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EFFECTS OF ANTIDEPRESSANTS ON GASTRIC FUNCTION IN PATIENTS WITH FUNCTIONAL DYSPEPSIA

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Abstract:

The most common functional gastrointestinal disorder with approximately 10 percent prevalence is known as Functional dyspepsia. Functional dyspepsia has remarkably disturbed the health care system. The statics indicates that almost 9.5 billion US dollar ascribable to the diagnosis of functional dyspepsia. Many studies reported that functional dyspepsia has linked with reduced quality of life. Two groups were made group A with 12 weeks trial of amitriptyline, escitalopram, and matching placebo in patients with FD. Age ranges from 18-65 both male and female were eligible the study. An informed consent was obtained from the participants after explaining the purpose of the study. PDS (post prandial fullness syndrome) was defined as having indigestion, feeling of fullness and early satiety two or more days per week. EPS (epigastric pain syndrome) was defined as weekly, or more frequent, epigastric pain or burning. The results have demonstrated that TCAs (amitriptyline) can be used to improve global FD symptoms. It will not induce or aggravate the delaying gastric emptying in FD patients.

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INTRODUCTION:

The most common functional gastrointestinal disorder with approximately 10 percent prevalence is known as Functional dyspepsia. Functional dyspepsia has remarkably disturbed the health care system. The statics indicates that almost 9.5 billion US dollar ascribable to the diagnosis of functional dyspepsia. Many studies reported that functional dyspepsia has linked with reduced quality of life. Symptoms of FD include epigastric pain or burning, postprandial fullness, early satiety, and in some studies, other symptoms including postprandial nausea and upper abdominal bloating. FD symptoms may develop due to a number of different pathophysiologic processes including abnormal fundic accommodation, delayed gastric emptying, rapid gastric emptying, visceral hypersensitivity, and duodenal eosinophilia. The most common identified pathophysiologic abnormalities in patients is delayed gastric emptying. Depending upon the method used to evaluate gastric motor function, delayed gastric emptying is present in 30% of FD patients. Functional dyspepsia has nonspecific symptoms which do not provide underlying pathophysiology surely it also includes delayed gastric emptying, whereas other studies indicate a link between symptoms and delayed gastric emptying. So that FD cannot be reliable to some specific symptoms which direct the underlying pathophysiologic abnormality based in symptom expression. The very first agent used to treat FD symptoms is proton pump inhibitors while being effective in only 7-10 percent individuals who were having FD as compared to placebo. Prokinetic agents are also used in health care system but in very limited use. To treat abdominal pain symptoms of functional dyspepsia Antidepressants, both tricyclic agents (TCAs) and selective serotonin reuptake inhibitors (SSRIs), are often used. Use of antidepressants which were acquired essentially from studies of patients having irritable bowel syndrome are supportive in the treatment of functional abdominal pain. Many patients present with overlapping symptoms of IBS and FD, until recently there were limited data to support the use of antidepressants for the treatment of FD symptoms. A large, multicenter, prospective, randomized controlled trial (FD Treatment Trial; FDTT) evaluated the efficacy and safety of antidepressant use in FD patients. The study concluded that TCA was having more efficacies than SSRI in improving the FD symptoms world widely. A small study of healthy volunteers indicted that TCAs could prompt delay in gastric emptying, so despite the fact of valuing the results many clinicians bothered about the use of TCAs to treat FD symptoms. Some data recommend that SSRIS increases the process of gastric emptying, so many clinicians are concerned with the use of SSRI to treat FDA symptoms. In such way FD patients have reported more aggravating symptoms with rapid gastric emptying. Gastric accommodation (GA) and sensation could potentially be affected by a TCA or SSRI, although in two small studies of healthy volunteers' amitriptyline did not affect gastric volumes. TCA or SSI has potentially affected the gastric accommodation and sensation whereas a small study conducted of healthy volunteers concluded that amitriptyline did not much influence the gastric volumes and paroxetine did not alter GA. The primary aim of the current study was to determine whether FD patients with delayed or rapid gastric emptying responded differently to antidepressant therapy compared to FD patients with normal gastric emptying.

METHODS:

It was randomized controlled study.

Two groups were made group A with 12 weeks trial of amitriptyline, escitalopram, and matching placebo in patients with FD. Age ranges from 18-65 both male and female were eligible the study. An informed consent was obtained from the participants after explaining the purpose of the study. PDS (post prandial fullness syndrome) was defined as having indigestion, feeling of fullness and early satiety two or more days per week. EPS (epigastric pain syndrome) was defined as weekly, or more frequent, epigastric pain or burning. Participants must have moderate FD symptoms which were evaluated by GI symptom rating scale Exclusion criteria were current antidepressant or anti-inflammatory agent use, symptoms responsive to anti-secretory therapy, a history of peptic ulcer disease, esophagitis, erosive gastritis, current drug or alcohol abuse, pregnancy, breast feeding, major abdominal surgery, or major physical illness. Subjects who were in group (a) were supposed to receive 25 mg amitriptyline for the first week to reduce the potential side effects. Rapid gastric emptying is defined as decreased capacity of holding the food for at least one hour. Delayed gastric emptying was defined as inability to quickly move the food in GI tract. An intent-to-treat analysis included all randomized subjects. Logistic regression was used to analyze the symptoms with adequate relief as the binary dependent variable. ANCOVA model was used to evaluate the effect of treatment on gastric emptying. P value of <0.05 was considered statistically significant. The associations among the physiological assessments were assessed using Spearman correlations.

