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Original Research Article

The Effect of Oral Pancreatic Enzyme Supplementation on the Course and Outcome of Pancreatic Exocrine Deficiency

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Abstract:

Background: 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 also high likely to develop deficiencies in micronutrients and lipid-soluble vitamins.

Objective: The present study is done to diagnose the exocrine deficiency of pancreas with various means and effect of oral pancreatic enzyme supplementation on the course and outcome in the patients with PEI.

Methods: The study population consisted of all inpatients and outpatients of Department of General Surgery, Civil Hospital, Ahmedabad attached to B.J. Medical College. This study consisted of 50 consecutive cases who met the criteria for exocrine deficiency of pancreas. Diagnosis of PEI was made on basis of history, examination, laboratory and CECT findings. Each patient was supplemented with oral pancreatic enzyme supplements and was followed up for a period of 1 year with three visits – 3 months, 6 months and 12 months. At each visit, the patients were evaluated to assess changes in clinical features of PEI, changes in nutritional status and compliance with therapy.

Results: In our study the patients were mostly males (74%) with age group ranging from 18-79 years. Most common etiology being higher intake of alcohol and majority of patients with symptoms like abdominal discomfort (94%), flatulence, increased stool frequency >2 per day (78%) with liquid consistency (diarrhea/ steatorrhea) (76%) and weight loss (86%). The average BMI of study sample at the time of diagnosis is 20.64 kg/sq m (SD 2.65) which improved to 21.402 kg/sq m at the end of study. Mean hemoglobin of study sample improved from 10.4 g/dl (SD 1.54) to 10.76 g/dl and average serum albumin had improved from 3.0 g/dl (SD 0.44) at primary survey to 3.3 g/dl at the end of study. CECT done in patients with severe acute pancreatitis with CTSI >8/10 had multiple etiologies causing significant destruction of pancreatic acini resulting in PEI. Laboratory and radiological findings also correlated with clinical features of exocrine deficiency of pancreas. Upon supply of oral pancreatic enzyme supplementation there is a significant improvement in overall clinical conditions of patients with PEI.

Conclusion: The clinical, laboratory and radiological parameters will help in diagnosis, detecting the extent of disease process and helps in understanding the patients with PEI and their response to treatment with the therapy. In the present study, significant statistical correlation is found with the clinical outcome in terms of improvement in abdominal discomfort, weight gain, stool consistency, BMI and hematological parameters in patients using oral enzyme supplements. Oral pancreatic enzyme replacement therapy (PERT) has a significant role in improving the symptomatic conditions in patients with PEI.

Keywords: pancreatic exocrine insufficiency (PEI), Oral pancreatic enzyme replacement therapy (PERT).

Introduction

Pancreatic secretion contains multiple enzymes for digesting all of three major types of food: proteins,

carbohydrates, and fats [1]. They play a pivotal role in digestion and absorption of nutrients. The pancreatic juice consists of bicarbonate and water secreted by ductal cells and several enzymes, secreted by acinar cells, with the specific capacity to digest proteins, carbohydrates and fats. Pancreatic exocrine insufficiency (PEI) can be defined as a 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. Evaluation of exocrine deficiency of pancreas requires complex, tedious and expensive laboratory evaluations which include fecal elastase, 13 C mixed triglyceride breath test, fecal fat estimation or invasive techniques directly evaluating pancreatic juices aspirated from the duodenum. These tests are not practically feasible and are expensive. Clinical evaluation with respect to symptomatology and overall nutritional status have 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.

Aims and Objectives

1. To study the etiology, pathogenesis, severity indices and complications of pancreatitis.
2. To study exocrine deficiency of pancreas.
3. To study diagnosis modalities to establish pancreatic exocrine deficiency.
4. To study the effects of oral pancreatic enzyme supplementation on the course and outcome of pancreatic exocrine deficiency.

Materials and Methods

The study population consisted of all inpatients and outpatients of Department of General surgery, civil hospital, Ahmedabad. The study consisted of 50 consecutive cases. Diagnosis of pancreatic exocrine deficiency was made on basis of history, examination, laboratory and CECT findings.

Inclusion Criteria

1. All patients with symptoms of pancreatic exocrine deficiency, with previous history of at least one episode of acute pancreatitis.
2. All patients with CT findings suggestive of chronic pancreatitis with dilated main pancreatic duct, ductal or parenchymal calcification or parenchymal atrophy.
3. All patients of acute pancreatitis with CTSI > 8/10, after resolution of the acute phase.
4. Age more than 18 years.

Exclusion Criteria

1. Hemodynamically unstable patients.
2. All those patients during active phase of acute pancreatitis.
3. All those patients who have undergone operative intervention for chronic pancreatitis.
4. Age less than 18 years.

