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Dumping Syndrome: Updated Perspectives on Etiologies and Diagnosis


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Dumping syndrome (DS) has historically been associated with gastric surgery and vagotomy, as well as diabetes mellitus (DM). This article provides an update on the etiologies and clinical spectrum that represent the current DS patient population. A retrospective chart review was conducted of patients who were referred to a tertiary GI motility center and met criteria for DS. 35 patients met the diagnostic criteria for DS. 10 patients had comorbid DM (8 type II), 5 had a previous Nissen fundoplication with presumed vagal damage, and 1 had a gastric bypass. 19 (54%) patients were determined to have "idiopathic" DS. Of these idiopathic patients, 32% were able to describe an event consistent with a viral or bacterial gastroenteritis which immediately preceded the onset of DS symptoms. Among all patients with DS, 37% patients had been previously labeled with a diagnosis of gastroparesis prior to their referral.

INTRODUCTION

Dumping syndrome (DS) has long been associated with surgical procedures involving the stomach and small bowel. It was first described in 1913 as a condition which persistently afflicted a minority of gastric surgery patients. These patients exhibited postprandial gastrointestinal and vasomotor symptoms in connection with the rapid transit of chyme through the stomach. Before H. pylori was identified as the predominate etiology of chronic peptic ulcer disease, DS commonly developed after vagotomies and partial gastrectomies, which were routinely performed for the management of that condition. DS, therefore, received abundant attention in the literature during this time and valuable progress was made toward understanding its pathogenesis.

DS is the result of the rapid transit of chyme from the stomach to the duodenum. This causes the delivery of a large and hyperosmolar concentration of chyme into the small intestine. This may result in substantial hormonal and neural changes that shift fluid from general circulation to the intestinal lumen and the intestinal venous supply.[i] Indeed, the degree of rapid gastric transit has been positively correlated with the degree of blood volume contraction.[ii] Due to the release of hormones (such as VIP, serotonin, norepinephrine, and GLP-1) and autonomic responses to intestinal distension, the change of arterial blood

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volume may then result in the vasomotor symptoms such as weakness, faintness, and dyspnea. In addition, widespread reflex sympathetic activation may also mediate symptoms such as sweating and increased heart rate.[i] GI symptoms such as abdominal cramping, bloating, and diarrhea, characterize early DS, which typically begin within 30 minutes of eating.

In late DS, as in early DS, rapid gastric transit results in hyperosmolar chyme being expelled into the lumen of the small intestine. This hyperosmolarity causes a massive release of GIP and insulin in anticipation of substantial glucose absorption.[i, iii] The humoral response turns out to be disproportionate to the occasion, however, and a reactive hypoglycemia develops. The symptoms of late dumping syndrome are explained by this reactive hypoglycemia, and include sweating, shakiness, difficulty concentrating, decreased consciousness, hunger, and sometimes syncope. The diagnosis of late dumping syndrome is made by the clinical presentation of late dumping symptoms and can be confirmed by an oral glucose test demonstrating low glucose levels sometimes less than 60 mg/dL at 2 or 3 hours.

Although the surgical treatment of peptic ulcer disease declined following the development of proton pump inhibitors, these surgeries are still performed for intractable disease. Additionally, accidental vagal nerve damage during Nissen fundoplications, as well as an increased number of gastric bypass surgeries, have kept DS very pertinent to current clinical practice.

DS may also be associated with non-surgical etiologies, the most prominent being diabetes.[iii] Diabetes is a well-recognized etiology of rapid gastric emptying [iii, iv] and is attributed to early vagal damage from Wallerian nerve degeneration. Of course, more advanced neurodegeneration developing over time can lead to gastroparesis.

Due to the evolving etiologies of rapid gastric transit, as well as our improved understanding of its etiologies, a new characterization and profile of the symptomatic patient population with rapid gastric emptying (RGE) is warranted. This article reviewing our study further examines the distinct patient populations with RGE in the current era, with special attention to the clinical spectrum of the DS, new etiologies of DS, and diagnostic challenges.

