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ORIGINAL PAPER

IMPACT OF COMPREHENSIVE THERAPY ON GASTROINTESTINAL SYMPTOMS AND NUTRITIONAL STATUS IN ELDERLY PATIENTS WITH CHRONIC PANCREATITIS

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Summary

Background. Chronic pancreatitis is a progressive condition that impairs pancreatic function and is particularly challenging to manage in elderly patients.

Material and methods. The study included 59 elderly patients with chronic pancreatitis who were monitored by their primary care physician. Participants were divided into two groups: Group 1 (n=29), who received treatment according to a standard chronic pancreatitis management protocol, and Group 2 (n=30), who received the same standard treatment plus intracellular systemic enzyme therapy.

Results. Fecal α-elastase increased by 12.18% in Group 1 and 19.97% in Group 2, with Group 1 5.73% lower post-treatment (p<0.05). The Gastrointestinal Symptom Rating Scale (GSRS) scores showed greater reductions in Group 2, including abdominal pain (-39.04% vs. -30.53%) and indigestion (-31.83% vs. -26.39%) (p<0.05). Nutritional indicators improved more in Group 2, with higher total protein (+6.27% vs. +2.51%) and retinol levels (+57.58% vs. +28.13%) (p<0.05).

Conclusions. The study found that intracellular systemic enzyme therapy significantly improved outcomes in elderly patients with chronic pancreatitis, including improved fecal α-elastase levels and better coprogram and ultrasound scores. Additionally, the therapy led to notable improvements in gastrointestinal symptoms and biochemical markers, suggesting its potential as a beneficial addition to chronic pancreatitis management.

Keywords: intracellular systemic enzyme therapy, fecal α-elastase, GSRS, chronic pancreatitis, elderly patients

Introduction

Chronic pancreatitis is a debilitating condition characterized by persistent inflammation of the pancreas, leading to progressive damage and functional impairment [1-3]. The chronic inflammation results in the gradual destruction of pancreatic tissue, which can severely impact endocrine and exocrine functions, leading to diabetes mellitus and digestive disorders, respectively [4-7]. The management of chronic pancreatitis is particularly challenging in elderly patients due to age-related physiological changes, which can exacerbate the disease's progression and complicate treatment [8]. As individuals age, they often experience diminished organ function, altered drug metabolism, and an increased prevalence of comorbidities such as cardiovascular disease and diabetes, which can further complicate the management of chronic pancreatitis [9-12].

Traditional treatment approaches primarily focus on symptomatic relief and dietary modifications [13-15]. They include pain management, pancreatic enzyme replacement therapy, and dietary adjustments to alleviate symptoms and improve nutritional status [16,17]. However, the methods often fall short in addressing the complex needs of elderly patients who may have

multiple health issues and require a more comprehensive treatment plan [18,19]. This necessitates a holistic approach to their care [20,21].

Moreover, dietary modifications, while essential, may not fully address the underlying inflammation or improve pancreatic function [22]. Therefore, there is a growing need for adjunctive therapies that can offer more substantial benefits [23]. The intracellular systemic enzyme therapy exhibits a range of pharmacological properties that contribute to its therapeutic efficacy [24,25]. Intracellular systemic enzyme therapy involves the use of enzyme preparations containing proteolytic enzymes such as bromelain, papain, and trypsin, often combined with antioxidants or anti-inflammatory compounds like rutin [24,25]. This contributes to the better circulation and overall cardiovascular health [26]. Additionally, the enzyme therapy enhances fibrinolysis and lipolysis by activating plasminogen and improving blood rheology, thereby reducing blood viscosity and cholesterol levels [27,28]. The enzyme mixture also modulates immune responses by improving the clearance of pathogenic immune complexes and stimulating phagocytic activity [24,27]. Further research is needed to explore the use of intracellular systemic enzyme therapy, especially in the management of elderly patients.

Aim of the work

The aim of the work is to address the gap by evaluating the effects of intracellular systemic enzyme therapy in elderly patients with chronic pancreatitis.

Material and methods

The study included 59 elderly patients with chronic pancreatitis who were monitored by their primary care physician. Participants were divided into two groups: Group 1 (n=29), who received treatment according to a standard chronic pancreatitis management protocol, patients were prescribed antispasmodics, prokinetics, proton pump inhibitors, and enzyme agents (pancreatin) in general therapeutic doses as needed; Group 2 (n=30), who received the same standard treatment plus intracellular systemic enzyme therapy Wobenzym®, Mucos Pharma, Germany 5 pills three times a day for 6 weeks. Active ingredients of intracellular systemic enzyme: 1 enteric-coated tablet contains: pancreatin – 300 Prot. units (100 mg); papain – 90 FIP-Units (18 mg); bromelain – 225 FIP-Units (45 mg); triacylglycerol lipase – 34 FIP-Units (10 mg); amylase – 50 FIP-Units (10 mg); trypsin – 360 FIP-Units (12 mg); chymotrypsin – 300 FIP-Units (0.75 mg); rutoside – 50 mg;

Inclusion criteria included a clinical diagnosis of chronic pancreatitis, age ≥ 65 years, and a stable medical condition. Exclusion criteria included malignancies, other severe gastrointestinal disorders, recent use of intracellular systemic enzyme therapy, and withdrawal from participation in the study.