Methodology

In this study, data was taken from Civil Hospital, Ahmedabad attached to B.J. Medical College and each patient was evaluated for clinical features of pancreatic exocrine deficiency at the first visit. Data regarding patient's symptoms relevant to pancreatic exocrine deficiency diagnosis was collected. 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 (15000 lipase units) per meal, averaging thrice daily). Each patient was then followed up for a period of 1 year with three visits - 3 months, 6 months and 12 months. At each follow up visit, the patient was evaluated to assess changes in clinical features of pancreatic exocrine deficiency, change in nutritional status of the patient and compliance with therapy. All data thus collected was tabulated in Microsoft Excel and graphically represented. Analysis of collected data was performed using student T test for quantitative data and chi square test for qualitative data.

Primary Survey

Patient's 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, BMI, abdominal examination, hemoglobin, blood sugar, renal function, liver function, amylase, lipase (to exclude active inflammatory state) and albumin was documented. Contrast enhanced CT 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 developed by Balthazar was noted to include those with CTSI >8/10 as exocrine deficient.

Follow-up Study

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 are tabulated. Those with excessive alcohol intake, hospital admissions for pancreatitis or unrelated causes (more than 2) were excluded from the study. The general outlook of the patient and BMI were noted. Hemoglobin and serum albumin were evaluated and compared to previous visits.

Observations and Results

Table 1: Sex distribution of study sample

Sex	Number of cases	Percentage
Male	37	74%
Female	13	26%

In our study, overall the patients mostly males male (74%), 37 patients were male and 13 patients were female with a mean age of 41.7 years, ranging from youngest age of 18 years to the eldest at 79 years. The higher numbers in males can probably be attributed to higher intake of alcohol in males, which is one of the most common etiologies of chronic pancreatitis and exocrine deficiency.

Table 2: Age distribution

Age	Number of patients	Percentage
18-30	11	22
30-40	18	36
40-60	14	28
60 & above	7	14

Majority of the study population belongs to the age group 18-30 and 30-40 years which is the young population. This population is the one on who both the younger and older population depends on, and a morbidity in this population makes the entire society crippled.

Table 3: The presenting complaint

Presenting complaint	Number of patients	Percentage
Abdominal discomfort	47	94
Stool frequency (>2per day)	39	78
Stool consistency (Liquid)	38	76
Weight loss	43	86

The major symptoms that brought the patients to the health care centre were abdominal discomfort, flatulence, increased stool frequency, liquid stool consistency (diarrhea/ steatorrhea) and weight loss. Mean stool frequency in the study sample at time of initial evaluation was 3.18 per day. The consistency was relatively liquid type 6 or 7 (according to Bristol stool chart) in 38 patients (76%).

30 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. CTSI (Balthazar index) > 8 were considered to have a severely depleted exocrine pancreas and were considered for the study to be exocrine deficient. 20 patients had no such history of any acute episode, but presented with symptoms of maldigestion and upon evaluation were diagnosed with Chronic Pancreatitis based on CECT findings of a dilated main pancreatic duct, intraductal calcifications, parenchymal calcifications or parenchymal atrophy. 60% patients (blue) had a documented past history of severe acute pancreatitis, 40% patients (red) 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. 1 patient (2%) had history of autoimmune disease. Rest of the study population did not have history of any autoimmune disease in the patient or in the family.

Lifestyle Pattern

26 patients (52%) consumed a regular vegetarian diet, whereas 24 patients (48%) consumed a mixed Indian diet. Due to disease, 28 patients (56%) had a reduced appetite compared to previous disease-free time period. This was attributed to abdominal complaints and feeling of ill-health by the patients. 22 patients though had normal appetite and were comfortable during diet despite the abdominal complaints.

Examination

The average BMI of the study sample was 20.64 kg/sq m (SD 2.65). This shows that the study sample had lower BMI in comparison to the general population. Visibly, 18 patients (36%) were poorly nourished with 7 patients (14%) showing signs of muscle wasting. 22 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. Per abdomen examination showed no signs of acute inflammatory state or features of peritonitis.

