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Original article

Enzigest - An Effective and Safe Therapeutic Option for Symptomatic and Supportive Management of Exocrine pancreatic insufficiency

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Abstract

Background: *Exocrine pancreatic insufficiency (EPI) is characterized by reduced pancreatic enzyme activity, leading to fat malabsorption, nutritional deficiencies, and gastrointestinal (GI) disturbances. Pancreatic enzyme replacement therapy (PERT) is the standard of care. Enzigest™ (pancreatin 10000 minimicrospheres) is a newer PERT formulation designed for symptomatic and supportive management of EPI.*

Purpose: *This study evaluated the real-world effectiveness and safety of Enzigest™ in patients with EPI presenting with GI complaints.*

Materials and Methods: *A multicenter, interventional study was conducted across 46 outpatient clinics in India, enrolling 460 adult patients with symptoms suggestive of EPI. Enzigest™ was prescribed before meals for 30 days. Primary outcomes included changes in GI symptom severity, while secondary outcomes assessed health-related quality of life (HRQOL). Statistical analysis was performed at a 5% significance level.*

Results: *Treatment with Enzigest™ led to significant improvement in GI symptoms. Reductions were observed in abdominal pain (83.4%), nausea (84.2%), vomiting (86.1%), epigastric pain (76.4%), early satiety (79.6%), acidity (76.3%), and diarrhea (77.9%) (all $p < 0.001$). HRQOL measures also improved, including reductions in emotional distress (28.5%), sleep disturbance (35.2%), and work absenteeism (40.7%). Enzigest™ was well tolerated, with no major adverse events reported.*

Conclusion: *Enzigest™ demonstrated robust clinical effectiveness and safety in routine practice, offering significant symptom relief and improved quality of life for patients with EPI. These findings support its role as a valuable therapeutic option in the symptomatic and supportive management of EPI.*

Keywords: *Exocrine Pancreatic Insufficiency, Pancreatic Enzyme Replacement Therapy, Pancreatin Minimicrospheres, Gastrointestinal Symptom Relief*

Introduction

Exocrine pancreatic insufficiency (EPI) is a condition characterized by a reduction in pancreatic enzyme activity—primarily pancreatic lipase—in the intestinal lumen to levels below those required for normal digestion. This deficiency may arise from various mechanisms, including inadequate pancreatic stimulation, impaired secretion by pancreatic acinar cells, obstruction of pancreatic ducts, or defective mixing of enzymes with chyme in the intestine.[1] Patients with EPI commonly experience steatorrhea, flatulence, weight loss, and abdominal discomfort of varying severity and location. These symptoms reflect fat malabsorption and nutritional deficiencies. Beyond digestive

issues, EPI significantly impairs quality of life and is associated with increased risk of malnutrition-related complications, including bone demineralization and heightened mortality risk.[1]

EPI is prevalent in approximately 60% to 90% of patients with chronic pancreatitis (CP) within 10 to 12 years of disease onset.[1] Chronic pancreatitis itself affects an estimated 42 to 73 individuals per 100,000 in the United States and is considered the leading cause of EPI. In Asian populations such as Japan, China, and India, the prevalence ranges from 36 to 125 per 100,000.[1] Chronic pancreatitis is a progressive fibro-inflammatory disease of the pancreas marked by irreversible acinar cell damage and fibrosis. It accounts for most EPI cases in adults. Symptoms of EPI, such as steatorrhea and nutritional deficiencies, typically appear 5–10 years after CP diagnosis.[2]

In children, the most common cause of EPI is cystic fibrosis. CFTR gene mutations lead to thick secretions that obstruct pancreatic ducts, causing progressive acinar damage. Most infants with CF are exocrine-insufficient at birth and require lifelong pancreatic enzyme replacement therapy (PERT) along with high-fat nutritional support to maintain growth and survival.[2] EPI can also occur after acute pancreatitis, especially in necrotizing or alcoholic pancreatitis. The prevalence of EPI post-acute pancreatitis varies from 19% in mild to 33% in severe cases and results from necrosis, ductal obstruction, or impaired enzyme secretion.[2]

Pancreatic resections frequently lead to EPI due to parenchymal loss and altered gastrointestinal anatomy. Postoperative EPI rates can be as high as 94%, depending on the type and extent of surgery.[2] Gastrectomy is another surgical condition that may induce EPI by disrupting enzyme release and activation. Post-surgical patients often develop steatorrhea and benefit significantly from PERT.[3]

