J Nut Res (2016) 4(1):85-87
ISSN: 2348-1064

PPI & Prokinetics - Boon for Diabetic Gastroparesis

Parveen Malhotra*, Naveen Malhotra, Vani Malhotra, Aman Gupta, Pansi Gupta Ajay Chugh, Abhishek Chaturvedi, Parul Chandrika

Received: 03 August 2015 / Received in revised form: 05 February 2016, Accepted: 31 May 2016
Published online: 26 June 2016;

Abstract

Diabetes is one of the common causes of gastroparesis, with data suggesting that approximately 5 to 12% patients with diabetes have symptoms consistent with gastroparesis. A 60-year-old male, who was a known diabetic for last 20 years and had been on regular oral hypoglycemic, presented with complaints of early satiety, bloating, and abdominal distension for last 10 years on and off. He was being treated with proton pump inhibitors (PPIs) for long duration but without any substantial relief. In terms of biochemical parameters, patient was seen to be having uncontrolled glucose levels both in fasting and postprandial levels. The patient was diagnosed to be suffering from diabetic Gastroparesis and his oral hypoglycemic agents were changed so that his glucose levels were controlled. Further, to manage gastrointestinal symptoms and underlying gastroparesis due to which patient was symptomatic, he was put on combination of PPI (pantoprazole) plus levosulpiride 75 mg per day.

Keywords: Non-alcoholic fatty liver disease, Liver fibrosis, Liver biopsy, Diabetes Mellitus, Metabolic Syndrome

Introduction

Diabetes is one of the common causes of gastroparesis, with data suggesting that approximately 5 to 12% patients with diabetes have symptoms consistent with gastroparesis. The clinical condition of DG is characterized by upper gastrointestinal (GI) dyspeptic symptoms (including nausea, vomiting, bloating, early satiety, etc) in association with delayed gastric emptying. Postprandial fullness and abdominal or epigastric pain can also be present in DG. Importantly, DG may tend to persist despite amelioration of glycaemic control, and causes considerable morbidity and suffering to the patient. Though earlier thought to be occurring only in type 1 diabetes, DG is now seen more frequently in type 2 diabetes (Kashyap & Farrugia 2010; Shakil et al. 2008; Camilleri et al. 2011).

Parveen Malhotra*, Naveen Malhotra, Vani Malhotra, Aman Gupta, Pansi Gupta Ajay Chugh, Abhishek Chaturvedi, Parul Chandrika

Department of Medical Gastroenterology, Medicine, Gynae. & Obstetrics, Anesthesiology, Surgery & Pathology PGIMS Rohtak – 124001, Haryana

*Email: drparveenmalhotra@yahoo.com

Even though a wide range of dyspeptic symptoms are seen in patients with gastroparesis, abdominal bloating, and postprandial fullness are reliable predictors and are linked to delay emptying in DG. Managing DG requires a multidisciplinary approach, with emphasis on prevention and improved blood glucose control (Abrahamsson 2007).

Case report

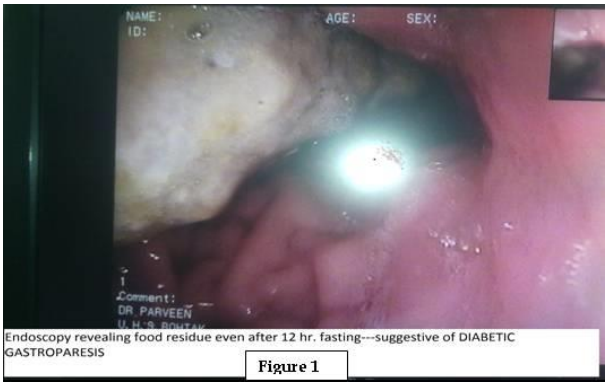
A 60-year-old male, who was a known diabetic for last 20 years and had been on regular oral hypoglycemic, presented with complaints of early satiety, bloating, and abdominal distension for last 10 years on and off. He was being treated with proton pump inhibitors (PPIs) for long duration but without any substantial relief. Her was diagnosed as a patient of diabetes 26 years back and was on oral hypoglycemic though he never took any insulin injections. It was ten years back when he started having gastrointestinal upsets and consulted various doctors, but his condition had not been managed satisfactorily. His compliance with oral hypoglycemic was not good. He had been treated with proton pump inhibitors (PPIs) for several years but did not get satisfactory relief. He had been advised lifestyle modifications in terms of diet and physical activity for diabetes, but patient never cared about it and was never compliant with it. He is a non-smoker but takes alcohol on and off though not regularly. Patient has a family history of diabetes. His father had diabetes, and had expired at an age of 68 yrs. after some kidney related complications, possibly renal failure. His General and systemic examination was found to be essentially normal.