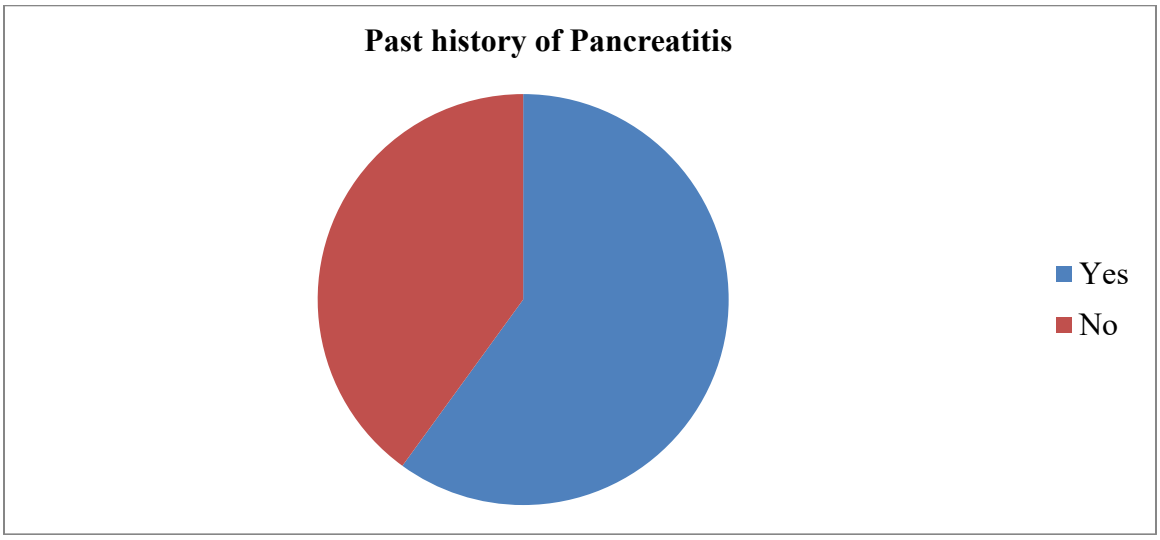

Figure 1: Past history of pancreatitis

The Blood Picture

Mean hemoglobin in the study population was 10.4 g/dL (SD 1.54), depicting an overall anemic study sample. 16 patients (32%) had a baseline hemoglobin of less than 10 g/dL with the lowest being 6.8 g/dL. Mean serum albumin in the study sample was 3.0 g/dL (SD 0.44), 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. Those with values three times above upper limit of normal were excluded from the study. Random blood sugar was done in all patients. 6 patients (12%) had readings above 200 mg/dL, suggestive of diabetes mellitus. 18 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. Those who were followed up as sequelae of acute severe pancreatitis had a Balthazar CTSI of 8 or more. The findings included parenchymal necrosis, multiple intra and peripancreatic fluidcollections suggestive of significant destruction of pancreatic acini resulting in pancreatic exocrine deficiency. In those with chronic pancreatitis, CECT showed the following findings of a dilated pancreatic duct intermixed with strictures with an average duct diameter of 6.7mm in 19 patients. Intraductal calculi were noted in 8 patients, parenchymal calcifications in 6 patients and parenchymal atrophy in 17 patients. All these findings depicted acinar injury with fibrosis resulting in pancreatic exocrine deficiency.

The first follow-up visit – at 3 months

Abdominal discomfort had reduced in 17 previously symptomatic patientsthough it persisted in 32 patients. Mean stool frequency had reduced from 3.18 per day to 2.34 per day. Stool consistency had improved, with only 18patients (36%) having liquid consistency stool in comparison to 76% at time of initial presentation. Average BMI had improved from baseline value of 20.648 kg/sq m to 20.674 kg/sq m. Average hemoglobin had improved from 10.40 g/dL to 10.52 g/dL and average serum albumin remained static at 3.0 g/dL.

The second follow-up visit– at 6 months

Abdominal discomfort had reduced in 20 previously symptomatic patients though it persisted in 27 patients. Mean stool frequency had reduced from3.18 per day (primary survey) to 1.7 per day. Stool consistency had improved, with only 12 patients (24%) having liquid consistency stool in comparison to 76%

at time of initial presentation. Average BMI had improved from baseline value of 20.648 kg/sq m to21.062 kg/sq m. Average hemoglobin had improved from 10.40 g/dL to 10.69 g/dL and average serum albumin had improved from 3.0 g/dL at primary survey to 3.1 g/dL.

