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Research Article

STUDY ON THERAPEUTIC APPROACH AND ITS OUTCOME WITH PROKINETICS AMONG DIABETES PATIENTS

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ABSTRACT

Gastroparesis is a chronic, symptomatic disorder of the stomach that is characterized by delayed gastric emptying in the absence of mechanical obstruction. Gastroparesis literally translated means "stomach paralysis. Gastroparesis is a digestive disorder in which the motility of the stomach is either abnormal or absent. In health, when the stomach is functioning normally, contractions of the stomach help to crush ingested food and then propel the pulverized food into the small intestine where further digestion and absorption of nutrients occurs. When the condition of Gastroparesis is present the stomach is unable to contract normally, and therefore cannot crush food nor propel food into the small intestine properly. Normal digestion may not occur. To study the demographic details and social history of diabetic induced gastropathy patients and need of the prokinetic agent. To find out how effective the prokinetic works in DM patient. To evaluate and compare the effectiveness of each prokinetic agent with lifestyle modifications and without the lifestyle modifications. A patient-based instrument called the gastroparesis cardinal symptom index (GCSI) has been developed to assess the severity of gastroparesis. The GCSI index is based on 3 symptom subscales 1.Nausea/vomiting [nausea, vomiting, retching's] 2.Postprandial fullness [not able to finish full meals, stomach fullness, loss of appetite, feeling excessively after meals] 2.Bloating[bloating, belly visible extremely large] of a larger upper gastrointestinal disorders–symptom severity index that was previously developed. These 3 scales were selected as part of the GCSI because they assess common symptoms related to gastroparesis- nausea/vomiting, postprandial fullness/early satiety, and bloating. The GCSI issued to rate symptom change by either the physician or the patient over a 2-6 week recall period. The scale was mention below (table 1). The findings of this study indicate that the GCSI is a reliable and valid instrument for measuring symptom severity in patients with gastroparesis. The patients who used prokinetics named itopride, levosulpiride, acotinamide who diagnosed with diabetic gastroparesis showed significant improvement in the symptoms.

Keywords :- Gerd, Peptic Ulcers, Gastritis, Gastroparesis, Prokinetics.

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INTRODUCTION

Gastroparesis is a chronic, symptomatic disorder of the stomach that is characterized by delayed gastric emptying in the absence of mechanical obstruction [1]. Gastroparesis literally translated means "stomach paralysis. Gastroparesis is a digestive disorder in which the motility of the stomach is either abnormal or absent. In health, when the stomach is functioning normally, contractions of the stomach help to crush ingested food and then propel the pulverized food into the small intestine where further digestion and absorption of nutrients occurs. When the condition of Gastroparesis is present the stomach is unable to contract normally, and therefore cannot crush food nor propel food into the small intestine properly. Normal digestion may not occur

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[2]. The 3 most common etiologies are diabetes mellitus, idiopathic, and postsurgical.[1] Other causes include medication, /Parkinson's disease, collagen vascular disorders, thyroid dysfunction, liver disease, chronic renal insufficiency, and intestinal pseudo-obstruction.[3] The prevalence of diabetic gastroperisis (DGP) appears to be higher in women than in men, for unknown reasons[4]. Autonomic neuropathy is also called as Gastroparesis with feelings of bloating, nausea, urinary retention impotence in men; postural hypotension, tachycardia and diahhorea with incontinence of stool .The presence of autonomic insufficiency may have profound effects on the patients responds to vasodilation drugs and ability to counter act hypoglycemia. Poor glycemic control with unexplained hypoglycemiamayresultfromthedisruptthedeliveryofthefo odtotheintestine; i.e. Glucose delivery does not correspond with prandial insulin action.as a result the blood glucose levels can be fluctuate easily[5].

DIABETIC GASTROPARESIS:

Diabetes gastroparesis is one of the complications of diabetes [1].this is also called as diabetic autonomic neuropathy [6].

Patients with diabetes in whom Gastroparesis develops often have had diabetes for at least 10 years and typically have retinopathy, neuropathy, and nephropathy. Diabetic Gastroparesis may cause severe symptoms and result in nutritional compromise, impaired glucose control, and a poor quality of life, independently of other factors such as age, tobacco use, alcohol use, or type of diabetes.[4] Symptoms attributable to Gastroparesis are reported by 5 to 12% of patients with diabetes[7].

