Etiologies of Nausea and Vomiting in Patients Referred to a Gastroenterology Motility Clinic

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Abbreviations used in this paper: GP-gastroparesis; GES - gastric electrical stimulation; GET - gastric emptying test; DM - Diabetes Mellitus; ID - idiopathic; ID-GP - idiopathic gastroparesis, DM-GP - diabetic gastroparesis;

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ABSTRACT

Background & Aims: There is a lack of comprehensive studies focusing on the different etiologies of nausea and vomiting among various racial/ethnic groups and specifically in Hispanics. The major entities identified as risk factors for the presence of nausea and vomiting are predominantly of upper gastrointestinal origin. Our study compared the etiologies responsible for nausea and/or vomiting, and the subsequent clinical presentations between Hispanic (H) and non-Hispanic white (NHW) patients referred for care to a gastrointestinal (GI) motility center in a tertiary medical center.

Methods: A retrospective cross-sectional analysis of patients with nausea and vomiting who were seeking outpatient care at a tertiary GI Motility Clinic from October 2009 to October 2010 was performed. Data from the clinical charts including comorbid conditions, current medications, results of specific laboratory tests and procedures were obtained for analysis.

Results: All obtained information from 121 (63 (52%) Hispanic (H); Female 95%) patients charts did not show any significant differences in the socio-demographic characteristics of H and NHW patients. Diabetes Mellitus (DM) was more prevalent among Hispanic patients as compared to non-Hispanic white patients (44% vs. 21% P=0.007), and diabetic gastroparesis was the major single diagnosis of nausea and vomiting in this group (28% vs. 12% P=0.042). Cyclic Vomiting Syndrome and post-surgical gastroparesis were more common etiologies among non-Hispanic white patients (21% vs. 5%; P=0.011), and the Gastric Electrical Stimulation System was implanted more frequently in non-Hispanic white as compared to Hispanic patients (15% vs. 6% NS).

Conclusions: Our retrospective analysis of more than one hundred patients revealed a disparity in the use of the gastric electrical stimulation in Hispanic patients with diabetic gastroparesis when compared to non-Hispanic whites. Our data provides support for earlier interventions in diabetic education and nutrition consultations in predominantly Hispanic community settings to prevent undesirable and serious complications of diabetes.

INTRODUCTION

There is a paucity of comprehensive studies highlighting the different etiologies of nausea and vomiting among various racial/ethnic backgrounds and specifically in Hispanic patients.

Nausea represents the subjective and unpleasant feeling of the desire to vomit. Vomiting describes the preprogrammed series of autonomic and motor responses that result in the forcible expulsion of gastrointestinal content through the mouth. Retching differs from vomiting by the absence of expulsion of gastric contents. In addition, patients may confuse vomiting with regurgitation, which is the effortless return of esophageal contents to the hypopharynx.¹

There are various risk factors for nausea and vomiting, but the major entities identified that are of upper gastrointestinal origin include: Gastroparesis of idiopathic, diabetic, or post-surgical origin (post-vagotomy); functional dyspepsia; Dumping Syndrome; Cyclic Vomiting Syndrome (CVS); drug-induced nausea/vomiting; Rumination Syndrome/Conditioned Vomiting, and other miscellaneous causes.

Gastroparesis is a chronic disorder resulting from weak gastric smooth muscle function leading to slow emptying of the stomach in the absence of mechanical obstructions. It is dominated by the symptoms of profound nausea, vomiting, early satiety, fullness, bloating, and epigastric pain. Of the recognized associations, Diabetes Mellitus and Idiopathic (unknown) origins have been reported as the most common.² Functional Dyspepsia, a less severe condition, is characterized as the feeling of postprandial fullness, early satiety, epigastric pain, and/or burning without any structural abnormality and normal rate of continued on page 15
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gastric emptying being recognized when less than 60% of food is retained in a stomach at 2, and less that 10% at 4 hours after ingestion of the study meal. Dumping Syndrome is another cause of nausea and vomiting, characterized by a cluster of postprandial symptoms including abdominal discomfort, diaphoresis, pallor, lethargy and diarrhea, and may occur after gastric surgery, in association with diabetes or it can be “idiopathic.” Its clinical picture is essentially indistinguishable from Gastroparesis. Cyclic Vomiting Syndrome (CVS) presents with recurrent and stereotyped episodes of severe nausea and vomiting separated by symptom-free periods that might last anywhere from a few weeks to months. There also are several medications that can induce nausea and vomiting. NSAIDs and aspirin can result in severe gastritis or even ulceration, and be associated with nausea and/or vomiting. In addition, opioids, chemotherapy agents, anticholinergics, digoxin, and dopamine agonists may trigger nausea and vomiting mainly via receptors located in the Chemoreceptor Trigger Zone. The most potent inhibitors of gastric motility and also agonists which can also induce nausea are opioids—commonly utilized for many GI and non-GI diseases. Byetta used for treating diabetes type 2, is a glucagon-like peptide-1 receptor agonist (GLP-1 RA) which may slow gastric emptying. Rumination Syndrome or Conditioned Vomiting is a disorder characterized by re-gurgitation of recently ingested food followed by re-chewing and re-swallowing or expulsion. The other diseases and disorders that can be observed in the setting of nausea and vomiting include: connective tissue diseases, scleroderma and lupus erythematosus, renal failure, migraine headaches, CNS entities including Parkinson’s disease and multiple sclerosis and constipation.