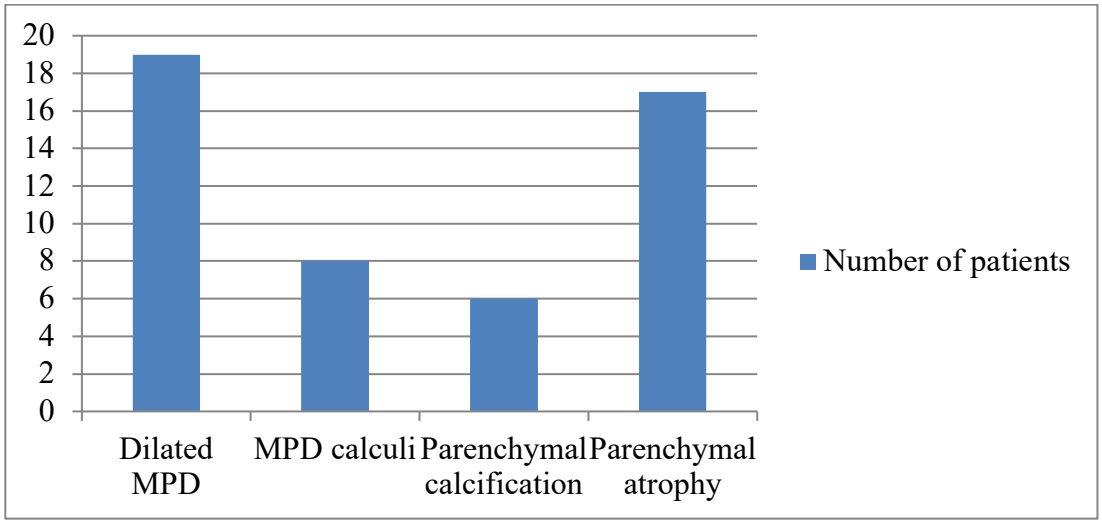

Figure 2: Imaging Results

The third follow-up visit– at 12 months

Abdominal discomfort had reduced in 30 previously symptomatic patients though it persisted in 17 patients. Mean stool frequency had reduced from 3.18 per day (primary survey) to 1.6 per day. Stool consistency had improved, with only 9 patients (18%) having liquid consistency stool in comparison to 76% at time of initial presentation. Average BMI had improved from baseline value of 20.648 kg/sq m to 21.402 kg/sq m. Average hemoglobin had improved from 10.40 g/dL to 10.76 g/dL and average serum albumin had 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 is impaired by approximately 60% or more, and clinically significant symptoms usually occur when pancreatic exocrine secretion is impaired by approximately 90%. Maldigestion in patients with PEI results in clinical symptoms such as increased stool frequency, changes in stool consistency, abdominal cramping, bloating, increased flatulence, abdominal pain often leading to sitophobia, and nutritional sequelae such as malnutrition, micronutrient deficiencies, and weight loss. These symptoms and signs occur secondary to maldigestion of ingested fats, carbohydrates, and proteins. Exocrine pancreatic insufficiency from CP results in decreased quality of life and increased morbidity and mortality. Evaluation of pancreatic exocrine deficiency can be done by direct and indirect means. All the methods involved in the evaluation are cumbersome, tedious, difficult to comply with and expensive. The clinical diagnosis is based on symptoms, laboratory markers of malnutrition including those for fat soluble vitamins (A, D, E and K), stool markers and imaging showing destruction of pancreatic acini [2]. Stool markers include coefficient of fecal fat and mean stool fat, evaluation of which is a tedious process. Patient compliance is very difficult, and the process is cumbersome. Hence these were not included in the study. The treatment of pancreatic exocrine deficiency is Pancreatic Enzyme Replacement Therapy (PERT). The questions that remain unanswered are how we can gauge the dose of PERT in correcting maldigestion and whether adequate supplementation is associated with changes in clinical symptoms of stool frequency and stool consistency, relief of abdominal pain, and decreased flatulence. Having effective answers to these questions will ultimately support a clinical determinant of the correct PERT dose to meet the clinical and nutritional needs of the patient. To date, the approach of relying solely on clinical symptoms for decision making regarding the adequacy and efficacy of PERT in CP remains controversial [3].