METHODS

A retrospective chart review was conducted of patients who were referred to one of the investigators (RWM) at a tertiary GI motility center in El Paso, TX. Of the 309 patients evaluated from March 2009 to June 2012, charts were reviewed for patients with a gastric emptying test (GET) demonstrating rapid gastric transit, as well as symptoms consistent with DS.

The gastric emptying time was assessed by the standard 4-h scintigraphic method, established by

Table 1. Diabetes Mellitus Patients

Age	Gender	Ethnicity	1-hour Retention (%)	Previous Diagnosis of Gastroparesis	Treated with domperidone	Treated with metoclopramide	Depression
44	F	C	42	Y	Y	Y	Y
41	F		38	Y	Y	Y	Y
53	F	H	10				
79	F	H	30				
56	F	H	40	Y			Y
60	M	C	25				Y
76	F	H	41	Y		Y	Y
80	F	H	33				
51	F	H	32	Y			Y
53	F	C	35	Y			

M: male; F: female; C: Caucasian; H: Hispanic; Y: yes; the first two had diabetes mellitus type I.

the consensus recommendations by the American Neurogastroentereology and Motility Society and the Society of Nuclear Medicine.[iii] This standardized method for assessing gastric emptying includes a scrambled egg substitute (120 g, equivalent to two large eggs, or 60 kcal) labeled with 99mTc sulphur-colloid, two slices of whole wheat bread (120 kcal), 30 g of jelly (75 kcal), and 120 ml of water. The meal has a total caloric value of 255 kcal (72% carbohydrate, 24% protein, 2% fat, and 2% fiber). Anterior and posterior images of the stomach were taken immediately after eating, and then hourly for 4 hours (see Figure 1). Gastric retention of gamma counts was calculated by the Department of Nuclear Medicine. The geometric mean was calculated by taking the square root of the number of counts recorded on the anterior and posterior images. Data was also corrected for isotope decay. Rapid gastric transit in this study was defined as <50% isotope retention at 1 hour for women, and <35% retention at 1 hour for men. These gender-specific cutoffs are based on a study by Tougas et al.,[iii] which analyzed gastric transit in individuals without GI disease, and demonstrated that these cutoffs represent the 90th percentile in terms of gastric transit speed.

35 (11%) patients met these criteria for rapid gastric

Figure 1: Gastric Emptying Test Demonstrating Rapid Gastric Emptying Images were taken immediately after egg meal ingestion, at 30 minutes, 1 hour, and 2 hours. Anterior (above) and posterior (below) images are displayed.

