revealed that the patient also suffered from occasional anxiety. Her symptoms did not improve with acid suppression therapy, and an upper endoscopy with biopsies was normal.

Over the course of a 1487-minute ambulatory I-pHM study, 26 GER episodes were detected; 18 (69.2%) were acidic (pH < 4) and 8 (30.8%) were nonacidic (pH ≥ 4). The acid reflux index was 0.8%, and the mean esophageal and gastric pH was 6.7 and 1.8, respectively. At the time of the I-pHM study, the patient was not taking any antireflux medications and did not have a fundoplication. Feeding periods were excluded from analyses.

Novel Application of I-pHM: Three copies of the unmarked I-pHM tracing were generated. In the first copy, SGBs were manually tagged to masquerade as GER episodes (Fig. 1) as recently described (3). Copies 2 and 3 were similarly marked for GBs and ASs, respectively.

Definitions: GER events were defined and evaluated using I-pHM as previously reported (Fig. 2) (4). SGBs were defined by an obvious rise in impedance (≥1000 Ω) in the proximal esophagus that moved initially in the caudal direction and then returned to baseline in the cranial direction (Fig. 3A) (5). ASs were defined as swallows that were immediately preceded by an air bolus (spike in impedance) that was ≥1000 Ω over baseline in the distal-most impedance channel (Z6) (Fig. 3B) (3, 6, 7). GBs were defined as air boluses of ≥1000 Ω that moved in the cranial direction (Fig. 3C). Hiccups were confirmed by the referring physician (H.K.M.) before I-pHM testing. A single person (F.W.W.) reviewed the entire study, but the events were confirmed by a second team member (K.W.).

The MMS/Laborie software was used to calculate the symptom association probability (SAP) values used to objectively assess the strength of the temporal relationship between each of the 4 esophageal disturbances (EDs) and hiccups. SAP values ≥95% were considered to be clinically significant.

Two of the 34 total hiccups occurred during feeding. Of the remaining 32, 4(12.5%) were not preceded by an ED, 10(31.2%) were preceded *only* by SGBs, 2(6.2%) were preceded *only* by ASs, 3(9.4%) were preceded *only* by GBs, and 1(3.1%) was preceded *only* by GER events; combinations of EDs preceding a hiccup are detailed in Table 1. Of the 28 hiccups that were associated with an ED, 27(96.4%) were associated with one or more of the 3 EAE types. It is important to note that of the 10 hiccups that were preceded by a GER event, only one hiccup episode was preceded by GER only.

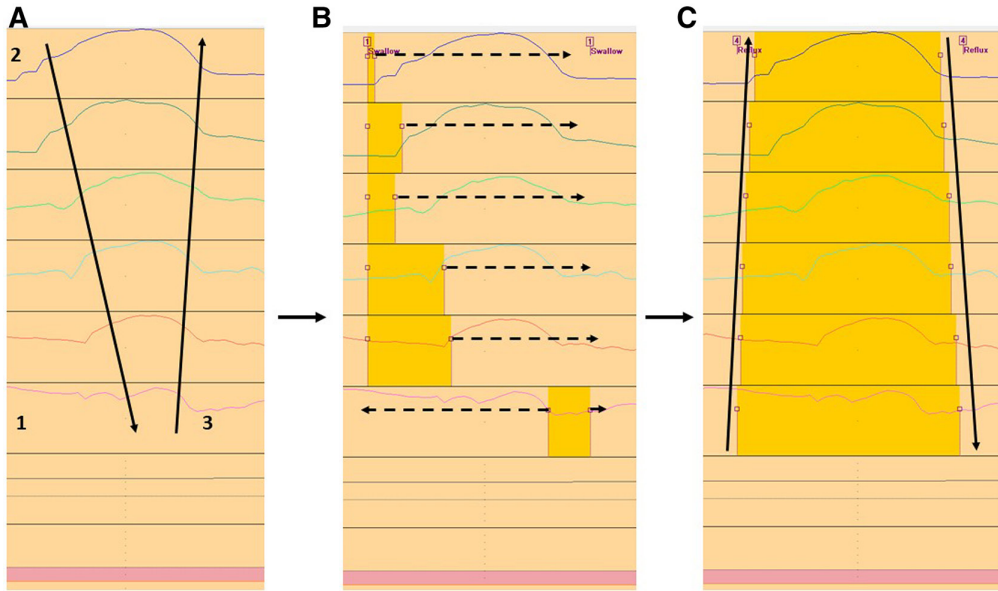


FIGURE 1. Supragastric belch tagged to masquerade as a reflux event. A) The series of left clicks (control key held) at position 1, 2, and 3 (then release control key). B) The results of the actions taken in (A), combined with the dotted arrows, that indicate the direction and extent to which the impedance lollipops are to be pulled in order to create the classic “pyramidal shape” that designates a reflux event (C).