Symptoms of the study sample

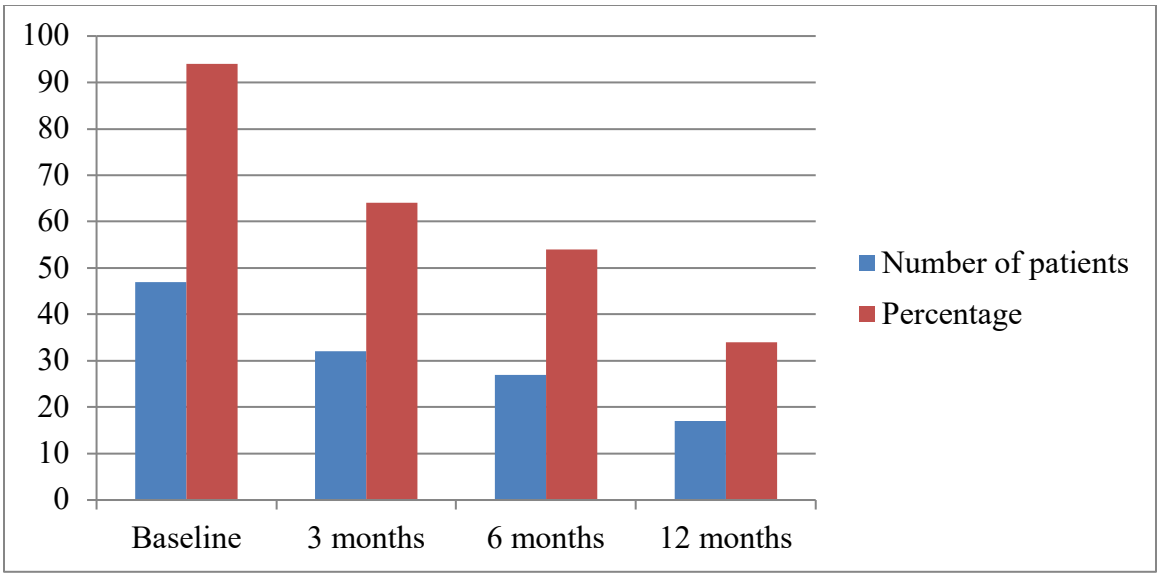

Figure 3: Decreasing trend of abdominal discomfort following PERT

In this study, one can note that 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. At the start of the study, 47 of the 50 patients had this symptom. With therapy, this reduced significantly to 32 patients (64%) at 3 months, 27 patients (54%) at 6 months and was limited to 17 patients (34%) at the end of the study period at 12 months. In a study by N Gubergrits et al [4], 6-month open label clinical trial, the percentage of subjects who reported no abdominal pain increased from 37.3% at baseline to 66% at the end. Improvement in abdominal pain was noted in 21 of the 47 subjects, though 5 of the 47 subjects reported worsening of pain.

In a study by Barkin et al [2], a 52 week follow up study, abdominal pain/ discomfort was noted to in 66% of subjects at the baseline and improving to 44% at 1 week and was limited to 19% subjects in 6 months.

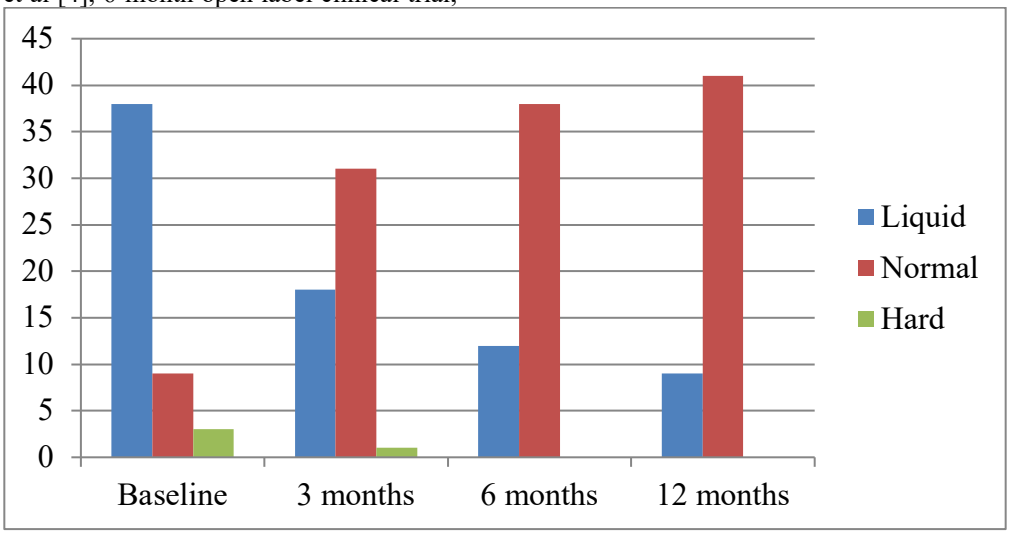

Figure 4: Stool consistency of study sample

The number of patients with liquid stool reduced from 38 to 18 in the first three months, to further improve to just 9 patients at the end of 12 months of PERT. Conversely, the proportion of patients with normal stool consistency increased from 9 patients to 41 over the course of 12 months, maximally increased in the first three months from 9 to 31 patients. In a study by N Gubergrits et al [4], 6 month

open label clinical trial, stool consistency improved from 21.6% subjects passing normal or solid stool at baseline to 61.8% subjects at 6 months. In Creon 10 trial by Safdi et al [5], stool consistency improved in 7 of the 13 subjects over a 2 week trial period.