PATHOPHYSIOLOGY OF DIABETIC GASTROPARESIS:

Normal Gastric Emptying:

The proximal stomach serves as the reservoir of food, and the distal stomach as the grinder. The physical nature, particle size, and fat and caloric content of food determine its emptying rate Non-nutrient liquids empty rapidly; the rate is fastest when there is a large volume. If there are increased calories in the liquid phase of the meal, emptying is relatively constant over time, with a maximum rate of 200 kcal per hour[8]. Solids are initially retained in the stomach and undergo churning while antral contractions propel particles toward the closed pylorus. Food particles are emptied once they have been broken down to approximately 2 mm in diameter. Thus, solids empty during two phases over 3 to 4 hours: an initial lag period (during which retention occurs), followed by a phase of relatively constant emptying. Glucose-regulating hormones are released when food arrives in different regions of the gut. Glucagon and incretins (e.g., amylin and glucagon-like peptide 1) retard gastric emptying, allowing for the delivery of food at a rate that facilitates digestion and controls postprandial glycaemia [9-11].

Impaired Gastric Emptying in Patients with Diabetes:

Diabetic Gastroparesis affects about 40% of patients with type 1 diabetes and up to 30% of patients with type 2 diabetes, especially those with long-standing disease. Both symptomatic and asymptomatic DGP seem to be associated with poor glycemic control by causing a mismatch between the action of insulin (or an oral hypoglycemic drug) and the absorption of nutrients. Diabetic Gastroparesis does not appear to be associated with an increased risk of death, however[11].In patients with diabetic Gastroparesis, mechanisms are changed, largely leads to the neuropathy affecting the vagus, reductions in the numbers of intrinsic inhibitory neurons that are critical for motor coordination and numbers of pacemaker cells the interstitial cells of Cajal**(ICCS**),and hormonal changes (e.g., increased glucagon levels[1]. Gastric enteric neurons are decreased in numbers of cell bodies are processes are shortened. These neurons are surrounded by an Immune infiltrate composed primilarly of type 2 macrophages, suggesting a role for the immune system and carbon monoxide in the pathogenesis of diabetic gastroparesis. The circular and longitudinal smooth muscle layers are normal or have very mild fibrosis [12,13].

COMPLICATIONS:

Complications of gastroparesis include esophagitis; Mallory-Weiss tear from chronic nausea and vomiting, malnutrition, volume depletion with acute renal failure, electrolyte disturbances, and bezoar formation [14].

AIMS & OBJECTIVES:

AIM:

- To know how effectively does the prokinetics work when strictly lifestyle modifications are followed in diabetes mellitus induced gastroparesis

OBJECTIVE:

- To study the demographic details and social history of diabetic induced gastropathy patients and need of the prokinetic agent.
- To find out how effective the prokinetic works in DM patient
- To evaluate and compare the effectiveness of each prokinetic agent with lifestyle modifications and without the lifestyle modifications.

MATERIALS & METHODS:

Inclusion criteria:

- Patients who are diabetic.[both Type-I and Type-II]
- Patients who are suffering from diabetic induced gastroperisis
- Patients who are prescribed with prokinetic agents

- Patients of adult ages i.e.25-55
- Patients who comply to participate in the study with a written informed consent.

Exclusion criteria:

- Patients not willing to participate in the study.
- Children, elderly patients i.e. above60yrs.
- Patients who previously undergone GI surgeries
- Patients with other comorbidities
- Patients with GERD, Peptic Ulcers, Gastritis.
- Patients who do not receive any Prokinetic agent.

MEASUREMENT OF GASTROPARESIS

A patient-based instrument called the gastroparesis cardinal symptom index (GCSI) has been developed to assess the severity of gastroparesis. The GCSI index is based on 3 symptom subscales 1.Nausea/vomiting [nausea, vomiting, retching's] 2.Postprandial fullness [not able to finish full meals, stomach fullness, loss of appetite, feeling excessively after meals] 2.Bloating[bloating, belly visible extremely large] of a larger upper gastrointestinal disorders–symptom severity index that was previously developed. These 3 scales were selected as part of the GCSI because they assess common symptoms related to gastroparesis-nausea/vomiting, postprandial fullness/early satiety, and bloating. The GCSI is used to rate symptom change by either the physician or the patient over a 2-6 week recall period. The scale was mention below (table 1) [15.16].

