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Randomized Controlled Trial

Effects of using symbiotics in the clinical nutritional evolution of patients with chronic pancreatitis: Study prospective, randomized, controlled, double blind

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SUMMARY

Patients with chronic pancreatitis (CP) present malabsorption and changes in nutritional status. In this prospective, randomized, controlled, double-blinded, intervention study, developed at the Clinic of Pancreas, we aimed to assess whether the use of symbiotics changes the nutritional status, the biochemical data and the intestinal rate of these patients. The intervention consisted of administering 12 g/day of symbiotics composed of *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Lactobacillus acidophilus*, *Bifidobacterium bifidum* and fructooligosaccharides to the intervention group and 12 g/day of medium absorption complex carbohydrate to the control group. The project was approved by the Ethics Committee of College of Technology and Science – FTC under the number process 0528-2008; reg. 498 e was registered under ClinicalTrials.gov Identifier with no. NCT00123456. We evaluated 60 patients and the intervention lasted for 3 months, with monthly monitoring. A statistically significant reduction was observed in the results by day in relation to the initial frequency ($x = 2.3$) and the use of symbiotics in the second ($x = 1.47$) and third ($x = 1.37$) months ($p = 0.001$). In the control group, there was no significant change in this frequency ($p = 0.157$). The results showed an increase in the levels of hemoglobin ($p < 0.001$), hematocrit ($p = 0.001$), red blood cells ($p < 0.001$), total lymphocyte count ($p < 0.002$), serum magnesium ($p < 0.001$), albumin (0.001) and total serum cholesterol reduction ($p < 0.001$) with the use of symbiotics. The changes were not observed in the nutritional status of both groups.

Conclusion: The use of symbiotics improved the clinical and laboratory profiles of the evaluated patients with CP, favoring the best clinical outcome, and may be a therapeutic option because of the low cost and therapeutic effectiveness in this population.

1. Introduction

Chronic pancreatitis (CP) is an inflammatory disease characterized by progressive fibrosis, destruction and canalicular distortions of the pancreas, which presents itself as a classic clinical situation comprised of abdominal pain, anorexia, vomiting, nausea and malabsorption [1,2]. These changes induce the exocrine pancreatic insufficiency, with reduction in the secretion of enzymes that participate in the digestive process [1,3,4].

The patients with CP show dysbiosis, characterized by greater growth of pathogenic bacteria along the bowel gastrointestinal tract (BGT) associated with changes in functions and in the integrity of the mucous barrier [5].

In CP, the dysbiosis occurs due to the reduction of pancreatic secretion that decreases the production of intestinal serotonin, provides proliferation of *Candida albicans*, and promotes the overgrowth of pathogenic bacteria [5].

The functional impairment of the BGT may favor the occurrence of diarrhea or promote the persistence of this symptom, inducing bile acid malabsorption and increasing intestinal permeability,

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aggravating the clinical and nutritional framework of these individuals, even though these patients properly use exogenous pancreatic enzymes [2,4,6–8].

Diarrhea, which is characteristic of CP, is associated with significant weight loss in 30%–50% of the patients, and malnutrition occurs in up to 50% of individuals with this disease [1,9,10].

Symbiotic prescription has been stimulated in patients with chronic TGI disturbance with the intention of promoting the control of malabsorption, intestinal microbiota balance, better absorption of iron, calcium and magnesium, and reducing episodes of diarrhea and blood levels of serum cholesterol and blood glucose in patients with symptoms, such as diarrhea and abdominal pain [11–16].

The use of probiotic strains, such as *Bifidobacterium bifidum*, *Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Lactobacillus casei*, *Lactobacillus acidophius*, *Lactobacillus plantarum*, *Streptococcus thermophilus and Saccharomyces boulardii*, administered individually or combined with prebiotic fructooligosaccharides, has been associated with reducing the episodes of diarrhea, malabsorption and dysbiosis [17–20].

The expected effect of symbiotic use in this population may be related to the restoration of the microbiota through the fermentation of fructooligosaccharides (FOS) and the consequent increase in Bifidobacteria and the reduction of pathogenic bacteria, by the competition for nutrients and for membership sites. The beneficial effects on intestinal motility were observed, in addition to reducing the intestinal transit time and stimulating the immunity of the host [8,14,15,20].

Therefore, the objective of the present study was to determine if the administration of the symbiotic compound with multiple strains can promote changes in the nutritional status, the biochemical data and the intestinal pace of individuals with CP.