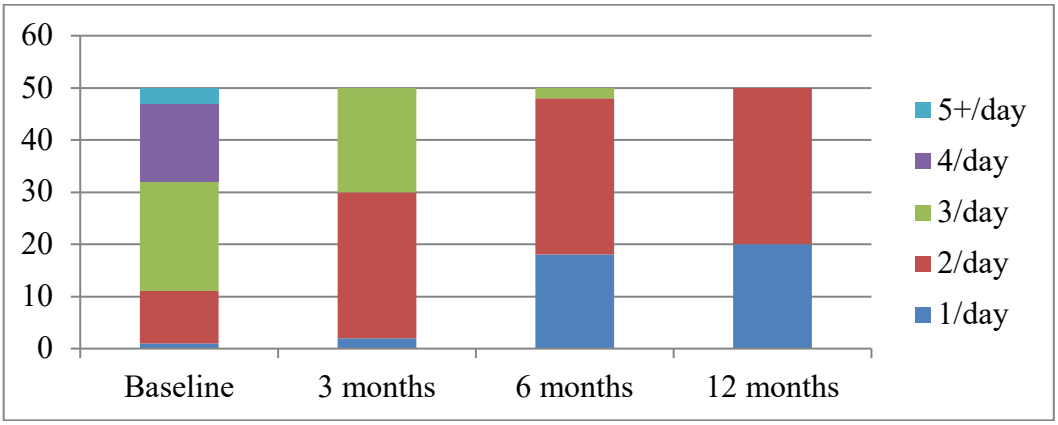

Figure 5: Stool frequency of study sample

With respect to the next symptom of stool frequency, there was a significant impact of PERT. The mean stool frequency average reduced from 3.18 per day to 1.6 per day. The distribution of stool frequencies is depicted in fig 5, which shows the trend of reducing stool frequency to 1 or 2 bowel movements per day. P value was significant (less than 0.05) at all three follow up visits. The results of our analysis presented here are in accordance with an earlier report by Safdi et al [5]. In a 2-week, randomized, double-blind study comparing pancrelipase (40,000 U with each meal) with placebo in 26 patients with CP, they found a significant decrease in stool frequency from 10.8 during placebo run in to 5.2 stools per day during double blind treatment in those receiving pancrelipase versus placebo. In a study by N Gubergrits et al [4], 6 month open label clinical trial, mean stool frequency at baseline was 2.8 per day. It improved to 2.1 per day at 3 months and 1.8 per day at the end of 6 months. In a study by Barkin et al [2] a 52 week follow up study, the mean stool frequency at baseline was 2.9 per day improving to 2.6 at the end of 1 week. On 52 week follow up, the mean stool frequency was 1.7 per day.

Table 4: Nutritional parameters during study period

Time	BMI Mean (SD)	HemoglobinMean (SD)	Albumin Mean (SD)
Baseline	20.64 (2.65)	10.4 (1.54)	3.0 (0.44)
3 months	20.67 (2.48)	10.52 (1.38)	3.0 (0.34)
6 months	21.06 (2.38)	10.69 (1.24)	3.1 (0.31)
12 months	21.4 (2.26)	10.76 (1.20)	3.3 (0.26)

Nutritional markers evaluated were, Body Mass Index (BMI), Hemoglobin, Serum albumin. 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.