This questionnaire asks you about the severity of symptoms you may have related to your gastrointestinal problem. There is no right or wrong answers. Please answer each question as accurately as possible. For each symptom, please circle the number that best describes how severe the symptom has been during the past 2 -6 weeks. If you have not experienced this symptom, circle 0. If the symptom has been very mild, circle 1. If the symptom has been mild, circle 2. If it has been moderate, circle 3. If it has been severe, circle 4. If it has been very severe, circle 5. Please be sure to answer every question. [17]Such a daily diary can aid patients who may have difficulty with remembering symptoms over a 2-6 week recall period.

RESULTS & DISCUSSION:

Total no of patients who enrolled into the study was 30 members. The 3 prokinetics are given according to the clinician prescription.20 patients were administrated with itopride (150mg) where as another 10 patients were administrated with levosulpiride (25mg) and acotinamide (100mg) of 5 each. We also included the drug such as itopride because of its less hepatic impairment, cardio vascular The patients who are using these 3 drugs are confirms to have gastroparesis by their endoscopy report. These 3 drugs were administered for a period of six-weeks. At the end of sixth week, 9 patients are seen to be recovered out of which 5 from itopride and 2 from levosulpiride and another 2 from acotinamide. And 21patients remained unchanged. As given in the table 2.

GCSI for nausea symptom:

The following symptoms were compared between before treatment of prokinetics and after 6 weeks treatment of prokinetics, with each symptom subscale. In which mild includes of no symptom. Whereasmoderate describe the symptom score from 1-3 which persists for month and severe describe symptom score of 4 and 5.as represented in table 3.

GCSI score for stomach fullness:

The following symptoms were compared between before treatment of prokinetics and after 6 weeks treatment of prokinetics, with each symptom subscale. In which mild includes of no symptom. Whereas moderate describe the symptom score from 1-3 which persists for month and severe describe symptom score of 4 and 5. As given in table 5.

GCSI score for Bloating:

The following symptoms were compared between before treatment of prokinetics and after 6 weeks treatment of prokinetics, with each symptom subscale. In which mild includes of no symptom. Whereas moderate describe the symptom score from 1-3 which persists for month and severe describe symptom score of 4 and 5. As given in table 7.

Table 1. Gastroparesis Cardinal Symptom Index (GCSI): 9 Symptoms of Gastroparesis Are Graded by the Patient According to Their Severity over the Prior 2-6 Weeks.

Symptoms	None	Very mild	Mild	Moderate	Severe	Very severe
1. Nausea (feeling sick to your stomach as if you were going to vomit or throw up)	0	1	2	3	4	5
2. Retching (heaving as ifto vomit, but nothing comesup	0	1	2	3	4	5
3.vomiting	0	1	2	3	4	5
4.stomach full ness	0	1	2	3	4	5
5. Not able to finish a normal-sized meal	0	1	2	3	4	5

6. Feeling excessively full after meals	0	1	2	3	4	5
7. Loss of appetite	0	1	2	3	4	5
8. Bloating (feeling like you need to loosen your clothes)	0	1	2	3	4	5
9. belly visible large.	0	1	2	3	4	5

Table 2: Total No of Patients Who Used Drugs

Type of drug	No of patients relived	No of patients unchanged
Itiopride	5	15
Acotinamide	2	3
Levosulpride	2	3
TOTAL	9	21

Table 3: GCSI Score for Nausea Before and After Treatment

nausea/vomiting	no of patients before treatment	Percentage	no of patients after treatment	Percentage
Mild	0	0	6	20
Moderate	11	36.67	10	33.33
Severe	19	63.33	14	46.67
Total	30	100	30	100

Table 4: Paired difference values

		Paired Differences					T	Df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	nv_before_treatment - nv_after_treatment	.067	.450	.082	-.101	.235	.812	29	.00423

Table 5: GCSI Score for Stomach Fullness Before and After the Treatment.