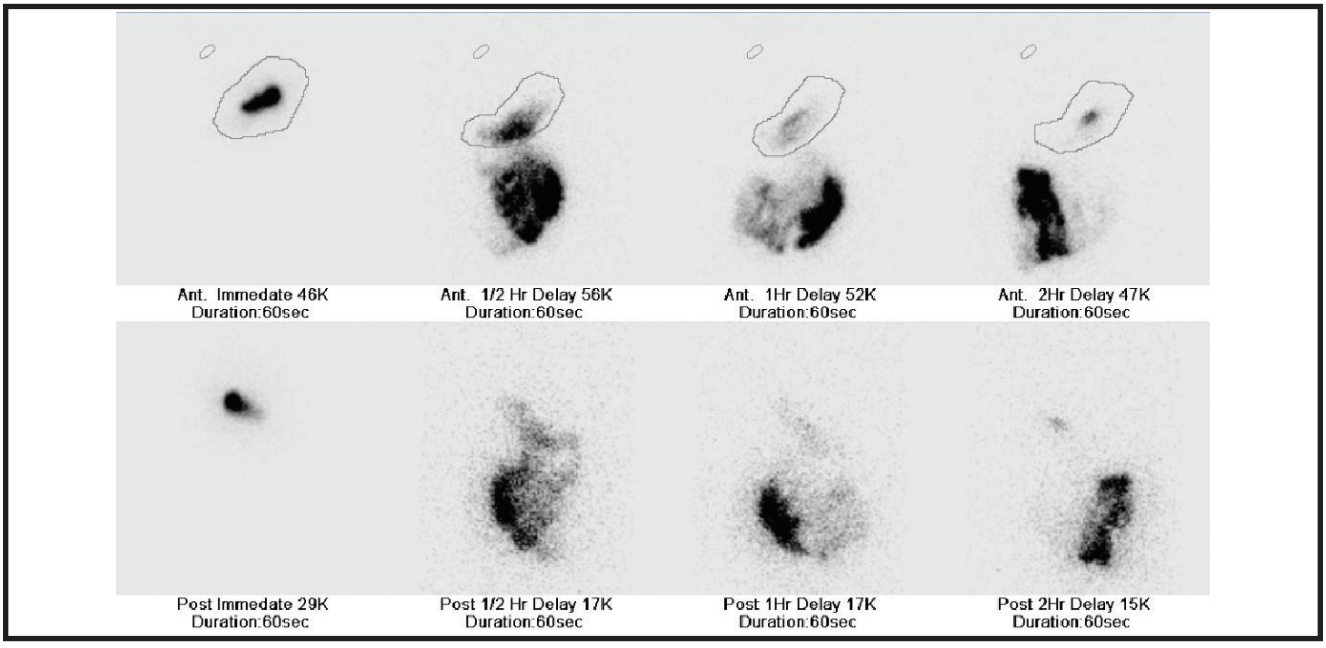

Table 2. Post-surgical Dumping Syndrome Patients

Age	Gender	Nissen Fundoplication	Gastric Bypass	Anxiety	Depression	1-hour Retention (%)
52	F	Y				18
58	F	Y		Y		7
59	M	Y				20
72	F	Y				46
60	F	Y		Y		20
63	F		Y		Y	25

M: male; F: female; Y: yes

Table 3. Idiopathic Patients

Age	Gender	Ethnicity	1-hour retention (%)	Anxiety	Depression	Migraines	Previous Diagnosis of Gastroparesis	Preceding Gastroenteritis
69	F		11		Y	Y		
63	F	C	42		Y	Y		Y
52	F	C	10		Y		Y	
69	F	H	49	Y	Y	Y	Y	Y
52	F	C	5		Y			
50	F	C	25				Y	Y
50	F	C	14				Y	
46	F	C	21					Y
46	F	H	31			Y	Y	Y
78	M	H	30					
24	F	C	10					
32	M		20	Y				
37	F	H	22					
41	F	A	13					
62	F	C	13		Y			
54	F	H	39					
75	F	H	48		Y			
43	F	H	32	Y			Y	
42	F	C	48	Y	Y		Y	

M: male; F: female; H: Hispanic; C: Caucasian; A: African-American; Y: yes

transit. These charts were reviewed with a focus on factors that could be attributed to the development and course of their pathophysiology. This included previous surgical procedures, diabetes mellitus, and preceding gastroenteritis-like illnesses in the period preceding the development of postprandial symptoms. In addition, attention was paid to comorbid conditions, medical treatments, and outcomes. When data on the chart was insufficient, telephone interviews were also conducted.

RESULTS

Of the 35 patients who met diagnostic criteria for DS, the mean age was 55, (ranging from 24-80 years), and 31 (88.6%) were females. The mean gastric retention at 1 hour was 27.9% for the women (5-49, SD ±15.8%) and 23.75% (20-30, SD ±4.1%) for the men.

In reviewing the etiologies of DS, we accertained that 10 patients (28.6%) had comorbid DM (8 type II, see Table 1), 5 (14.2%) had a previous Nissen fundoplication with presumed vagal damage, and 1 (2.9%) had another surgery which caused DS (a gastric bypass, see Table 2 for surgical causes of DS). Notably, 19 (54%) patients were determined to have "idiopathic" DS, defined as the lack of an identifiable etiology of DS (see Table 3). Of these idiopathic patients, 6 (32%) were able to recall and describe an event consistent with a viral or bacterial gastroenteritis which immediately preceded their DS symptoms.