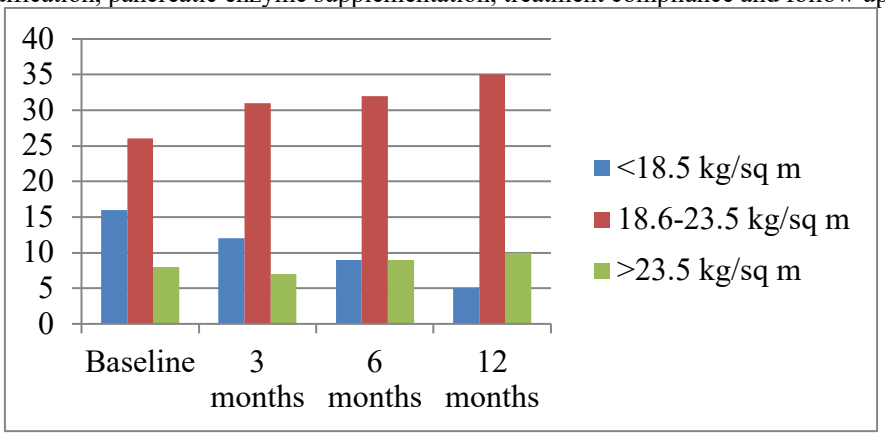

Figure 6: BMI of study sample

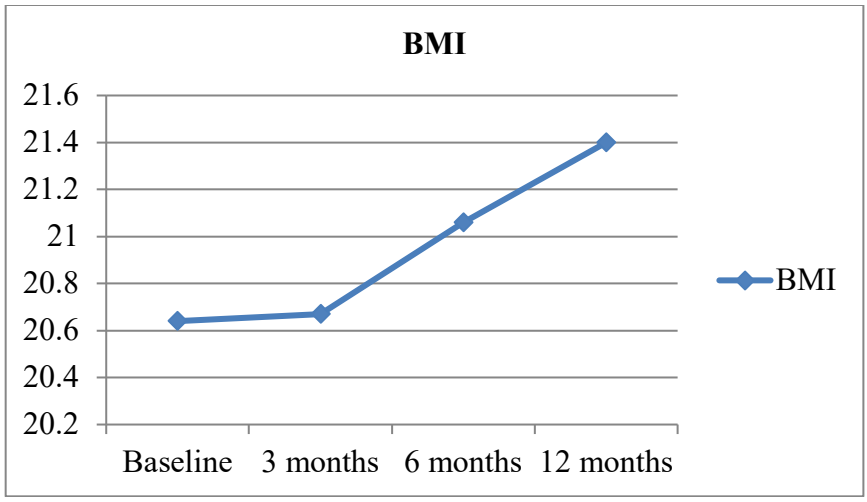

Figure 7: Mean BMI of study sample

Body mass index was analyzed and grouped in three categories <18.5 kg/ sq m = undernourished status, 18.6 - 23.5 kg/sq m = average nourishment status, > 23.5 kg/sq m = good nourishment status. 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 towards the end of the study period of 12 months.

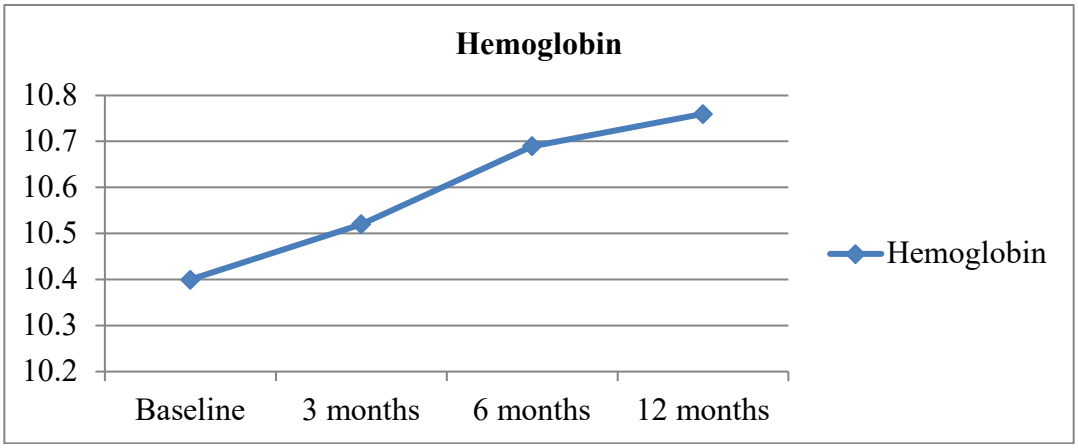

Figure 8: Mean Hemoglobin of study sample

Mean Hemoglobin of the study sample at the start of the study was 10.4 g/dL and increased to 10.76 g/ dL at the end of the study period.

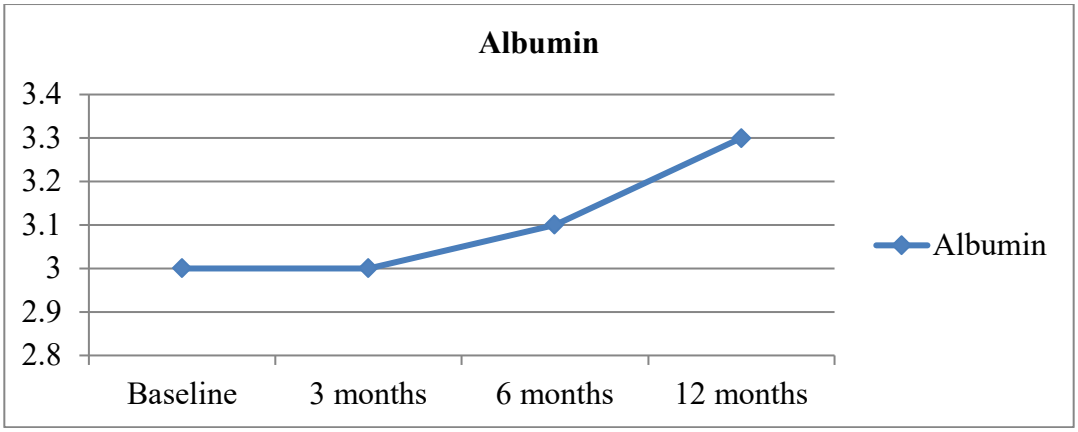

Figure 9: Mean serum Albumin of study sample

Mean serum albumin of the study sample increased from a baseline value of 3g/ dL to 3.3 g/dL at the of the study period of 12 months. Gain in BMI at the end of 3 months was not statistically significant, (p value 0.58) similar to rise in hemoglobin (p value 0.15) or rise in serum albumin levels (p value 0.26).
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 values less than 0.05. The study shows that patients symptoms improve in the first three 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, patient's nutritional status also improved in terms of BMI, hemoglobin and serum albumin values.