stomach fullness	no of patients before treatment	Percentage	no of patients after treatment	Percentage
Mild	3	10	17	56.67
Moderate	4	13.33	9	30
Table Severe	23	76.67	4	13.33
TOTAL	30	100	30	100

6: Paired Samples Test for stomachfullness before and after treatment

		Paired Differences					T	Df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	stoamachfullness_before_treatment - stomachfullness_after_treatment	.167	.747	.136	-.112	.445	1.223	29	.00231

Tab.7GCSI Scores for Bloating Before And After Treatment

Bloating	no of patients before treatment	Percentage	no of patients after treatment	Percentage
Mild	1	3.33	14	46.67
Moderate	12	40	8	26.67

Severe	17	56.67	8	26.67
TOTAL	30	100	30	100

Table 8. Paired Samples Test for bloating before and after treatment

		Paired Differences					t	Df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	bloating_before_treatment - bloating_after_treatment	.333	.606	.111	.107	.560	3.010	29	.005

Fig. 1: no of people and no of patients sufferedThe mean comparision between before and after treatment of nausea was found to be significant P <0.05. Tab.5.6.nausea before and after treatment.

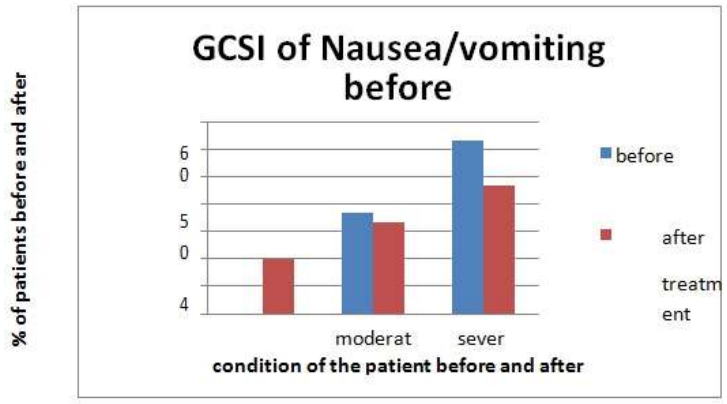


Fig 2. percentage people and no of patients suffered

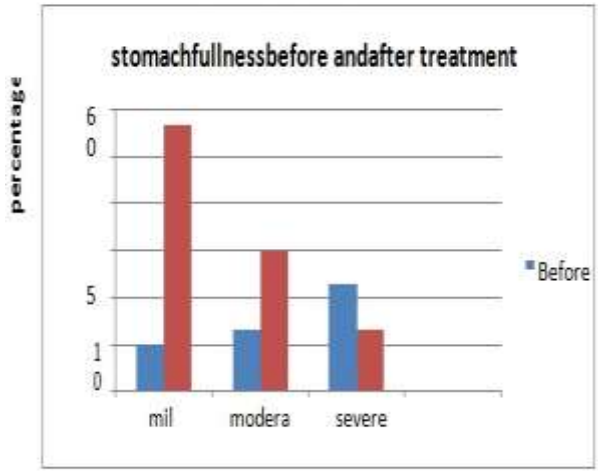
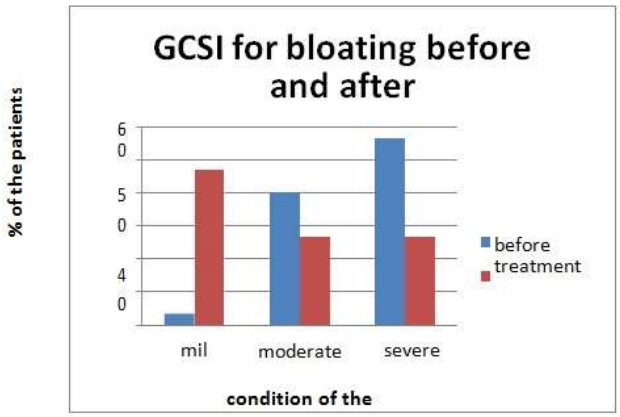


Fig. 3: percentage people and no of patients suffered.