The incidence of gastroparesis (GP) is estimated to affect about 4% of the population. It has long been known that GP is a complication of diabetes and it is often associated with long-standing Type I or Type II diabetes along with other complications such as retinopathy, nephropathy, and peripheral neuropathy.

Because of the high prevalence of diabetes among Hispanics, we hypothesized, that diabetic gastroparesis would be the major etiology for nausea and vomiting among our Hispanic patients. Our study investigated the etiology and clinical outcomes of nausea and/or vomiting among Hispanic (H) patients referred for care at a tertiary medical center and we compared this group with non-Hispanic white (NHW) patients also referred and seen at our GI Motility Center.

STUDY DESIGN AND METHODS

The study was a retrospective chart review of patients with nausea and vomiting who were seeking outpatient care from a single gastroenterologist from October 2009 to October 2010. The specific questions and research goals described in the IRB approved protocol and presented below, in addition to patient’s clinical presentations were extracted from review of the patients’ charts. We also investigated the outcomes related to the treatment options (medical, surgical, or other) that were implemented in the GI Motility Clinic. We reviewed participant charts looking for the following variables (if they were available): 1) Demographics: age, gender, socioeconomic status, co-morbidities, 2) History of Present Illness, Past Medical and Surgical History, 3) Past and current medications related to GI tract (prokinetics/antiemetic), 4) Labs: CBC, BMP, HbA1c, Liver function test, Lipase, Amylase, Vitamin B12, Folic acid levels, Iron panel studies, TSH, T3, T4, Cortisol, ACTH if available, 5) Other Studies: Results of endoscopy, Gastric Emptying Studies (4-hour Scintigraphy Test), CT scan of abdomen, double contrast upper GI X-ray, Ultrasound of the abdomen, IHDA scan, motility studies such as lactulose/glucose breath test for Small Intestine Bacterial Overgrowth (SIBO), if available.

This analysis represents retrospective chart review of 121 patients referred to one physician with the chief complaint of nausea and vomiting. All patients underwent extensive evaluation including endoscopy, colonoscopy, ultrasound, radiological tests, laboratory work (including HbA1c) and careful clinical assessment before they received a final diagnosis. Also, 4 hour scintigraphy gastric emptying test (GET) is an established standardized test diagnosing patients with gastroparesis based on greater than 60% retention at 4 hours and/or/10% retention of the isotope-labeled study meal at 4 hour time point. Dumping Syndrome is recognized when 65% or more of the meal is emptied by 1 hour, and 80% by 2 hours. Data were described using appropriate summary measures. The continuous variables were compared using unpaired t-test while categorical variables were compared using Fisher’s exact test. P-values less than 5% were regarded as significant results. Statistical analyses were carried out using Stata 12.1.

RESULTS

Our results are summarized in Table 1 “Comparisons of clinical characteristics of patients by ethnicity” and Table 2 “Special Characteristics of Patients with Diabetes Mellitus (n=40).” The results of the remaining laboratory tests and procedures, described in our methods section above, did not show any significant differences by ethnicity.

DISCUSSION

There have been limited publications addressing ethnic and racial aspects of nausea and vomiting in pregnant settings, and results have been inconsistent. After reviewing the literature, we concluded that there has not been a published study focusing on Hispanic white populations regarding the etiology of nausea/vomiting in non-pregnant settings. Even though there are many GI and non-GI related disorders that can manifest with nausea and vomiting, our research focused on gastrointestinal causes of these symptoms in patients being referred to the Motility Center where 85% of the population is Hispanic and almost 16% have been diagnosed with Diabetes.