The diagnosis of chronic pancreatitis was established in accordance with the current clinical protocol, as outlined in protocol No. 1204, dated July 4th, 2023, approved by the Order of the Ministry of Health of Ukraine. Chronic pancreatitis is defined as a progressive inflammatory disease of the pancreas characterized by irreversible structural changes, leading to persistent abdominal pain and/or exocrine and endocrine insufficiency. The diagnosis is typically based on clinical symptoms, imaging findings such as calcifications or ductal abnormalities on ultrasound,

CT, or MRI, and functional tests indicating pancreatic insufficiency, including reduced fecal α-elastase levels.

Fecal α-elastase levels were determined using the enzyme-linked immunosorbent assay (ELISA) method. The coprogram score for detecting exocrine pancreatic insufficiency was assessed using a scoring system, each pathological finding was assigned 1 point. According to the scale, 1 point was assigned to the following signs: the presence of undigested meat food residues (creatorrhea) in large quantities; the presence of undigested fats (steatorrhea) in the form of neutral fats; the presence of digested fiber and starch in feces (amylorrhea); a significant amount of mucus and leukocytes as evidence of an inflammatory process in the intestine; the presence of fungi, protozoa, helminths, and their waste products. In the assessment of ultrasound of the pancreas, the following signs obtained from ultrasound were taken into account: dilation of the duct of Wirsung more than 3 mm (a sign of ductal hypertension); tortuous course of the duct; intraductal echogenic formations with and without acoustic shadows (stones, wall calcifications, protein precipitates); hyperechoic (fibrously altered) duct wall; expansion of the lateral branches of the duct (periductal parenchymal fibrosis); inhomogeneous echo structure of the pancreatic parenchyma; zones of reduced echogenicity with small (13 mm) inclusions (inflammatory tissue edema); hyperechoic inclusions with acoustic shadows (calcification of the gland); linear heavy inclusions of various shapes and lengths (fibrosis); uneven tuberculate hyperechoic contour of the gland (fibrosis and atrophy); anechoic cavities (over 5 mm in size) - the presence of pseudocysts.

Gastroenterological symptoms were assessed using the Gastrointestinal Symptom Rating Scale (GSRS). The GSRS is a validated questionnaire designed to evaluate the severity of gastrointestinal symptoms in patients. It includes several domains: abdominal pain (AP), regurgitation symptoms (RS), diarrhea symptoms (DS), constipation symptoms (CS), and

indigestion symptoms (IS). Each domain is rated on a scale from 1 (no symptoms) to 7 (severe symptoms), providing a comprehensive assessment of gastrointestinal health.

Nutritional status indicators include: total protein, measured by the Biuret method, albumin by the Bromcresol Green method, transferrin by an immunoassay, ferritin by ELISA, and transferrin saturation is calculated as the ratio of serum iron to total iron-binding capacity multiplied by 100. The levels of tocopherol and retinol is determined using high-performance liquid chromatography (HPLC).

The Shapiro-Wilk test was employed to evaluate whether the data followed a normal distribution. Descriptive statistics were presented as the mean and standard error (M±m). For data meeting the normality assumption, Student's t-test was utilized to compare means between independent and dependent groups. For data not conforming to a normal distribution, non-parametric methods were applied: the Mann-Whitney U-test for comparing median ranks between independent groups and the Wilcoxon signed-rank test for comparing median ranks within dependent groups. Data processing and statistical analyses were conducted using Microsoft Excel 2016 and specialized statistical software, including STATISTICA® 8.0 (Stat Soft Inc., USA), IBM® SPSS® Statistics Version 23.0, GraphPad Prism® 8.0, and MedCalc® v.19.0.7.

Results

The analysis of the studied parameters revealed a statistically significant positive impact of intracellular systemic enzyme therapy in elderly patients with chronic pancreatitis. The analysis of exocrine pancreatic insufficiency (EPI) indicators showed significant changes in fecal α-elastase, coprogram scores, and ultrasound scores of the pancreas following treatment (Table 1).

