ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 16, Issue 1, 2023

Online - 2455-3891
Print - 0974-2441

Research Article

ROLE OF ORAL PANCREATIC ENZYME SUPPLEMENTATION IN PANCREATIC EXOCRINE DEFICIENCY

HITENDRA DESAI[1], ALPESH PATEL[2]*

[1]Department of Surgery, New Civil Hospital, B.J. Medical College, Ahmedabad, Gujarat, India. [2]Department of Pharmacology, Dr. Kiran C. Patel Medical College, Bharuch, Gujarat, India. Email: dr_alpeshpatel@yahoo.co.in

Received: 10 November 2022, Revised and Accepted: 15 December 2022

ABSTRACT

Objectives: The present study was carried out to study the role of oral pancreatic enzyme supplementation in pancreatic exocrine deficiency.

Methods: This study included 50 consecutive cases of pancreatic exocrine deficiency. Diagnosis of pancreatic exocrine deficiency was made based on history, clinical examination, and contrast-enhanced computed tomography findings. Each patient was supplied with oral pancreatic enzyme supplements. Each patient was followed up for 1 year with three visits (3 months, 6 months, and 12 months) to assess changes in clinical features of pancreatic exocrine deficiency, change in nutritional status of the patient, and compliance with therapy.

Results: At first follow-up visit (3 months), abdominal discomfort reduced in 17 previously symptomatic patients. Mean stool frequency reduced from 3.18 per day to 2.34 per day. Stool consistency improved with only 18 patients (36%) having liquid consistency stool in comparison to 76% at the time of initial presentation. Average body mass index (BMI) improved from baseline value of 20.648 kg/sqm to 20.674 kg/sqm. Average hemoglobin improved from 10.40 g/dL to 10.52 g/dL and average serum albumin remained static at 3.0 g/dL. At second follow-up visit (6 months), abdominal discomfort reduced in 20 previously symptomatic patients. Mean stool frequency reduced from 3.18 per day (primary survey) to 1.7 per day. Stool consistency improved with only 12 patients (24%) having liquid consistency stool in comparison to 76% at the time of initial presentation. Average BMI improved from baseline value of 20.648 kg/sqm to 21.062 kg/sqm. Average hemoglobin improved from 10.40 g/dL to 10.69 g/dL and average serum albumin improved from 3.0 g/dL at primary survey to 3.1 g/dL. At third follow-up visit (12 months), abdominal discomfort reduced in 30 previously symptomatic patients. Mean stool frequency reduced from 3.18 per day (primary survey) to 1.6 per day. Stool consistency improved with only 9 patients (18%) having liquid consistency stool in comparison to 76% at the time of initial presentation. Average BMI improved from baseline value of 20.648 kg/sqm to 21.402 kg/sqm. Average hemoglobin improved from 10.40 g/dL to 10.76 g/dL and average serum albumin improved from 3.0 g/dL at primary survey to 3.3 g/dL.

Conclusion: In follow-up visits, there was an improvement in symptoms over 12 months. Abdominal discomfort and stool frequency reduced. Stool consistency improved. Nutritional parameters showed statistically significant improvement. Mean BMI of the study sample, mean hemoglobin, and serum albumin increased. The study provides rationale for using these clinical symptoms as surrogate markers for the efficacy of Pancreatic Enzyme Replacement Therapy in patients with pancreatic exocrine insufficiency.

Keywords: Oral pancreatic enzyme supplementation, Pancreatic exocrine deficiency, Pancreatitis.

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INTRODUCTION

The pancreatic juice plays a pivotal role in the digestion and absorption of nutrients. Pancreatic exocrine insufficiency (PEI) can be defined as reduction in pancreatic enzyme activity in the intestinal lumen to a level that is below the threshold required to maintain normal digestion. Patients with untreated PEI not only suffer from impaired quality of life due to steatorrhea, weight loss, abdominal discomfort, and other PEI-related symptoms but are also highly likely to develop deficiencies of micronutrients and lipid-soluble vitamins.[1]

Evaluation of exocrine deficiency of pancreas requires complex, tedious, and expensive laboratory evaluation or invasive techniques which are not practically feasible and are expensive. Clinical evaluation with respect to symptomatology and overall nutritional status has been used as alternative ways to determine the role of pancreatic enzyme supplementation in patients expected to have exocrine deficiency based on radiological imaging of the pancreas.