The mean comparision between before and after treatment of nausea was found to be significant P = 0.05

CONCLUSION:

The findings of this study indicate that the GCSI is a reliable and validinstrument formeasuring symptom severity in patients withgastroparesis. The patients who used prokinetics named itopride,levosulpiride, acotinamide who diagnosed with diabetic gastroparesisshowed significant improvement in the symptoms.

REFERENCES

1. Holtman G, Talley N, lievregts, et al. (2006) A Placebo controlled trial of Itopride on functional Dyspepsia. *NEngl Jmed.*, 354, 832-840.

2. Tsuchihara M, Suga T, Nurashima Y, et al. (1993) Therapeutic effect of Itopride Hydrochoride for upper abdominal digestive symptoms associated with chronic Gastrities. *Medical construction and new remedies*, 30(11);2125-2131.
3. Kim YS, Kim TH, Choi CS, et al. (2005) Effect of itopride A new Prokinetic, in patients with mild GERD-A pilot study. *World J Gastroenterol.*, 11(27), 4210-4214.
4. NortitakeM, Kikuchi Y, Ohtsubo T, et al. (1997) Effect of itiopride Hydrochloride on diabetic gastroparesis. *Clinical report*, 31(8), 2787-2791.
5. Talley NJ, Stanghellini V, Heading RC, Koch KL, Malagelada J-R, Tytgat GN. (1999) Functional gastroduodenal disorders. *Gut*, 45(suppl II), S37–S42
6. Talley NJ, Silverstein MD, Agre´us L, Nyren O, Sonnenberg A, Holtmann G. (1998) AGA technical review: evaluation of dyspepsia. *Gastroenterology*, 11, 582–595.
7. Mearin F, Cucala M, Azpiroz F, Malagelada JR. (1991) The origin of symptoms on the brain-gut axis in functional dyspepsia. *Gastroenterology*, 101, 999–1006.
8. Bennet EJ, Beaurepaire J, Langeluddecke P, Kellow J, Tennant C. (1991) Life stress and non-ulcer dyspepsia: a case control study. *J Psychosom Res*, 35, 579–590.
9. Bennet EJ, Piesse C, Palmer K, Badcock CA, Tennant CC, Kellow JE. (1998) Functional gastrointestinal disorders: psychological, social, and somatic features. *Gut*, 42, 414–420.
10. Tack J, Caenepeel P, Fischler B, Piessevaux H, and Janssens J. (2001) Hypersensitivity to gastric distention is associated with symptoms in functional dyspepsia. *Gastroenterology*, 121, 526–535.
11. Stanghellini V, Tosetti C, Paternico A, Barbara G, Morselli- Labate AM, Monetti N, Marengo M, Corinaldesi R. (1996) Risk indicators of delayed gastric emptying of solids in patients with functional dyspepsia. *Gastroenterology*, 110, 036–1042.
12. Talley NJ, Meineche-Schmidt V, Pare P, Duckworth M, Raisanen P, Pap A, Kordecki H, Schmid V. (1998) Efficacy of omeprazol in functional dyspepsia: double-blind, randomised, placebo- controlled trials (the Bond and Opera studies). *Aliment PharmacolTher*, 12,1055–1065.
13. Bytzer P. (2002) H_2 Receptor antagonists and prokinetics in dyspepsia: a critical review. Gut 2002; 50(supplIV):S58–S62.
14. Allescher HD, Bo¨ckenhoff A, Knapp G, Wienbeck M, Hartung J. (2001) Treatment of non-ulcer dyspepsia: a meta-analysis of placebo controlled prospective studies. *Scand J Gastroenterol*, 36, 934–941.
15. Moayyedi P, Soo S, Deeks J, Delaney B, Innes M, Forman D. () Pharmacological interventions for non-ulcer dyspepsia. *Cochrane Database Syst Rev*, 1.2003
16. Finney JS, Kinnersley N, Hughes M, OBryan-Tear CG, Lothian J. (1998) Meta-analysis of antisecretory and gastrokinetic compounds in functional dyspepsia. *J ClinGastroenterol*, 36, 312–320.
Veldhuyzen van Zanten SJO, Jones MJ, Verlinden M, Talley NJ. (2001) Efficacy of cisapride and domperidone in functional(nonulcer) dyspepsia: a meta-analysis. *Am J Gastroenterol*, 96, 689– 696?

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