RESULTS:

Total 199 participants who met the inclusion criteria were recruited in the study. Mean age of the participants were 42 years in which 85% were male and 76% were female. 74% were having ulcer like functional dyspepsia whereas 26% were having

dysmotility like FD. According to post hoc classification 21% were having post-prandial distress syndrome, 45% met the criteria of both PDS and EPS whereas 19% had epigastric pain syndrome. Moreover 42 participants were met the criteria of FD but could not be recognized into any three mentioned categories. It has reported that 52% globally improvement in patients treated with amitriptyline those having FD symptoms as compared to 35% treated with escitalopram and 45% treated with placebo. Demographics of those with delayed gastric emptying were similar to those with normal emptying with regard to age, gender, and FD subtype.

Treatment with ESC did not enhance gastric emptying in any of the 71 patients with normal emptying at baseline at week 12. Means of t 1/2 by treatment arm and FD subtype did not differ.

Gastric emptying and symptom response Patients with delayed gastric emptying at baseline was less likely overall to respond to antidepressant therapy for their FD symptoms than patients with normal gastric emptying. The symptoms response was not related to any kind of antidepressant used. Both AMI and ESC reported similar and improved baseline as compared to placebo. The nutrient drink test result for symptoms of bloating was improved after 12 weeks of antidepressant therapy as compared to placebo. When amitriptyline was compared escitalopram there was no difference observed.

The symptoms of abdominal pain were improved with antidepressants specifically more significant with AMI.

Analysis of patients using FD subtypes (PDS vs. EPS vs. PDS– EPS overlap) found that the PDS–EPS groups were more likely to have an abnormal satiety test than either the PDS group (62%) or the EPS group compared to both groups. Seventy six participants underwent gastric accommodation baseline, while 22% women having gastric ulcer; 71% dysmotility. Individuals having dysmotility had undergone for more testing as compared to ulcer like subtype. Eight patients had abnormal GA at baseline. There was found no significant correlation of GA with FD symptoms. No differences in GA were identified based on age, gender, BMI, presence of absence of delayed gastric emptying, and FD subtype (EPS vs. PDS vs. both). Antidepressant therapy did not affect fasting gastric volume; Fasting gastric volume did not get affected from antidepressants whereas it enhances the postprandial gastric volume. Fed volume was seen improved by both AMI and ESC than placebo. However, there was no remarkable difference between both antidepressants.

DISCUSSION:

The most common functional gastrointestinal disorders is FD. Treatment of FD is still a difficult part because of unknown underlying pathophysiologic processes and the arising symptoms are not specific to single pathophysiologic abnormality. By using number of methods including breath test, delayed gastric emptying has found in 30% of patients with functional dyspepsia. Because the symptoms do not exactly reflect the fundamental pathophysiology, treating FD symptoms has been a difficult. Many treatment options are available to treat multiple symptoms of FD however there is no authentic treatment algorithm exists. Due to the given ease of access, acceptable safety profile and many overlapping of FD symptoms with gastrointestinal reflux; proton pump inhibitors are first to use. Abdominal pain associated with functional bowel disorders are often used with tricyclic antidepressants. A very limited data has been posted in the favor of their use. The recent NIH FDTT demonstrated that a TCA (amitriptyline) was superior to an SSRI (escitalopram) at improving the global symptoms of FD.

A recent study has compared the use of TCA and SSRI for the treatment of FD. The results concluded that TCA had meaningful in formation on the use of TCAs for the treatment of FD. Whereas theoretical study demonstrates that it could slow down the gastric emptying hence aggravating or inducing the dyspeptic symptoms. Another small study conducted on healthy volunteers has concluded that slowing stomach emptying did not worsen meal related symptoms. No prospective studies have evaluated the effects of TCAs and SSRIs on both gastric emptying and symptoms in a large sample of well-characterized FD patients. The current study found that antidepressants, whether a TCA or an SSRI, did not delay gastric emptying. More specifically, for those patients with delayed gastric emptying at the start of the study, the use of a TCA did not alter gastric emptying as measured by a physiologically relevant scintigraphic study. Importantly, the use of a TCA did not slow gastric emptying in those with normal gastric emptying at the start of the study period. These findings provide important information to clinicians who are reticent about using TCAs for the treatment of FD due to theoretical concerns about changing gastric motor function. This study also determined that escitalopram did not transform those with normal gastric emptying into rapid emptying. Although the sample size is small, these findings should diminish theoretical concerns about the use of SSRIs worsening gastric symptoms due to accelerating gastric emptying. The nutrient drink test was the

physiologic test most likely to be abnormal in this large study of FD patients. Correlation between the nutrient drink test, GA, and gastric emptying was only poor, however. This highlights the fact that the symptom of satiation represents a complex physiologic process not entirely based on either GA or gastric emptying. Correlations with the Somatic Symptom Checklist with symptoms during the nutrient drink test suggest a psychological component contributes to the perceived symptoms. An important finding of this study was the general improvement in aggregate FD symptoms (i.e., abdominal pain, fullness, nausea and bloating), measured during the nutrient drink test, in those patients treated with either AMI or ESC. In addition, the prevalent and bothersome post-prandial symptom of bloating was improved in FD patients treated with either AMI or ESC. GA and post-prandial symptoms, as assessed by the nutrient drink test, improved with antidepressant therapy. One of the most bothersome symptoms of FD, postprandial bloating, improved with antidepressant therapy, and these results should encourage clinicians to use these agents more routinely.

The results have demonstrated that TCAs (amitriptyline) can be used to improve global FD symptoms. It will not induce or aggravate the delaying gastric emptying in FD patients.

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