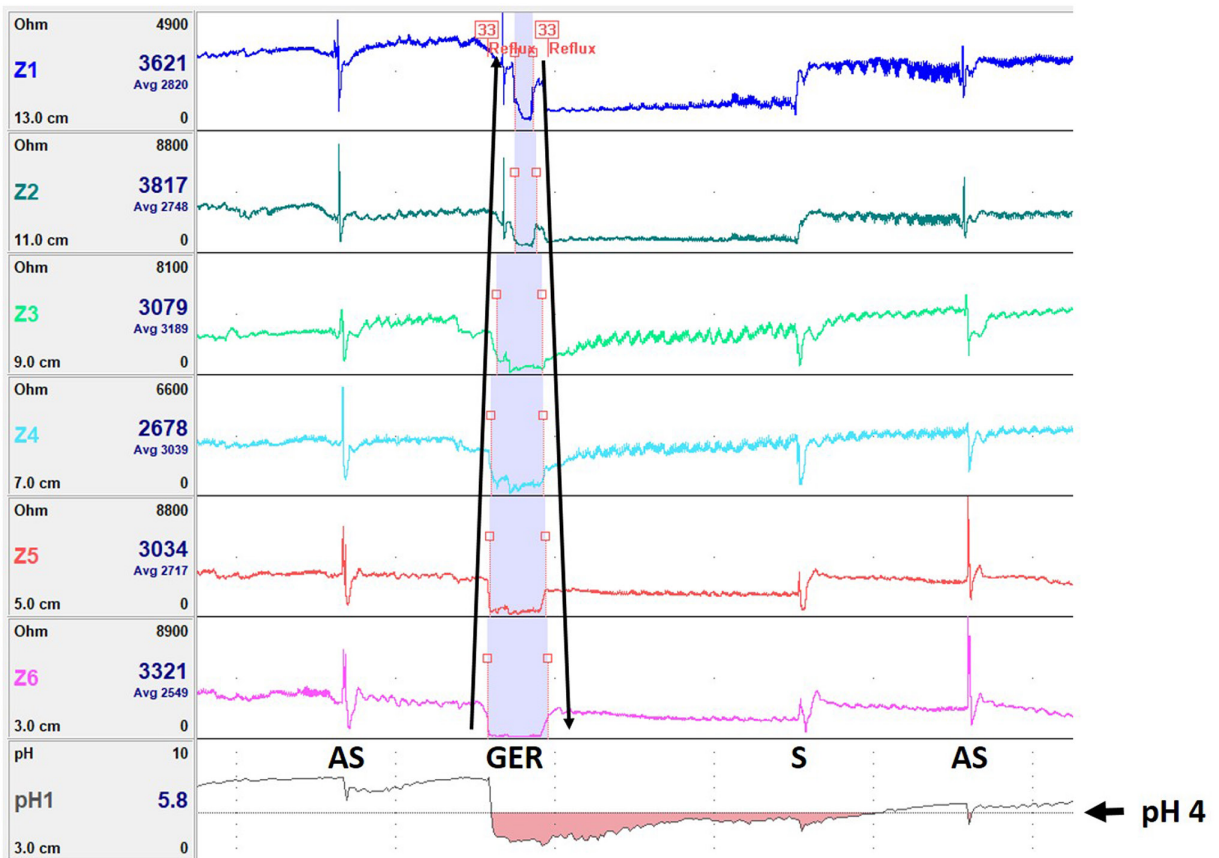


FIGURE 2. Acid gastroesophageal reflux event. Image above depicts an acid gastroesophageal reflux event (GER), flanked on the left by an air swallow (AS) and on the right by both a swallow (S) and an air swallow (AS). Vertical black arrows indicate the direction of intraluminal flow of the GER event and the thicker horizontal black arrow indicates the pH 4 threshold, signifying the acidity of the GER event.

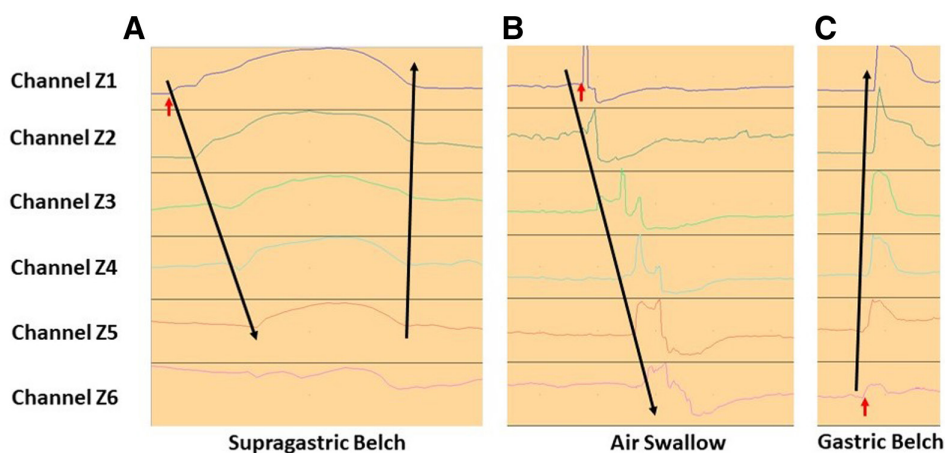


FIGURE 3. Esophageal air events. Black arrows indicate the direction of gas flow. Red arrow mark event start times.