Important co-existing conditions among this patient group included 14 (40%) who reported depression, and 8 (22.9%) who reported an anxiety disorder. Additionally, 17 (48.6%) were treated for concomitant small bowel bacterial overgrowth. Migraines were identified in 5

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(14.3%), and IBS had previously been diagnosed in 5 (14.3%).

It was noted that 13 patients (37.1%) had been previously labeled with a diagnosis of gastroparesis prior to their referral to our motility center, and 6 (46%) of those had been treated with metoclopramide or domperidone with suboptimal outcomes.

The treatment approaches for these patients included dietary modifications in all, dicyclomine (Bentyl) in 26 patients (74.3%), and somatostatin (Octreotide) in 6 (17.1%).

DISCUSSION

Our cutoff for defining rapid gastric transit in men and women was based on number of studies, which have demonstrated a significant difference between gastric emptying times in women and men, with women having slower transit times.[iii iv v] The standardized scintigraphic technique, utilized by Tougas et al., had demonstrated this discrepancy, and provided cutoff values for the 90th percentile in both men and women. We adopted these 90th percentile values as our cutoffs for defining rapid gastric transit in women and men (<35% retention at 1 hr in men; <50% retention at 1 hr in women). However, further studies will be needed to assess whether these 90% percentile cutoffs offer the optimal diagnostic sensitivity and specificity.

Our report highlights a patient population with a strong representation of non-surgical etiologies of DS. Our experiences with these patients underscore the importance of recognizing DS in those without a prior gastric surgery. Indeed, 29 patients were referred to our center over the 3 years from which data was obtained, with DS without a surgical cause. It is important to note here that our medical center does not specialize in a common cause of DS in the current era, namely bariatric surgery. This fact serves as an explanation for why our patient group was predominantly non-surgical DS. In general, surgery may lead to DS by reducing the volume of the stomach (such as in partial gastrectomy), inhibiting receptive relaxation (e.g. fundoplication), or disrupting the neural mechanisms which retard gastric emptying (occurring occasionally with vagotomy).

As we examined the non-surgical DS patients, we found a large proportion were "idiopathic"- an unexpected finding. In fact, our study involves the most idiopathic DS patients of any published study to our knowledge. As we focused on this group, we realized that although there was no demonstrable cause of the condition in these patients, the reality of their gastrointestinal dysfunction could not be overlooked. Many had severe, sometimes disabling symptoms, which was the reason for their referral to our center. In addition, previous interventions had usually not been helpful. These observations, and the proportion of patients in our study with truly idiopathic DS, underscore the importance of the awareness of this "new kid on the block" when explaining why dumping syndrome can develop. Our expectation is that increased awareness will contribute to appropriate management and referrals for these patients, and treatments with anti-motility instead of promotility agents.

In the past, it is possible that many in the idiopathic subgroup were diagnosed with non-ulcer dyspepsia. Indeed, non-ulcer dyspepsia has been associated with both rapid gastric transit and delayed.[iii, iv] However, Rome III criteria for functional dyspepsia only encapsulate postprandial fullness, satiety, epigastric burning, and epigastric pain.[iii] Therefore, DS can be clinically distinguished from non-ulcer dyspepsia on the basis of more severe abdominal cramping, as well as systemic symptoms (sweating, weakness, palpitations, etc.). If there is uncertainty about the diagnosis, and symptoms are severe, DS should be considered. In these cases a scintigraphic study can establish the diagnosis. Treatments such as diet, dicyclomine, and octreotide, rely on an accurate diagnosis of DS.