Other causes of EPI include diabetes mellitus, celiac disease, inflammatory bowel disease, bariatric surgery, HIV/AIDS, and various genetic and congenital disorders[1]. Toxic-metabolic factors, such as chronic alcohol consumption, smoking, hypercalcemia, hyperlipidemia, and chronic kidney disease, also contribute to the pathogenesis of pancreatic insufficiency[1]. Idiopathic cases represent approximately 25% of EPI diagnoses and are increasingly linked to underlying genetic mutations.[1]

Drug-induced EPI has been reported in rare instances, with furosemide being one of the implicated agents. The mechanism is not fully understood but may involve pancreatic hypoperfusion due to diuresis or an immunologic hypersensitivity reaction.[4]

Importantly, not all causes act via the same pathophysiological mechanisms. While CP, CF, pancreatic tumors, and resections cause direct acinar loss, other conditions such as periampullary tumors, small bowel inflammation, or post-gastrectomy changes may impair pancreatic stimulation or synchronization of enzyme secretion.[5]

Pancreatic enzyme replacement therapy (PERT) is the mainstay of treatment for EPI and is associated with improved fat absorption, symptom relief, quality of life, and even survival.[5] Modern PERT formulations typically consist of enteric-coated porcine-derived pancrelipase, which remains effective even in patients without overt symptoms of maldigestion.[6]

Materials and Methods

An interventional, real-world evidence study was conducted across 46 outpatient clinics, where patients were followed up for one month. The study was approved by institutional review board and adhered to the ethical principles. Adults over 18 years of age presenting with one or more of the following symptoms—abdominal pain, acidity, diarrhea, nausea, or dyspepsia (based on ROME III criteria)—were considered eligible. These individuals had a clinical history of gallstones, hypertriglyceridemia, alcohol consumption, use of diuretics (Furosemide or Thiazide), or prior abdominal surgery. Patients were excluded if they had a history of substance abuse, were pregnant or lactating, had any severe illness, or were otherwise deemed unfit for the study. Written informed consent was obtained from all participants prior to screening. The study product, Enzigest™10000 (manufactured by Wallace Pharmaceuticals Pvt Ltd), was prescribed to be taken before each meal for a duration of one month. Participants were instructed to refrain from using any Ayurvedic, herbal, homeopathic dietary supplements, or alternative therapies during the treatment period, and any concurrent medications were documented.

The primary outcome measures included assessment of gastrointestinal symptoms at baseline and at the end of 30 days of treatment. Health-related quality of life (HRQOL) was evaluated as a secondary outcome at both the beginning and conclusion of therapy. A sample size of 460 patients across 46 centers was deemed appropriate for assessing both effectiveness and tolerability. Statistical analysis included the use of the Chi square test to evaluate treatment efficacy, while

demographic data were analyzed using descriptive statistics. All statistical tests were conducted at a 5% level of significance.

Results

Parameters	n (no of patients)	Percentage (%)
Gender: Male	339	73.7
Female	121	26.3
Gallstones	207	45
Alcohol Consumption	232	50.4
Use of Diuretics	97	21.1
Hypertriglyceridemia	141	30.7
Undergone Abdominal Surgery	110	23.9
Any concomitant Medications	24	5.2

Table 1: Baseline Demographic Details

Table 1: Among 460 patients with exocrine pancreatic insufficiency, 73.7% were male and 26.3% were female. Alcohol consumption was observed in 50.4%, gallstones in 45%, hypertriglyceridemia in 30.7%, history of abdominal surgery in 23.9%, and diuretic use in 21.1%. Concomitant medication use was reported in 5.2%. Alcohol and gallstones were the most common risk factors.

Primary Outcomes:

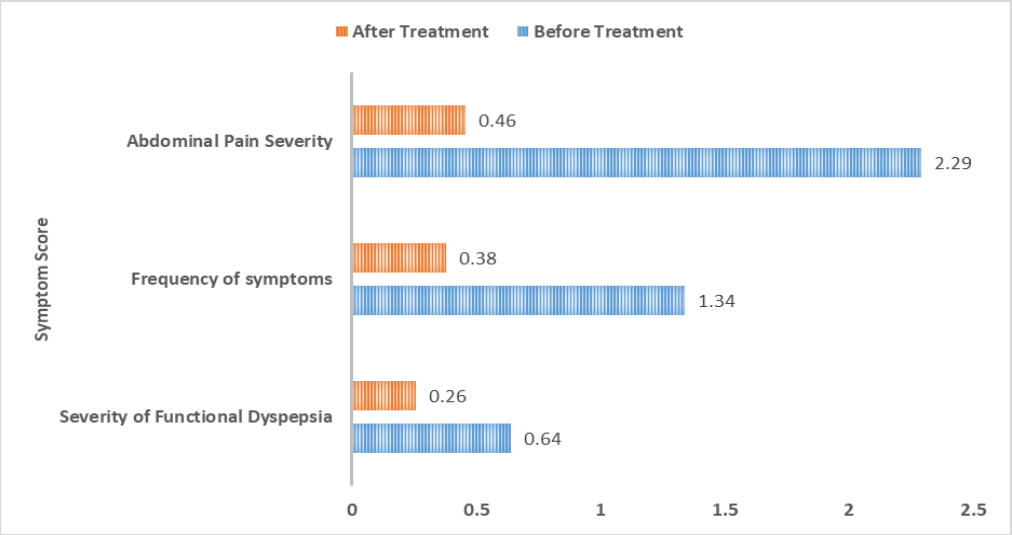


Figure 1: Improvement in Symptom and Severity

Figure 1 shows improvement in functional dyspepsia parameters after 30 days of Wallace Enzigest therapy. Abdominal pain severity reduced from 2.29 to 0.46, frequency of symptoms decreased from 1.34 to 0.38 and Overall severity of functional dyspepsia declined from 0.64 to 0.26.

Figure 2: Pancreatin Symptom Improvement

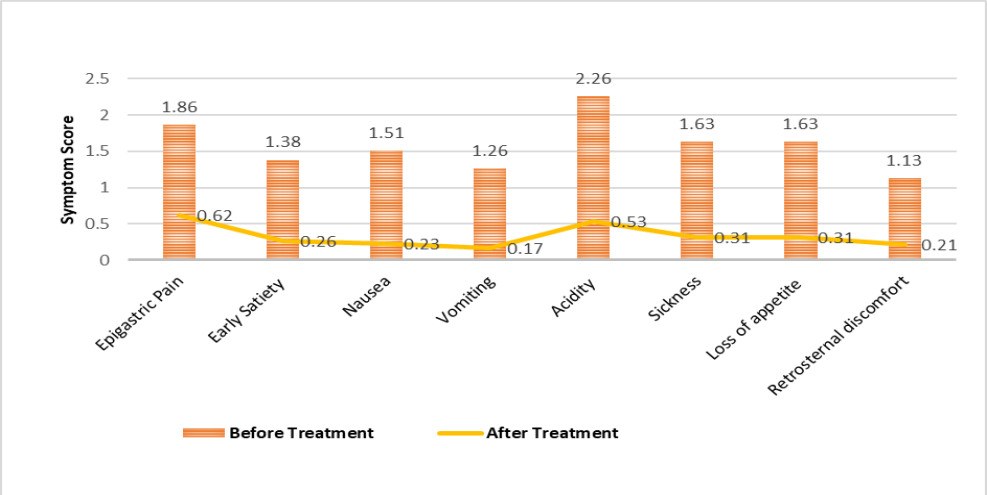


Figure 2 shows improvement in gastrointestinal symptoms after 30 days of Wallace Enzigest therapy. Vomiting reduced from 1.26 to 0.17, nausea from 1.51 to 0.23, early satiety from 1.38 to 0.26, acidity from 2.26 to 0.53, and epigastric pain from 1.86 to 0.62. Sickness, loss of appetite, and retrosternal discomfort also showed significant reductions.