On evaluation, his routine hematological results were normal. In terms of biochemical parameters, patient was seen to be having uncontrolled glucose levels both in fasting and postprandial levels. HbA1C levels were also high suggesting patient was not maintaining within normal glucose levels in past 3 months. Liver function tests revealed raised transaminases levels. Serum triglycerides and LDL cholesterol levels were also high. Kidney parameters were, however, normal.

Table 1. Biochemical Parameters

Random plasma glucose	196 mg/dL
Fasting plasma glucose	134 mg/dL
Postprandial plasma glucose	242 mg/dL
HbA1C	8.0
Serum triglycerides	278 mg/dL
High-density lipoprotein cholesterol (HDL-C)	38 mg/dL
Low density lipoprotein cholesterol (LDL-C)	208 mg/dL
Total cholesterol	262 mg/dL
ALT	90
AST	80
Blood urea nitrogen	34 mg/dL
Serum creatinine	1.0 mg%

Viral screening for hepatitis and HIV was done (HBsAg, Anti HCV, and Anti HIV), but came out to be negative**.** Ultrasonogram of abdomen revealed grade 1 fatty liver. Upper G.I. endoscopy revealed changes of diabetic gastroparesis i.e. presence of food in stomach even after 12 hours of fasting (Figure 1)



Endoscopy revealing food residue even after 12 hr. fasting---suggestive of DIABETIC GASTROPARESIS

Figure 1

Diagnosis & Management

The patient was diagnosed to be suffering from Diabetic Gastroparesis and his oral hypoglycemic agents were changed so that his glucose levels were controlled. Further, to manage gastrointestinal symptoms and underlying gastroparesis due to which patient was symptomatic, he was put on combination of PPI (pantoprazole) plus levosulpiride 75 mg per day

Clinical course and follow up

Patient responded well to therapy and within one month duration, he showed significant improvement. His blood sugar came under control and all his symptoms related to diabetic gastroparesis massively improved. The patient was being maintained on pantoprazole plus levosulpiride combination for next 3 months. Even after stopping the treatment, the patient has been asymptomatic, and no gastrointestinal symptoms have been seen. In terms of diabetes control, patient is maintaining normal blood glucose on oral hypoglycemic agents. Patient was asked to come for monthly follow-up or if and when any gastrointestinal symptoms come back. Patient was advised to meet a diabetologist and diet counselor (dietician) to keep his blood sugar levels under control, through lifestyle modifications and oral hypoglycemic agents.

Discussion

Pharmacologically, proton pump inhibitors (PPIs) are advocated to relieve dyspeptic symptoms of nausea, bloating, vomiting, and pain. PPIs like pantoprazole have shown to effectively manage dyspeptic symptoms in DG. The role of Prokinetics (like levosulpiride) is extremely useful in managing delayed gastric emptying associated with DG and is considered mainstay treatment. Prokinetics not only stimulate peristalsis and improve delayed emptying by influencing antral contractility, rhythm, and antroduodenal coordination, but also help in glycaemia control. Hence, use of Prokinetics is advantageous in patients of DG even in the absence of significant symptom relief (Kashyap & Farrugia 2010; Aljarallah 2011). Pantoprazole has good efficacy in managing dyspeptic symptoms and is effective and well tolerated both in children as well as elderly. Improved quality of life (QoL) and high satisfaction levels has been shown with pantoprazole in dyspeptic patients. Pantoprazole has advantageous safety-tolerability, as it appears to be safest of all PPIs with lowest risk of hepatic-based interactions. A study evaluated pantoprazole in combination with 5HT4 agonist (itopride; a prokinetic) in DG, and demonstrated good efficacy of the combination therapy in managing dyspeptic symptoms (nausea, vomiting, early satiety, bloating, postprandial fullness, and regurgitation). Therapy was rated good to excellent, with significant improvement in severity as well as frequency of all symptoms (Venkatesh & Kulkarni 2008).