Diabetes is one of the most common non-communicable diseases, with an estimated 347 million people living with diabetes worldwide (CDC, Report 2013). Type 1 diabetes is much less common than type 2, consisting of 10% of all cases of diabetes. While type 2 diabetes has been increasing among African-American and Hispanic adolescents, the highest rates of type 1 diabetes are found among Caucasian youth. This same report indicates that Diabetes Mellitus is two to three times more common in Mexican American and Puerto Rican adults than in non-Hispanic whites and that the prevalence of DM by race/ethnicity is 7.1% of NHW and 11.8% of HW with 13.3% of them being for Mexican Americans. Therefore, we believe that DM is a serious health concern for
Table 1.
Comparisons of clinical characteristics by ethnicity.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Total n=121</th>
<th>Hispanics=63</th>
<th>Non-Hispanics=58</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (range)</td>
<td>51(18-89)</td>
<td>51(18-83)</td>
<td>50 (20-89)</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>94 (75%)</td>
<td>46 (73%)</td>
<td>45 (76%)</td>
<td>NS</td>
</tr>
<tr>
<td>Male</td>
<td>31 (25%)</td>
<td>17 (27%)</td>
<td>13 (24%)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean Weight (range)</td>
<td>165 (88-259)</td>
<td>170 (107-259)</td>
<td>159 (88-240)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean BMI (range)</td>
<td>27(15-43)</td>
<td>27 (18-43)</td>
<td>26 (15-39)</td>
<td>NS</td>
</tr>
<tr>
<td>Total DM patients</td>
<td>40 (33%)</td>
<td>28 (44%)</td>
<td>12 (21%)</td>
<td>0.007</td>
</tr>
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</table>

Etiologies of Nausea & Vomiting

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Total n=121</th>
<th>Hispanics=63</th>
<th>Non-Hispanics=58</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic Gastroparesis (DM-GP)</td>
<td>25 (21%)</td>
<td>18 (28%)</td>
<td>7 (12%)</td>
<td>0.042</td>
</tr>
<tr>
<td>Idiopathic Gastroparesis (ID-GP)</td>
<td>15 (12%)</td>
<td>5 (8%)</td>
<td>10 (17%)</td>
<td>NS</td>
</tr>
<tr>
<td>Dumping Syndrome (DS)</td>
<td>19 (16%)</td>
<td>9 (14%)</td>
<td>10 (17%)</td>
<td>NS</td>
</tr>
<tr>
<td>Cycling Vomiting Syndrome (CVS)</td>
<td>15 (12%)</td>
<td>3 (5%)</td>
<td>12 (21%)</td>
<td>0.011</td>
</tr>
<tr>
<td>Ruminatin and Conditioned Vomiting</td>
<td>8 (7%)</td>
<td>1 (2%)</td>
<td>7 (12%)</td>
<td>0.027</td>
</tr>
<tr>
<td>Post-surgical (fundoplication)</td>
<td>12(10%)</td>
<td>3 (5%)</td>
<td>9 (16%)</td>
<td>NS</td>
</tr>
<tr>
<td>All Other Diagnosis (see more details in “Discussion” section)</td>
<td>27 (22%)</td>
<td>24 (38%)</td>
<td>3 (5%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Prokinetics

<table>
<thead>
<tr>
<th>Prokinetic</th>
<th>Total n=121</th>
<th>Hispanics=63</th>
<th>Non-Hispanics=58</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide</td>
<td>22 (18%)</td>
<td>13 (21%)</td>
<td>9 (15%)</td>
<td>NS</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>2 (2%)</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>NS</td>
</tr>
<tr>
<td>Domperidone</td>
<td>16 (13%)</td>
<td>8 (13%)</td>
<td>9 (15%)</td>
<td>NS</td>
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</table>

Anti-Emetics

<table>
<thead>
<tr>
<th>Anti-Emetic</th>
<th>Total n=121</th>
<th>Hispanics=63</th>
<th>Non-Hispanics=58</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenergan</td>
<td>12(10%)</td>
<td>6 (9%)</td>
<td>6 (10%)</td>
<td>NS</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>6 (5%)</td>
<td>3 (5%)</td>
<td>3 (5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Zofran</td>
<td>19(16%)</td>
<td>4 (6%)</td>
<td>15(26%)</td>
<td>0.005</td>
</tr>
<tr>
<td>PPIs</td>
<td>52 (43%)</td>
<td>31 (49%)</td>
<td>38 (65%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Surgical Procedures