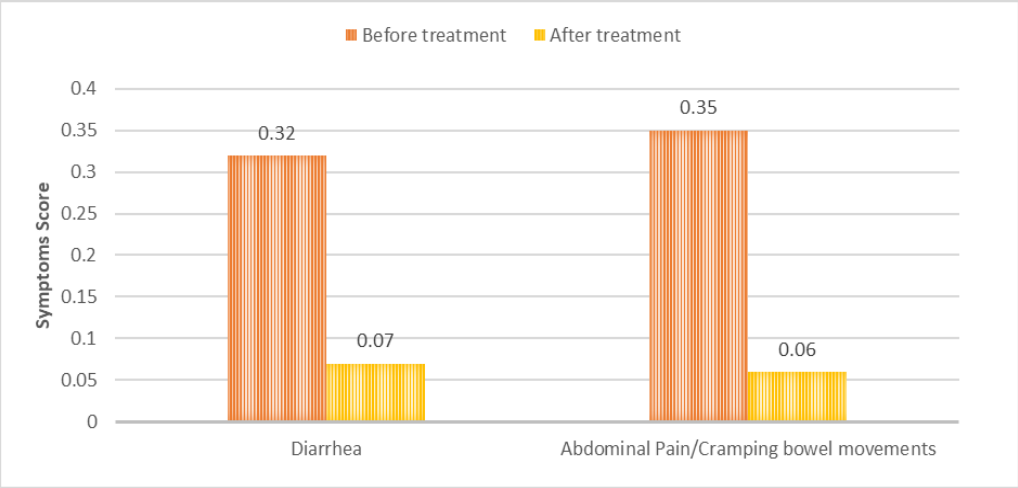


Figure 3 : Reduction in diarrhea

Figure 3 shows reduction in gastrointestinal disturbances after 30 days of Wallace Enzigest therapy. Diarrhea scores decreased from 0.32 to 0.07. Abdominal pain and cramping during bowel movements reduced from 0.35 to 0.06.

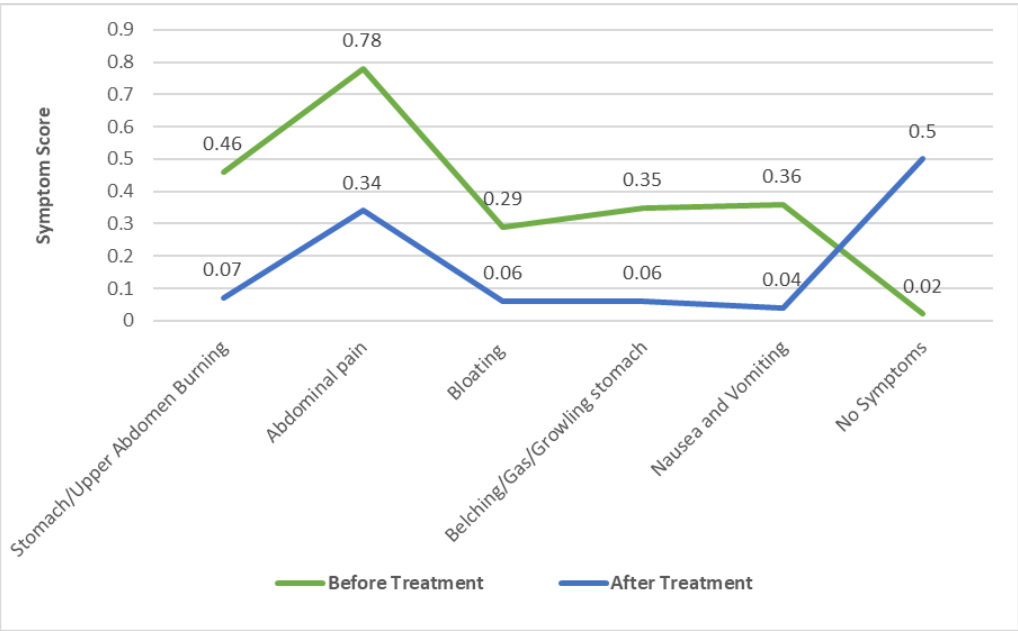
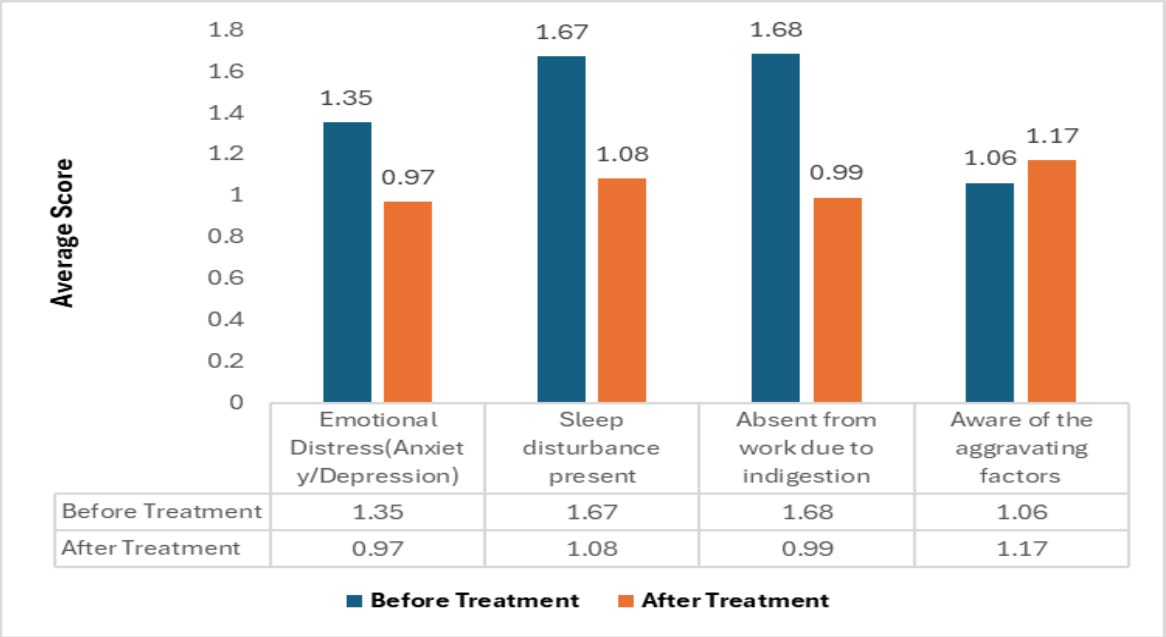