Similarly, in a randomized, double-blind, placebo-controlled, international study comparing 2 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 [6] found significant increases in body weight and body mass index and improvements in stool consistency, flatulence, and abdominal pain, which again support our findings. The gain in weight over a period of 3 weeks was 0.38kg, corresponding to a rise in BMI of 0.13 kg/sq m at the low dose in comparison to a weight gain on 0.5 kg, equivalent to a rise in BMI of 0.16 kg/sq m. In the study by N Gubergrits et al [4], mean BMI of 78 patients improved from baseline value of 22.8 kg/ sq m to 23.1 kg/ sq m over a period of 6 months. Our findings are also in agreement with those of the meta-analysis by de la Iglesia-Garcia et al [7]. They reported on a total of 511 patients from 17 studies and found that PERT reduced fecal fat excretion and fecal weight. In addition, PERT reduced abdominal pain, especially at doses comparable to those used in our study, which showed a trend toward greater efficacy. Our findings are also in agreement with those of the meta-analysis by de la Iglesia-Garcia et al [7].

They reported on a total of 511 patients from 17 studies and found that PERT reduced fecal fat excretion and fecal weight. In addition, PERT reduced abdominal pain, especially at doses comparable to those used in our study, which showed a trend toward greater efficacy. It is worth noting that studies also exists that report no significant effects of PERT on stool frequency in patients with PEI or that symptom improvement may occur independently of changes in CFA. In a 1986 study of 10 patients with CP and diarrhea, Armbrecht et al [8] found a significant reduction in fecal fat excretion, but a nonsignificant decrease in daily bowel movements after PERT (mean, 3.16 during placebo period vs 2.32 after therapy). Suarez et al [9] examined the effects of pancreatic supplementation on gastrointestinal symptoms after a high-fat meal in healthy subjects. Although no changes were observed in stool frequency, significant improvement in bloating was reported, suggesting symptom reduction occurred independently of changes in fat assimilation in subjects with normal pancreatic function. However the measure of bloating is subjective in nature, whereas stool frequency provides an objective assessment of gastrointestinal symptoms and likely represents a more reliable surrogate marker for clinical improvement in patients with CP and PEI. In addition, all of these small studies are more than 20 years old and were conducted before the approval of any standardized PERT formulations, so any inferences should be drawn cautiously. Our findings also provide further evidence supporting the United European Gastroenterology evidence-based guidelines by Dominguez-Munoz et al [10] for the therapy of CP and the Italian consensus guidelines for the management of CP by Frulloni et al [11].

Conclusion

The mean age of the study sample was 41.7 years (ranging 18 years to 79 years) with a gender distribution of 74% male predominance. The bulk of the sample belonged to age group 18-40 years. The presenting complains were abdominal discomfort (94%), increased stool frequency (78%) with average 3.18 bowel movements per day, liquid stool consistency (76%) and weight loss (86%). 30 patients had a documented previous attack of acute pancreatitis with CTSI > 8/10 requiring hospital admission. 20 patients had no acute episode but had features of chronic pancreatitis on CECT with symptoms of maldigestion. 28 patients (56%) had reduced appetite and poor oral intake. On examination, the average BMI was 20.64 kg/ sq m with 14% subjects having signs of muscle wasting, 20% subjects having pallor and 26% having malnutrition related pitting pedal edema. Mean Hemoglobin of the study sample was 10.4 g/dL with 32% subjects having hemoglobin less than 10 g/ dL. Mean serum albumin level was 3g /dL, which is lower than lower limit of normal. In those with chronic pancreatitis, CECT abdomen had findings of dilated MPD in 19 patients with average diameter of 6.7mm; MPD calculus in 8 patients, parenchymal calcification in 6 patients and parenchymal atrophy in 17 patients. In the 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% subjects, stool frequency reduced from 3.18 per day to 1.6 per day. Nutritional parameters also showed statistically significant improvement. Mean BMI of the study sample in-

creased from20.64 kg/ sq m to 21.40 kg/ sq m ($p<0.05$). Mean Hemoglobin increased from 10.4 g/ dL to 10.76 g/dL ($p< 0.05$) and serum albumin increased from 3.0 g/dL to 3.3 g/dL ($p< 0.05$) over the course of 12 months. The study provides the rationale for using these clinical symptoms as surrogate markers for the efficacy of PERT in patients with PEI.

Ethical approval: The study was approved by the Institutional Ethics Committee

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