SAP calculations indicated that each of the 4 EDs was significantly correlated with hiccups, with SGBs being temporally associated with more than half of them (Table 2).

DISCUSSION

Under normal circumstances, the diaphragm pulls down to draw air into the lungs, and then it pushes back up to expel inhaled air. When the diaphragm is irritated, it can spasm, causing air to be quickly pulled into the mouth against the larynx, causing it to close, thus producing the noise that is characteristic of a classic “hiccup” (1). Hiccups are physiologically normal but can become pathological when they occur with increasing regularity or for extended periods of time (1). The occurrence of hiccups is mediated through a reflex arc that consists of 3 basic branches: (1) afferent/sensory limb involving vagal, phrenic, and sympathetic nerves; (2) medulla and possibly the cervical spine (8) where central processing occurs; and (3) efferent/motor limb involving motor fibers of phrenic nerves and accessory nerves that innervate the diaphragm and intercostal muscles,

TABLE 1. Hiccup episodes preceded by esophageal disturbance(s)

	Number	Percentage
SGB	10	31.20
AS	2	6.20
GB	2	6.20
GER	1	3.10
SGB + AS	2	6.20
GER + SGB	3	9.40
GER + GB	1	3.10
GER + AS	1	3.10
GB + AS	1	3.10
SGB + AS + GER	1	3.10
GB + AS + GER	3	9.40
SGB + GB + AS + GER	1	3.10
Hiccups occurring with no esophageal disturbance	4	12.50
Total hiccups	32	100

ASs = air swallows; GB = gastric belch; GER = gastroesophageal reflux; SGB = supragastric belch.

respectively (1, 9). A hiccup may be caused by any disturbance that triggers one of these branches (1).

Belching may be associated with hiccups in patients with gastroesophageal reflux disease (GERD) (2). Hopman and colleagues’ report of I-pHM in the 74-year-old man showed an acid reflux index of 50% (45% upright and 57% supine), low distal baseline impedance (<1000 Ω), and a total of 188 SGBs (2). While proton pump inhibitor (PPI) treatment and behavioral therapy resulted in reduction of the acid index (to 27%) and the number of SGBs (from 188 to 17) after just 1 month, a 1-year follow-up revealed minor and fleeting improvement in the frequency of hiccups (2).

We initially tried treating this patient’s hiccups with acid suppression. When symptoms persisted despite H₂ blocker, PPI, and cyproheptadine therapy, I-pHM confirmed minimal GER and allowed us to focus instead on other treatments: behavioral techniques, diaphragmatic breathing, and baclofen. Ultimately, treatment

TABLE 2. Objective assessment of the association of GER, ASs, SGBs, and GBs with symptoms

Symptom (No. events of episodes)	Number of associated events, SAP value (%)			Esophageal pH	
	Combined	P	pH < 4	pH \geq 4	
GER					
Hiccups (32)	10, 100%	<0.0000	8, 100%	2, 94.4%	
ASs					
Hiccups (32)	10, 99.7%	0.0031	0, 0.0%	10, 99.7%	
SGBs					
Hiccups (32)	18, 100%	<0.0001	3, 100%	16, 100%	
GBs					
Hiccups (32)	8, 100%	<0.0001	1, 95.6%	7, 100%	

Table above depicts the number of associated symptom events, the corresponding symptom association probability value and the P value corresponding to the combined acid + nonacid values. Data in parenthesis are the total number of hiccup events. The number before the comma is the number of hiccups that were temporally associated with the esophageal disturbance. The number following the comma is the SAP value. One hiccup episode was associated with 2 separate SGBs (one when the esophagus was acidified and one when the esophagus was not acidified).

ASs = air swallows; GB = gastric belch; GER = gastroesophageal reflux; SGB = supragastric belch.

with baclofen resulted in marked improvement of hiccup symptoms (10), which included a reduction in both frequency and severity of hiccups, from multiple times per day to only occasional episodes each month, thus allowing for fuller participation in daily activities, school, and extracurricular activities.

As previously suggested for a pair of infants who had numerous GERD-like symptoms that were significantly associated with EAEs (3), we posit that esophageal distention caused by the EAEs may lead to sensory-motor activation of vagal reflexes that trigger the hiccups in our patient (11–13).

Our observations with this patient underscore the importance of considering multiple EDs, in addition to GER, when developing strategies for clinical management of patients who show signs of esophageal involvement. The fact that GER alone was associated with only one hiccup event may explain why acid suppression alone did not alleviate our patient's hiccups. Our data show that novel application of the I-pHM technology (to tag other EDs [GBs, SGBs, and ASs] in addition to GER) permits objective assessment of the strength of the temporal associations between multiple EDs and symptoms. These observations are important because they can direct clinical management to include alternate medical and behavioral treatment modalities such as baclofen and controlled abdominal breathing and swallowing, respectively (2).

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F.W.W. conceived and designed the study and performed all measurements (with the help of K.W.) and analyzed data. Subject was provided for by K.W., C.D.L., and H.K.M. Clinical guidance was provided by K.W., C.D.L., and H.K.M. F.W.W. wrote the first draft, and K.W., C.D., and H.K.M. were involved in the critical revisions.

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