Table 1. Dynamics of EPI indicators in patients with chronic pancreatitis under the influence of different treatment programs

Indicator	Comparison group			
	Group 1 (n=29)		Group 2 (n=30)	
	Before treatment	After treatment	Before treatment	After treatment
Fecal α-elastase, μg/g	98.83±2.87	110.87±1.15#	97.71±2.99	117.22±1.17#&
Coprological score, points	4.65±0.20	3.31± 0.12#	4.62±0.22	3.07±0.10#&
Pancreatic ultrasound score, points	4.77±0.26	4.39±0.10#	4.79±0.27	4.16±0.11#&

Notes: # – indicates a statistically significant difference compared to the same post-treatment group (p<0.05); & – indicates a statistically significant difference compared to another post-treatment group (p<0.05).

After treatment, fecal α-elastase levels increased by 12.18% in Group 1 and 19.97% in Group 2, with both increases statistically significant (p<0.05). Group 1's levels were 5.73% lower than Group 2's post-treatment (p<0.05). Coprogram scores decreased by 28.82% in Group 1 and 33.55% in Group 2 (p<0.05), with Group 1 scoring 7.25% higher in post-treatment (p<0.05). Pancreatic ultrasound scores improved by 7.97% in Group 1 and 13.15% in Group 2 (p<0.05), with Group 1's scores 5.24% higher in post-treatment (p<0.05).

Significant reductions in GSRS questionnaire scores were observed in post-treatment across several symptom scales (p<0.05) (Table 2).

Table 2. Dynamics of GSRS questionnaire scores in patients with chronic pancreatitis under the influence of different treatment programs

Indicator	Comparison group			
	Group 1 (n=29)		Group 2 (n=30)	
	Before treatment	After treatment	Before treatment	After treatment
AP, points	4.75±0.29	3.30±0.15#	4.79±0.33	2.92±0.21#&
IS, points	5.57±0.28	4.10±0.17#	5.53±0.26	3.77±0.15#&
DS, points	4.59±0.27	3.14±0.16#	4.54±0.28	2.85±0.11#&
CS, points	4.05±0.20	3.76±0.08#	4.02±0.17	2.57±0.09#&
RS, points	5.02±0.24	4.61±0.16#	5.05±0.26	3.29±0.14#&

Notes: # – indicates a statistically significant difference compared to the same post-treatment group ($p<0.05$); & – indicates a statistically significant difference compared to another post-treatment group ($p<0.05$).

In post-treatment, AP scores decreased by 30.53% in Group 1 and 39.04% in Group 2 ($p<0.05$). Group 1's AP scores were 11.52% higher than Group 2's ($p<0.05$). IS scores decreased by 26.39% in Group 1 and 31.83% in Group 2 ($p<0.05$), with Group 1's IS scores 8.05% higher than Group 2's ($p<0.05$). DS scores reduced by 31.59% in Group 1 and 37.22% in Group 2 ($p<0.05$), with Group 1's DS scores 9.24% higher than Group 2's ($p<0.05$). CS scores improved by 7.16% in Group 1 and 36.07% in Group 2 ($p<0.05$), with Group 1's CS scores 31.65% higher ($p<0.05$). RS scores decreased by 8.17% in Group 1 and 34.85% in Group 2 ($p<0.05$), with Group 1's RS scores 28.63% higher ($p<0.05$).

Nutritional status indicators also demonstrated significant changes post-treatment (Table 3).

Table 3. Dynamics of integral nutritional status indicators in patients with chronic pancreatitis under the influence of different treatment programs

Indicator	Comparison group			
	Group 1 (n=29)		Group 2 (n=30)	
	Before treatment	After treatment	Before treatment	After treatment
Total protein, g/L	67.31±0.47	69.00±0.21#	67.27±0.49	71.49±0.26#&
Albumin, g/L	40.15±0.32	41.69±0.19#	40.10±0.35	42.90±0.21#&
Transferrin, mg/dL	529.32±6.21	492.81±4.15#	529.78±6.29	483.76±4.27#&
Ferritin, ng/mL	47.81±1.21	50.99±0.95#	47.76±1.24	53.73±0.76#&
Transferrin saturation with iron, %	24.60±0.75	26.89±0.51#	24.56±0.81	28.98±0.57#&
Retinol, mg/L	0.32±0.05	0.41±0.03#	0.33±0.04	0.52±0.05#&
Tocopherol, mg/L	5.12±0.12	6.07±0.11#	5.18±0.15	6.57±0.16#&

Notes: # – indicates a statistically significant difference compared to the same post-treatment group ($p<0.05$); & – indicates a statistically significant difference compared to another post-treatment group ($p<0.05$).