METHODS

The study population consisted of all in patients and out patients of department of general surgery. This study consisted of 50 consecutive cases. Diagnosis of pancreatic exocrine deficiency was made based on history, examination, and contrast-enhanced computed tomography (CECT) findings. Inclusion criteria were patients with symptoms of pancreatic exocrine deficiency with the previous history of at least one episode of acute pancreatitis, patients with computed tomography (CT) finding suggestive of chronic pancreatitis with dilated main pancreatic duct ductal or parenchymal calcification or parenchyma atrophy, patients of acute pancreatitis with CISI > and 10, after resolution of the acute phase, age more than 18 years, patients fulfilling the above, and consenting to be part of the study. Exclusion criteria were hemodynamically unstable patients, patients during active phase of acute pancreatitis, patients who have undergone operative intervention for chronic pancreatitis, age <18 years, and patients not consenting or complying to the study.

Approval of ethics committee was obtained for this study. In this study, each patient was evaluated for clinical features of pancreatic exocrine deficiency at the first visit. Nutritional status of the patient, anemia, hypoalbuminemia, and symptomatology were considered surrogate markers of malabsorption due to exocrine deficiency. Each patient was then supplied with oral pancreatic enzyme supplements (standardized at one tablet of Pankreatoflat (15000 lipase units) per meal, averaging thrice daily). Each patient was followed up for a period of 1 year. Analysis of collected data was performed using student T test for quantitative data and Chi-square test for qualitative data.

During primary survey, patients demographic details, symptoms related to malabsorption, history of weight loss, previous attack of acute pancreatitis, history of diabetes mellitus, history of alcohol intake, awareness of the disease, and knowledge about oral enzyme supplementation were documented. Baseline parameters of nutritional status, body mass index (BMI), abdominal examination, hemoglobin, blood sugar, renal function, liver function, amylase, lipase (to exclude active inflammatory state), and albumin was documented. CECT scan was performed as part of institute protocol in all patients of acute/chronic pancreatitis. Pancreatic duct dilatation, duct calculi, parenchymal calcification, or atrophy were documented in chronic pancreatitis in acute pancreatitis, modified CT severity index (CTSI) developed by Balthazar was noted to include those with CTSI >8/10 as exocrine deficient.

During follow-up survey, each patient was followed up for a period of 1 year at intervals of 3 months, 6 months, and 12 months. At each follow-up visit, the symptoms of malabsorption, compliance to oral enzyme therapy, persisting alcohol consumption, number of hospital visits, or admissions were tabulated The general outlook of the patient and BMI was noted. Hemoglobin and serum albumin were evaluated and compared to the previous visits.

RESULTS

Overall, the patients were mostly male with a mean age of 41.7 years, ranging from youngest age of 18 years to the eldest at 79 years (Table 1). The major symptoms were abdominal discomfort, flatulence, increased stool frequency, liquid stool consistency (diarrhoea/steatorrhea), and weight loss (Table 2).

Thirty patients had past history of severe acute pancreatitis requiring hospital admission for at least a week. Confirmation included documents showing an increased serum level of amylase and lipase at the time of admission with a CECT of the abdomen confirming the diagnosis CT severity index (CTSI) (Balthazar index) more than eight were considered to have a severely depleted exocrine pancreas and were considered for the study to be exocrine deficient. Twenty patients had no such history of any acute episode, but presented with symptoms of maldigestion and on evaluation were diagnosed with chronic pancreatitis based on CECT findings of a dilated main pancreatic duct, intraductal calcifications, parenchymal calcifications, or parenchymal atrophy. About 60% of patients had a documented past history of severe acute pancreatitis, 40% ofpatients had no such history, 6 patients (12%) had been diagnosed to have diabetes mellitus and were on either oral hypoglycemic drugs or subcutaneous insulin therapy. One patient (2%) had history of auto immune disease.