Figure 4 : Improvement in Troublesome Indigestion Symptoms

Figure 4 shows improvement in indigestion symptoms after 30 days of Wallace Enzigest therapy. Abdominal pain reduced from 0.78 to 0.34. Stomach/upper abdomen burning decreased from 0.46 to 0.07. Bloating reduced from 0.29 to 0.06, belching/gas/growling stomach from 0.35 to 0.06, and nausea and vomiting from 0.36 to 0.04. "No symptoms" increased from 0.02 to 0.50, indicating overall relief.

Secondary Outcomes:



	Emotional Distress(Anxiety/Depression)	Sleep disturbance present	Absent from work due to indigestion	Aware of the aggravating factors
Before Treatment	1.35	1.67	1.68	1.06
After Treatment	0.97	1.08	0.99	1.17

Figure 5 : Improvement in Quality of Life

Figure 5 shows that all quality-of-life parameters improved notably after 30 days of Wallace Enzigest therapy. Emotional distress decreased from 1.35 to 0.97. Sleep disturbance reduced from 1.67 to 1.08. Absence from work due to indigestion declined from 1.68 to 0.99. Awareness of aggravating factors increased from 1.06 to 1.17.

Parameters	Before Treatment (Mean ± SD)	After Treatment (Mean ± SD)	Change %	p-value
Primary Outcomes				
Severity of Functional Dyspepsia	0.64 ± 0.76	0.26 ± 0.44	59.46%	<0.001
Frequency of symptoms	1.34 ± 0.54	0.38 ± 0.49	71.52%	<0.001
Abdominal Pain Severity	2.29 ± 2.83	0.46 ± 0.27	83.39%	<0.001
Overall Assessment of the Patient with Functional Dyspepsia	0.72 ± 0.79	2.27 ± 0.77	215.28% *	<0.001
Epigastric/Abdominal Pain	1.86 ± 1.05	0.62 ± 0.61	76.40%	<0.001
Early Satiety	1.38 ± 1.20	0.26 ± 0.52	79.57%	<0.001
Nausea	1.51 ± 1.28	0.23 ± 0.54	84.20%	<0.001
Vomiting	1.26 ± 1.26	0.17 ± 0.48	86.11%	<0.001
Acidity (Regurgitation/ Heart Burn)	2.26 ± 1.01	0.53 ± 0.61	76.34%	<0.001
Sickness	1.63 ± 1.12	0.31 ± 0.56	80.90%	<0.001
Loss of appetite	1.63 ± 1.12	0.31 ± 0.56	80.90%	<0.001
Retrosternal discomfort	1.13 ± 1.18	0.21 ± 0.54	80.84%	<0.001
Diarrhea	0.32 ± 0.47	0.07 ± 0.26	77.85% *	<0.001
Abdominal Pain/Cramping with your bowel movements	0.35 ± 0.48	0.06 ± 0.24	82.82% *	<0.001
How have your stools been	1.74 ± 0.96	1.20 ± 0.41	31.17% *	<0.001
Secondary Outcomes (HRQOL)				
Most troublesome symptoms of indigestion	1.51 ± 1.28	0.24 ± 0.54	84.2% *	<0.001
Emotional Distress (Anxiety/Depression)	1.35 ± 0.66	0.97 ± 0.29	28.5% *	<0.001
Patient Sleeping Pattern affected by health condition	1.67 ± 0.63	1.08 ± 0.39	35.2% *	<0.001
Absent from work due to indigestion	1.68 ± 0.61	0.99 ± 0.28	40.73% *	<0.001
Patients are aware of the factors precipitating or aggravating indigestion	1.06 ± 0.79	1.17 ± 0.79	10.02%	0.0416
Complication associated with drug use in indigestion	0.31 ± 0.51	0.07 ± 0.25	78.5% *	<0.001