<table>
<thead>
<tr>
<th>Surgical Procedure</th>
<th>Total n=121</th>
<th>Hispanics=63</th>
<th>Non-Hispanics=58</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric Stimulation</td>
<td>13 (11%)</td>
<td>4 (6%)</td>
<td>9 (15%)</td>
<td>NS</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>29 (24%)</td>
<td>16 (25%)</td>
<td>13 (22%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Hispanic women, who have a higher prevalence than men (19). Gastroparesis affects up to 2.3 million adults with DM in the US. An NIH/NIDDK study showed that the majority of gastroparetic patients were women (83% overall) regardless of etiology. In a different paper the same authors also noted that out of 243 patients diagnosed with Idiopathic GP prevalence was reported as 4 times more prevalent in woman than men, with mean age of diagnosis being 41 years old. This observation is consistent with previously published data showing that females diagnosed with GP outnumber males by a ratio 4:1. Interestingly, in our study women dominated the referral pattern for nausea and vomiting of all etiologies both in NHW (76%) and Hispanic whites (73%). This suggests that the female GI tract has more susceptibility and underlining hormonal predispositions to develop impairment of neuromuscular function than males. This female dominance is well reported in the literature in NHW gastroparesis, but our study is the first one showing that female gender dominance is also present in Hispanic gastroparetic patients.

Hispanic patients in our study had a higher frequency of diabetes (44% vs. 21%) with a mean glucose of 142 mg/dl and a mean HbA1c of 8.7%, as compared to NHW with a mean glucose of 117 mg/dl and a mean level of HbA1c of 5.9%. They also had a higher frequency of gastroparesis secondary to diabetes when compared to non-Hispanic whites (29 % vs. 12%). It was also noted that 15% of NHW patients with severe gastroparesis underwent surgical implantation of gastric electrical stimulation (GES) system as compared to 6% of Hispanic patients. The availabilities or lack of health insurance and economic status of these patients may explain the disparity between HW and NHW patients being treated with GES Therapy for severe, drug refractory symptoms of gastroparesis.

Dumping Syndrome was also an important contributor to nausea and vomiting among our Hispanic patients, and was related to the spectrum of earlier diabetest causing rapid gastric emptying (< then 70% retention of the study meal at 30 min, and <35% at 60 min). Specifically, dumping syndrome is regarded as the degree of an earlier presentation of GP symptoms resulting from substantial hormonal (such as VIP, Continued on page 17
serotonin, norepinephrine, and GLP-1), arterial blood volume and neural changes including vagal nerve injury.

On the other hand Idiopathic and Post-surgical etiologies were more predominant among NHW patients. Other etiologies of N/V, besides GP, which were also more common in this group as compared to the Hispanic population, were: CVS 21% vs. 5%, and Rumination/Conditioned Vomiting 12% vs. 2%.

Since the proportion of Hispanics throughout the USA is growing, it is very important to recognize the specific etiologies of nausea and vomiting in this population. It is anticipated that the incidence of diabetes will continue to increase. The major factors probably influencing this prediction are related to: population growth, aging, urbanization, obesity, unhealthy dietary habits and physical inactivity. Diabetes is very comparable to “a silently ticking bomb” in our society, requiring serious medical attention with preventive measures and education. A very good example is that about 675,000 Hispanic Americans have diabetes but do not know they have the disease, with about 25 to 30% being either diagnosed or undiagnosed with DM.15 The lack of access to health care due to lack of health insurance, and not seeking health care at all, are the primary reasons why these diabetes cases are usually missed.

Based on our study, gastroparesis has been identified as the most common etiology of nausea and vomiting in the diabetic Hispanic patients. However, only 1/3 of our patients were taking prokinetics and antiemetics, reflecting under-recognition of gastroparesis. PPIs use was very common in both groups suggesting that gastric acid suppression is a primary care approach to upper GI symptoms, hence delaying any diagnostic tests. Also the lack of dietary education in gastroparetic patient was very evident in chart reviews of all patients seen in the clinic. Furthermore, the evidence of high mean glucose 142 mg/dl and HbA1c 8.7 emphasizes that special attention with nutritional education and lifestyle modification should be provided to diabetics in Hispanic white population.

CONCLUSIONS
Some of the etiological factors for nausea and vomiting among Hispanic patients were found to be different among non-Hispanic white patients referred to a tertiary motility clinic. Our study suggests there is a need for life style intervention to reduce the comorbidities associated with nausea and vomiting in a predominantly Hispanic group of patients. We believe, genetic predispositions, high calories, low fiber diet, socio-economical and educational levels, with the lack of insurance coverage, limiting an early access to medical care are the major reasons causing some inequality among our patients. Our analysis of more than one hundred patients also demonstrated a disparity in the use of the gastric electrical stimulator therapy for refractory gastroparesis among Hispanic patients when compared to non-Hispanic patients. Our data provides support for earlier intervention in diabetic education and nutrition consultations in predominantly Hispanic community settings, which could prevent further undesirable and serious complications of diabetes.

REFERENCES

Continued on page 18
Etiologies of Nausea and Vomiting in Patients Referred to a Gastroenterology Motility Clinic (Continued)


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