The average BMI of the study sample was 20.64 kg/sqm (SD 2.65). Eighteen patients (36%) were poorly nourished with 7 patients (14%) showing signs of muscle wasting. Twenty-two patients (44%) were averagely nourished whereas only 10 (20%) were well nourished.

Pallor was noted in 10 patients (20%) and pitting pedal edema was noted in 13 patients (26%). Both these signs are characteristic of nutritional deficiency.

Mean hemoglobin in the study population was 10.4 g/dL. Sixteen patients (32%) had a baseline hemoglobin of <10 g/dL with the lowest being 6.8 g/dL. Mean serum albumin in the study sample was 3.0 g/dL lower than the normal limits, suggesting a state of chronic malnutrition. Total leukocyte count, renal function, and liver function tests were done to rule out patients with altered parameters as they would interfere with the study.

Serum amylase and lipase were done in all patients to rule out a state of acute inflammation of the pancreas. Random blood sugar was done in all patients. Six patients (12%) had readings above 200 mg/dL, suggestive of diabetes mellitus. Eighteen patients (24%) had blood sugar readings between 140 and 200 mg/dL suggestive of impaired glucose tolerance or pre-diabetic stage.

CECT abdomen was the standard investigation performed in all patients to diagnose acute severe pancreatitis and chronic pancreatitis with findings resulting in pancreatic exocrine deficiency.

During first follow-up visit at 3 months, abdominal discomfort reduced in 17 previously symptomatic patients though it persisted in 32 patients. Mean stool frequency reduced from 3.18 per day to 2.34 per day. Stool consistency improved, with only 18 patients (36%) having liquid consistency stool in comparison to 76% at time of initial presentation. Average BMI improved from baseline value of 20.648 kg/sq m to 20.674 kg/sq m. Average hemoglobin improved from 10.40 g/dL to 10.52 g/dL and average serum albumin remained static at 3.0 g/dL. During second follow-up visit at 6 months, abdominal discomfort reduced in 20 previously symptomatic patients though it in 27 patients. Mean stool frequency reduced from 3.18 per day (primary survey) to 1.7 per day. Stool consistency improved, with only 12 patients (24%) having liquid consistency stool in comparison to 76% at time of initial presentation. Average BMI improved from baseline value of 20.648 kg/sq m to 21.062 kg/sq m. Average hemoglobin improved from 10.40 g/dL to 10.69 g/dL and average serum albumin improved from 3.0 g/dL at primary survey to 3.1 g/dL. During third follow-up visit at 12 months, abdominal discomfort reduced in 30 previously symptomatic patients though it persisted in 17 patients. Mean stool frequency reduced from 3.18 per day (primary survey) to 1.6 per day. Stool consistency improved, with only 9 patients (18%) having liquid consistency stool in comparison to 76% at time of initial presentation. Average BMI improved from baseline value of 20.648 kg/sqm to 21.402 kg/sqm. Average hemoglobin improved from 10.40 g/dL to 10.76 g/dL and average serum albumin improved from 3.0 g/dl at primary survey to 3.3 g/dl.

DISCUSSION

In patients with CP, PEI begins when pancreatic exocrine secretion impaired by approximately 60 or more and clinically significant symptoms usually occur when pancreatic exocrine secretion is impaired approximately 90%. Maldigestion in patients with PEI results in clinical symptoms. Exocrine pancreatic insufficiency from CP results in decreased quality of life and increased morbidity and mortality.

All the methods involved in the evaluation of pancreatic exocrine deficiency are cumbersome, tedious, difficult to comply with, and expensive. The clinical diagnosis is based on symptoms, laboratory markers of malnutrition, and imaging showing destruction of pancreatic acini. The treatment of pancreatic exocrine deficiency is pancreatic enzyme replacement therapy (PERT).