In post-treatment, total protein levels increased by 2.51% in Group 1 and 6.27% in Group 2 ($p<0.05$), with Group 1's levels 3.61% lower than Group 2's ($p<0.05$). Albumin levels increased by 3.84% in Group 1 and 6.98% in Group 2 ($p<0.05$), with Group 1's albumin 2.90% lower than Group 2's ($p<0.05$). Transferrin levels decreased by 6.33% in Group 1 and 8.69% in Group 2 ($p<0.05$), with Group 1's transferrin 1.84% higher than Group 2's ($p<0.05$). Ferritin levels increased by 6.65% in Group 1 and 12.5% in Group 2 ($p<0.05$), with Group 1's ferritin 31.08% lower than Group 2's ($p<0.05$). Transferrin Saturation with iron increased by 9.31% in Group 1 and 18.00% in Group 2 ($p<0.05$), with Group 1's levels 7.77% lower than Group 2's ($p<0.05$). Retinol levels increased by 28.13% in Group 1 and 57.58% in Group 2 ($p<0.05$), with Group 1's retinol 26.83% lower than Group 2's ($p<0.05$). Tocopherol levels increased by 18.55% in Group 1 and 26.83% in Group 2 ($p<0.05$), with Group 1's tocopherol 8.24% lower than Group 2's ($p<0.05$).

Discussion

The study highlights the potential benefits of intracellular systemic enzyme therapy in the management of chronic pancreatitis in elderly patients, demonstrating significant improvements in clinical and biochemical markers. The observed reduction in fecal α-elastase levels suggests enhanced pancreatic exocrine function through increased digestive enzyme activity. Additionally, improved coprogram scores indicate better digestion and nutrient absorption, while positive changes in ultrasound findings reflect reductions in pancreatic inflammation and structural improvements. Significant reductions in gastrointestinal symptoms, as measured by the GSRS questionnaire, further emphasize the therapy's ability to alleviate gastrointestinal distress and improve patients' quality of life. Moreover, improvements in nutritional status indicators suggest the therapy's potential to positively impact overall nutritional outcomes.

Intracellular enzymatic therapy, particularly the use of combined enzymatic preparations, represents a promising approach in the treatment of chronic inflammatory diseases, as the therapies can reduce the levels of inflammatory cytokines, improve tissue metabolism, and stimulate the regeneration of damaged cells. The effectiveness of the therapy, in comparison to traditional treatment methods, is supported by clinical research findings that demonstrate significant improvements in patients' quality of life and a reduction in symptom severity [27,29].

Intracellular systemic enzyme therapy has demonstrated benefits in managing other conditions [24,25]. Previous research has found that intracellular systemic enzyme therapy significantly improved symptoms and quality of life in patients with osteoarthritis, suggesting its anti-inflammatory and analgesic effects extend beyond pancreatic disorders [27,29]. Intracellular systemic enzyme therapy has also been investigated for its use in the treatment of recurrent

obstructive bronchitis. Research findings suggest that the therapy may enhance recovery and reduce inflammation in patients with recurrent obstructive bronchitis, highlighting its potential in managing inflammatory respiratory conditions [24]. Intracellular systemic enzyme therapy is also beneficial in the treatment of gynecological diseases and chronic sexually transmitted infections [25,26]. Furthermore, studies have indicated that intracellular systemic enzyme therapy can enhance recovery and reduce inflammation in patients with chronic sinusitis and other inflammatory conditions [30]. The findings underscore the broader therapeutic potential of intracellular systemic enzyme therapy and its utility in a range of inflammatory and degenerative diseases.

Despite the promising results, the study has limitations including a relatively small sample size and a limited follow-up duration of 6 weeks. The study also did not assess long-term outcomes or potential side effects of intracellular systemic enzyme therapy. Future research should address the gaps through larger, multi-center trials with extended follow-up periods to confirm the findings and explore the long-term safety and efficacy of intracellular systemic enzyme therapy in managing chronic pancreatitis and other conditions. Such studies are essential to fully understand the therapeutic potential of intracellular systemic enzyme therapy and its role in comprehensive treatment strategies.

The small number of patients and the relatively short follow-up period is a limitation of our study.

Conclusions

The study identified that intracellular systemic enzyme therapy significantly improved outcomes in elderly patients with chronic pancreatitis. Key findings include substantial reductions in fecal α-elastase levels and enhanced coprogram and ultrasound scores in the therapy group. Notable improvements in gastrointestinal symptoms, such as abdominal pain, indigestion, and reflux, were observed with intracellular systemic enzyme therapy. Additionally, biochemical markers, including total protein, albumin, and ferritin, transferrin saturation with iron, retinol, tocopherol, also improved more with intracellular systemic enzyme therapy. The results suggest that intracellular systemic enzyme therapy may be a beneficial addition to the management of chronic pancreatitis.

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Informed consent was obtained from all participants prior to their involvement. The study received ethical approval from the Bioethics Committee of I. Horbachevsky Ternopil National Medical University Ministry of Health of Ukraine (Protocol No. 75, November 1st, 2023).

Artificial intelligence (AI) was not used in the creation of the manuscript.

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