2. Material and methods

The intervention study, which was randomized, prospective, controlled, and double-blinded, was developed at the University Clinic of Reference for Diseases of the Pancreas during a 9-month period.

Outpatients with a diagnosis of chronic pancreatitis were eligible to participate in the study if they met the clinical criteria associated with bioimaging data [1,5] and were aged ≥18 years. The PC was previously diagnosed characterized by abdominal pain and/or evidence of endocrine pancreatic insufficiency (diabetes) and/or exocrine (steatorrhea), associated with changes in the bio-imaging scans of pancreatic: dilation and tortuosity loss of branching Wirsung and/or pancreatic and/or pseudocysts calcification.

The exclusion criteria were as follows: patients over the age of 70 years; a history of intestinal surgeries; or pancreas surgery; and other chronic diseases not associated with the underlying disease.

The sample of convenience and composed of all the patients registered at the referral center, where they attend to receive quarterly revenue to receive enzymes SUS system.

Sixty-nine patients fulfilled the inclusion criteria; of the 69 patients, two patients refused to participate in the study, five patients showed no conditions to attend all queries, two patients reported prior history of cancer, totaling 60 patients with PC who complied fully with the intervention protocol.

2.1. Intervention

For the intervention protocol, the patients were randomly sorted into two groups: the symbiotic group, which was administered the symbiotics composed of fructooligosaccharides, *L. casei*, *L. rhamnosus*, *Lactobacillus acidophilus*, *and B. bifidum*. The control group was administered maltodextrin, classified as average absorption and complex carbohydrate (Tables 1 and 2).

Both products were packaged in identical sachets that were identified only by code numbers and contained 6 g each and were stored in a temperature-controlled environment at 24 °C and 45% humidity conditions. Identification numbers for a table of random numbers was used and this work was done by a professional statistics. The products were administered to the patients at a dose of 12 g/day for three months, and the contents of the sachets and the nature of the intervention group were unknown to the researchers. The sachets were identical and came from the factory this way straight to the statistical professional.

Monitoring was conducted using 4 queries with 1-month interval between them for the purposes of tracking and receiving sufficient quantity of their products for 1 month of use. The patients were provided verbal and written instructions regarding the use of the products, conservation care, use of 6 g per day in the morning and 6 g per day in the evening; and they were instructed to return the empty sachets after every query, for the purpose of controlling adherence to treatment. The membership was considered to be acceptable when there was a minimal devolution of 90% of empty envelopes, indicating appropriate consumption of supplements.

The safe use of the products was monitored through biweekly telephone contact and in every query, when the presence of adverse effects was investigated, such as fatigue, bloating, feelings of bloating and stomach irritation, headache, and altered sleep patterns. The patients were instructed to feel free and telephone the researchers to notify them of unpredictable side effects.

2.2. Nutritional evaluation

The patient's weight was measured using the technique of Lohman [21]; the patient's height was measured using a stadiometer (Model 31, Filizola®).

The body mass index (BMI) was calculated according to the formula of Quetelet, and the anthropometric nutritional status classification was made according to World Health Organization (WHO) (1995) for adults and according to Lipschitz (1994) for the elderly [22].

The evaluation of muscle mass for adults was conducted using the corrected arm muscle area (AMAc), and the reservation of adipose tissue was obtained by analyzing body fat percentage [22].

For anthropometric assessments of the elderly, the TSF (triciptal skin fold) and the muscular arm circumference (MAC) were used, and the results were evaluated according to NHANESIII, 1988–1991 [22].

Body composition using bioelectrical impedance (BIA) was assessed in the first query and in the last query, using the electrical bioimpedance tetrapolar device (Model 450, Biodynamics®), followed by preparations required for hydration and nutrition. The phase angle was calculated and the value below 5 was considered to be associated with malnutrition; the values between 5 and 10

Table 1
Symbiotic composition used.

Composition	
Components	Amount
Frutooligossacarídeo	6 g
Lactobacillus casei	10^9 a 10^8[a] CFU[b]
Lactobacillus rhamnosus	10^9 a 10^8 CFU
Lactobacillus acidophilus	10^9 a 10^8 CFU
Bifidobacterium bifidum	10^9 a 10^8 CFU

[a] Lot standardization log.
[b] CFU, forming unit of Cologne.

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