In this study, the patient's symptoms improving over the course of the year with the use of enzyme supplementation. Abdominal discomfort in the form of dull aching pains, dyspepsia, bloating, and flatulence was the most common symptom. With therapy, this reduced significantly which is also reported in the study by Barkin and Barkin [2]. The number of patients with liquid stool reduced from 38 to 18 in the first 3 months, to further improve to just nine patients at the end of 12 months of PERT Conversely, the proportion of patients with normal stool consistency increased from nine patients to 41 over the course of 12 months, maximally increased in the first 3 months from 9 to 31 patients. This trend of improvement in stool consistency is also reported in a study by Gubergrits *et al*. [3] and Creon 10 trial by Safdi *et al*. [4]. There was a significant impact of PERT on stool frequency. The mean stool frequency average reduced from 3.18 per day to 16 per day. The results of our analysis are in accordance with an earlier report by Safdi *et al*.

Nutritional parameters were evaluated as a measure to assess improvement in digestion by the study design which included lifestyle modification, diet modification, pancreatic enzyme supplementation treatment compliance, and follow-up. Nutritional markers evaluated were BMI, hemoglobin, and serum albumin. The study sample showed that with compliant treatment to proposed protocol, patients improved in weight and thus BMI. The number of under nourished patients

reduced with more patients settling at the average nourishments status toward the end of the study period of 12 months. Hemoglobin and serum albumin are good indicators of nutritional status of the patient. Both parameters showed a stable increase in value over the course of 12 months. In the analysis of data involving follow-up visits at 6 months and 12 months, gain in BMI, increase in hemoglobin, and serum albumin levels were all statistically significant with $p<0.05$.

The study shows that patients symptoms improve in the first 3 months in terms of reduced abdominal discomfort, reduced stool frequencies, and improved stool consistency, though nutritional markers do not show statistically significant improvement over time, as noted in follow-up at 6 and 12 months, patients nutritional status also improved in terms of BMI hemoglobin and serum albumin values. Similarly in a randomized double-blind, placebo-controlled, and international study comparing two doses of pancrelipase (140.000 U/d vs. 35,000 U/d Zenpep. Allergan USA Inc, Irvine, Calif) with placebo in 72 patients, Toskes *et al*. [5] found significant increases in body weight and BMI and improvements in stool consistency, flatulence, and abdominal pain, which again support our findings. Our findings also provide further evidence supporting the United European Gastroenterology evidence-based guidelines by Dominguez-Munoz *et al*. [6] for the therapy of CP and the talian consensus guidelines for the management of CP by Frulloni *et al*. [7].

CONCLUSION

The presenting complaints were abdominal discomfort, increased stool frequency, liquid stool consistency, and weight loss. CECT abdomen showed sequence of acute pancreatitis with CTSI of 8 or more according to Balthazar scoring system in 30 patients. In those with chronic pancreatitis, CECT abdomen had findings of dilated MPD in 19 patients with average diameter of 6.7 mm, MPD calculus in eight patients, parenchymal calcification in six patients, and parenchymal atrophy in 17 patients. In follow-up visits, there was an improvement in symptoms over 12 months. Abdominal discomfort reduced from 47 patients to 17 patients. Stool consistency improved in 58% of subjects. Stool frequency reduced from 3.18 per day to 1.6 per day. Nutritional parameters showed statistically significant improvement. Mean BMI of the study sample increased from 20.64 kg/sqm to 21.40 kg/sqm. Mean hemoglobin increased from 10.4 g/dL to 10.76 g/dL. Serum albumin increased from 3.0 g/dL to 3.3 g/dL. The study provides rationale for using these clinical symptoms as surrogate markers for the efficacy of PERT in patients with PEI.

AUTHORS' CONTRIBUTION

Preparation of manuscript, literature search, and review of literature.

CONFLICTS OF INTEREST

Nil.

AUTHOR'S FUNDING

Nil.

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