An interesting finding in our study among our idiopathic group was that 32% of idiopathic patients had experienced a preceding gastroenteritis. Although further studies would be needed to establish the veracity of this relationship, as well as the mechanism, a possible explanation for this is that these illnesses induced injury to duodenal receptors, namely fat and osmotic receptors which control gastric emptying. Another possibility is vagal nerve damage resulting in decreased fundic relaxation and accomodation, facilitating rapid emptying.

Among etiologic factors of DS in our patient group, DM was the most common. As previously mentioned, we would expect that at medical centers specializing in bariatric surgery, surgical causes of DS would make a bigger contribution. Additionally, the population of El Paso, Texas (the location of our motility center) is predominantely Hispanic, which nationality has a well-established genetic susceptibility to DM2. With the increasing prevalence of DM2, it is likely that the

number of Americans with GI motility disorders will increase as well. Thus, the importance of the DM2 DS population cannot be ignored. Although long-standing DM has classically been associated with gastroparesis, previous studies have demonstrated that DM of shorter duration is linked to rapid gastric emptying.[vi, vii] It is speculated that this RGE is due to early vagal damage, probably distal vagal damage, with gastroparesis evolving after more complete vagal loss. Although this temporal relationship is what is described in the literature, we observed DS in diabetes of long standing duration as well.

Another important conclusion to draw from our study is the utility of the scintigraphic GET. This test is key in distinguishing the diagnosis of gastroparesis from DS. Many of the patients in our study were previously labeled with gastroparesis, and indeed, some of the symptoms of gastroparesis are the same as in DS (e.g. nausea, vomiting, abdominal pain, and bloating). Some clinical differentiation may rest in the higher chance of nausea and vomiting in gastroparesis, and less severe abdominal pain than is present in DS. However, the past diagnosis of gastroparesis made in many of our patients emphasizes that gastroparesis symptoms can be almost indistinguishable from DS. Therefore gastric scintigraphy should be utilized when possible to definitively distinguish between gastroparesis and DS. Almost half our patients who had been previously labeled with gastroparesis had received prokinetics (domperidone or metoclopramide) before referral to our center. In these cases, we can assume that these treatments were not only ineffective, but also potentially worsened the symptoms. This finding underscores the usefulness of the GET.

The number of patients who identified themselves as having depression or anxiety in our study was high (49%). This finding is not surprising as it reinforces the well-known association of psychiatric disturbances with GI disease. For instance, CVS also has a high association with anxiety and depression.[iii] Similarly, IBS has a strong association with psychiatric illness; we have also found this to be a common comorbid condition in patients with DS. These associations between functional bowel disease and psychiatric illness emphasize the common pathogenic processes between mental health and the enteric nervous system. However, the lack of a specific diagnosis or poor response to misdirected therapies may have also contributed to the mental status of our frustrated and long suffering patients.

CRITIQUE

A potential limitation of our study was the criteria we used in the assessment of rapid gastric transit. In particular, because most studies on gastric transit testing have focused on delayed transit criteria, sufficient attention has not been paid to the early stages of the test. The early stages (first 30 minutes) are important, perhaps the most important, as this is the time frame during which early DS occurs. Thus, further studies outlining criteria for rapid emptying during earlier phases of the test might provide a more optimal method of diagnosing DS.

Our study design was not effective at identifying response to treatment in our patients. Studies addressing the effectiveness of anti-motility agents such as dicyclomine and somatostatin in DS patients would be helpful.

CONCLUSION

Many patients without a surgical history exhibit disabling DS symptoms in the setting of rapid gastric emptying. This included patients with DM2, those with a preceding gastroenteritis illness, and also those who had no predisposing factors for their symptoms. These findings emphasize a crucial role for scintigraphic GET in patients who have the symptoms of DS, even in the absence of a recent gastric surgery. This is essential to make the diagnosis of DS and effectively treat patients with this condition. Particularly in patients with DM and GI symptoms, a GET distinguished between gastroparesis and DS. With more precise diagnoses, this patient population will be better treated with focused therapies. ■

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