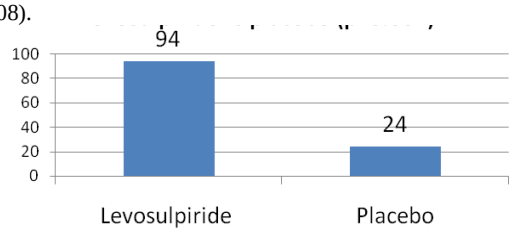


Figure 2: Signifiannntly higher reduction in gastric emptying time (in min) seen with levosulpiride vs placebo ($p<0.0010$.

Levosulpiride (a dopamine antagonist) helps in DG by its prokinetic action and manages DG by accelerating gastric emptying. Studies demonstrated that prokinetic levosulpiride (25 mg three times a day) is as effective as 5HT4 receptor agonists in relieving nausea/vomiting in gastroparesis. A study evaluating levosulpiride in DG patients, demonstrated levosulpiride to significantly reduce gastric emptying time (from 416 to 322 min) as compared to placebo where not much change much was observed (396 *vs.* 372 min) ($p<0.001$) (Fig. 2). Levosulpiride demonstrated an accelerating effect on gastric emptying and effectively relieved dyspeptic symptoms in DG patients with slow gastric emptying time. Levosulpiride also helped achieve better blood glucose control by reduction of gastric emptying time (Mansi et al. 1995).

Comparative efficacy of Prokinetics (levosulpiride with 5HT4 agonist) on dyspeptic symptoms and gastric emptying rates in patients with functional dyspepsia and delayed gastric emptying was studied. Levosulpiride demonstrated similar efficacy to 5HT4 agonist in significantly shortening gastric emptying time ($P<0.001$). Further, levosulpiride was significantly more effective ($P<0.01$) than 5HT4 agonist in improving patient's everyday activities (QoL parameters) and individual symptoms such as nausea, vomiting and early postprandial satiety. Side effect profile was similar with both medications (Mansi et al. 2000).

Summary and Conclusion

Levosulpiride is a useful agent in DG and should be used in addition to PPIs in managing associated dyspeptic symptoms (nausea, vomiting, bloating, postprandial fullness and early satiety), along with delayed gastric motility. As we could see

that the patient was earlier not responding to PPI alone, but addition of prokinetic, levosulpiride, led to amelioration of symptoms associated with delayed gastric emptying. However, apart from symptomatic control, pharmacological management of DG also includes effective glycemic control and needs emphasis. A combination of PPI and prokinetic is advantageous in managing DG; as was seen in this patient in which levosulpiride was used in combination with pantoprazole. Reports of similar success in managing DG with pantoprazole with levosulpiride have also come from various other researchers-clinicians.

References

Abrahamsson H. Treatment options for patients with severe gastroparesis. *Gut.* 2007 June; 56(6): 877–883

Aljarallah BM. Management of diabetic gastroparesis. *Saudi J Gastroenterol.* 2011 Mar-Apr;17(2):97-10

Camilleri M, Bharucha AE, Farrugia G. Epidemiology, mechanisms, and management of diabetic gastroparesis. *Clin Gastroenterol Hepatol.* 2011 Jan;9(1):5-12

Kashyap P, Farrugia G. Diabetic gastroparesis: what we have learned and had to unlearn in the past 5 years. *Gut.* 2010 Dec; 59(12):1716-1726.

Mansi C, Borro P, Giacomini M, *et al.* Comparative effects of levosulpiride and cisapride on gastric emptying and symptoms in patients with functional dyspepsia and gastroparesis. *Aliment Pharmacol Ther.* 2000 May; 14(5):561-569.

Mansi C, Savarino V, Vigneri S. Gastro kinetic effects of levosulpiride in dyspeptic patients with diabetic gastroparesis. *Am J Gastroenterol.* 1995 Nov; 90(11):1989-1993.

Shakil A, Church RJ, Rao SS. Gastrointestinal complications of diabetes. *Am Fam Physician.* 2008 Jun 15; 77(12):1697-1702.

Venkatesh V, Kulkarni KP. Itopride and pantoprazole outcomes in diabetic gastroparesis trial (IPOD trial). *J Indian Med Assoc.* 2008 Dec; 106(12):814-815.