This table 2 shows statistically significant improvement ($p < 0.001$) in all major parameters after 30 days of Wallace Enzigest therapy. Severity of functional dyspepsia (59.46%), symptom frequency (71.52%), abdominal pain severity (83.39%), epigastric pain (76.40%), early satiety (79.57%), nausea (84.20%), vomiting (86.11%), acidity (76.34%),

sickness (80.90%), loss of appetite (80.90%), retrosternal discomfort (80.84%), diarrhea (77.85%), abdominal cramping with bowel movements (82.82%), stool consistency (31.17%), most troublesome symptoms (84.2%), emotional distress (28.5%), disturbed sleep (35.2%), work absence (40.73%), and drug-related complications (78.5%) all showed significant reduction. Patient awareness of aggravating factors slightly increased (10.02%, p=0.0416).

Discussion

This real-world, multicenter interventional study evaluated the clinical effectiveness of Enzigest™ (pancreatin 10000 minimicrospheres) in patients with symptoms suggestive of exocrine pancreatic insufficiency (EPI). After 30 days of therapy, statistically significant improvements ($p < 0.001$) were observed in both primary outcomes (gastrointestinal symptom relief) and secondary outcomes (quality-of-life measures), underscoring the utility of pancreatic enzyme replacement therapy (PERT) in routine clinical settings.

Primary Outcomes:

The study demonstrated marked reduction in dyspeptic and gastrointestinal symptoms. Notably, abdominal pain severity reduced by 83.39%, nausea by 84.20%, vomiting by 86.11%, epigastric pain by 76.40%, early satiety by 79.57%, and acidity by 76.34%. The frequency of symptoms declined by 71.52%, and severity of functional dyspepsia dropped by 59.46%. These primary outcomes are consistent with those reported by Desai et al., who found that Enzigest significantly reduced the severity of functional dyspepsia by 88.67%, and improved abdominal pain (81.58%), epigastric pain (83.09%), nausea (84.35%), and vomiting (89.62%) in patients with EPI of varied etiologies including alcohol use, gallstones, and hypertriglyceridemia (Desai A, et al.).[7]

The improvement in stool-related parameters—such as reductions in diarrhea (77.85%) and abdominal cramping with bowel movements (82.82%)—further supports the digestive efficacy of Enzigest. This aligns with findings from García et al., who reported that PERT reduced fecal fat excretion, nitrogen loss, and stool volume, while alleviating abdominal pain and improving overall gastrointestinal function in patients with pancreatic insufficiency (García L, et al.).[8]

Secondary Outcomes:

In addition to symptom relief, this study showed significant improvements in secondary outcomes related to health-related quality of life (HRQOL). Emotional distress was reduced by 28.5%, sleep disturbance by 35.2%, and absenteeism from work due to indigestion by 40.73%. These findings are in accordance with those of Czakó et al., who reported that enzyme therapy in chronic pancreatitis patients improved not only steatorrhea and pain, but also working ability, cognitive function, financial burden, and overall QoL. Their study also showed that improvements in quality of life correlated with weight gain and decreased stool frequency (Czakó L, et al.).[9]

Risk Factor Association:

The current study also identified common risk factors for EPI, including alcohol consumption (50.4%), gallstones (45%), hypertriglyceridemia (30.7%), diuretic use (21.1%), and prior abdominal surgery (23.9%). These risk factors are consistent with those seen in the populations studied by Desai and Czakó, where chronic alcohol use and metabolic disturbances were prominent contributors to pancreatic insufficiency. The therapeutic response observed

across these subgroups reinforces the applicability of enzyme supplementation across a spectrum of EPI etiologies.[7,9]

In conclusion, treatment with Enzigest™ resulted in significant improvements in both primary outcomes (gastrointestinal symptoms) and secondary outcomes (quality of life) in patients with EPI-related digestive complaints. Enzigest™ represents an effective and well-tolerated therapeutic option in the symptomatic and supportive management of EPI in routine practice. Future studies should assess long-term outcomes of Enzigest™, including sustained symptom control, nutritional benefits, and complication prevention. Comparative and dose-optimization trials across EPI etiologies, along with patient-reported outcomes and cost-effectiveness analyses, will further define its clinical and economic value.

Acknowledgment

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