

## ВНУТРЕННИЕ БОЛЕЗНИ

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**Dry protein composite mixture enriched with calcium of dairy origin, in the dietary treatment of certain diseases of the digestive system accompanied by malabsorption syndrome**A. Yu. Baranovsky<sup>1</sup>, A. L. Maslyanskiy<sup>1,2</sup><sup>1</sup> St Petersburg State University,

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The aim of this study is to evaluate the effectiveness of diet therapy with the inclusion of a specialized food product of a dry protein composite mixture enriched with calcium of dairy origin in patients with enteral malabsorption syndrome. 66 patients with various diseases of the digestive system (chronic atrophic gastritis, condition after gastric resection, chronic pancreatitis, etc.), aged 47 to 79 years, were examined. All patients were divided into 2 groups: the study group (40 patients) and the control group (26 patients). All patients underwent comprehensive treatment according to the profile of their underlying disease, as well. Medical nutrition was prescribed according to the Order of the Ministry of Health of the Russian Federation #330 2003 with the inclusion of 27 g of a dry protein composite mixture according to the order of the Ministry of Health of the Russian Federation #395n 2013. For the patients of the study group, dry protein composite mixture was enriched with 1.85 g of calcium of dairy origin. The duration of treatment is 12 weeks. In patients of the study group, in comparison with the control group, all clinical signs of statistically significantly improved, the absorption function of enterocytes was proved to be activated, the dynamics of recovery of metabolic disorders was noted faster. Conclusion: it has been shown for the first time that the use of calcium-enriched dry protein composite mixture of dairy origin as part of the dietary program of complex therapy of patients with malabsorption syndrome significantly improves the functional state of the small intestine, provides rapid dynamics of regression of the malabsorption syndrome clinic and metabolic disorders of the patients' body.

**Keywords:** malabsorption syndrome in diseases of the digestive system, diet therapy, dry protein composite mixture enriched with calcium of dairy origin.

## Introduction

The national project “Healthcare”, as one of the state priority projects in the Russian Federation, approved by the President of the Russian Federation in the interests of preserving and strengthening the health of the inhabitants of our country, involves the fundamental improvement of all methods and means of providing and improving the quality of medical care to patients [1]. Therapeutic and dietary nutrition, as a basic method of treatment programs at all stages of the course of any diseases, has every opportunity to increase its therapeutic and preventive significance and effectiveness in the context of new modern achievements of fundamental and applied sciences. This can be achieved by personifying the content of diets, their pathogenetic orientation, clinical validity, the introduction of a functional nutrition system, including the development and use of appropriate composite food formulations.

The development of malabsorption syndrome in some diseases of the gastrointestinal tract is a fairly common and progressive phenomenon, developing due to a violation of the digestive and transport functions of the small intestine, which in turn leads to pathological changes in metabolism. It is known that the causes of malabsorption can be both acute severe, including postoperative processes that violate the consistency of the digestive conveyor, as well as chronic diseases of the digestive organs accompanied by degradation of secretory activity of the digestive glands and/or severe dyskinetic processes in the stomach and small intestine. The formation of manifestations of malabsorption syndrome requires not only adequate treatment of diseases that contributed to the development and progression of digestive failure, but also, first of all, pathogenetically based individualized therapeutic nutrition.

One of the principles of optimizing therapeutic nutrition is the use in standard diets of specialized food mixtures of protein composite dry (hereinafter referred to as SBCS), intended for dietary therapeutic and dietary preventive nutrition as a component for the preparation of ready meals. SBCS do not affect the organoleptic properties and taste qualities of ready meals, they allow to increase the nutritional density and biological value of an individual dish or the diet as a whole.

Numerous studies have shown that the bioavailability of calcium from milk and dairy products is significantly higher compared to other sources of calcium [2]. That is why the inclusion of a specialized SBCS food product enriched with calcium of dairy origin could provide adequate compensatory intake into the body of patients with malabsorption syndrome not only protein, essential and interchangeable amino acids, but also the necessary amount of calcium in a ratio with phosphorus and zinc equal to that in natural milk, which, in turn, creates conditions for high digestibility of calcium — one of the key macronutrients.

The purpose of the study: to evaluate the effectiveness of diet therapy with the inclusion of a specialized food product of a dry protein composite mixture enriched with calcium of dairy origin in patients with chronic diseases of the gastrointestinal tract accompanied by malabsorption syndrome.

## Materials and methods

Sixty-six patients with various diseases of the digestive system (progressive chronic atrophic gastritis, a condition after gastric resection, chronic pancreatitis with pancreatic insufficiency, enteropathy of various genesis, including celiac disease, radiation enteropa-

thy, etc., irritable bowel syndrome), aged 47 to 79 years, were examined. Women — 43, men — 23 patients. All patients showed signs of malabsorption as a symptom complex of disorders of the motor, secretory and suction functions of the small intestine. The diagnosis of the underlying disease in all patients was made on the basis of data from a comprehensive application of laboratory studies (general clinical and biochemical blood analysis, coprogram, bacteriological analysis of feces), fibrogastroduodenoscopy, fibroejunoscopia, fibrocolonoscopy, electrogastroenterography, MRI of abdominal organs, histological and histochemical studies of biopsies of the gastric mucosa, duodenum and small intestine. Verification of malabsorption syndrome was based on a comprehensive assessment of the characteristic clinical manifestations and laboratory evidence of malabsorption in the small intestine and deficiency in the blood of many nutrients.

The frequency of clinical manifestations of malabsorption in the cohort of examined patients was as follows: poor appetite in 64 out of 66 patients, a decrease in the blood content of many nutrients in 61 out of 66 patients, weight loss in 60 out of 66 patients, including protein-energy deficiency of I and II degrees in 21 out of 66 patients, bloating, diarrhea in 50 out of 66 patients, severe fatigue, progressive fatigue in 47 out of 66 patients, nausea and/or vomiting in 38 out of 66 patients, as well as anemia in 37 out of 66 patients. Data were obtained on the development of anemia in combination with a decrease in the blood content of erythrocytes in 58 of 66 patients, a high concentration of fat in feces in 59 of 66 patients, creatorrhea in 48 of 66 patients.

A high frequency of metabolic disorders was revealed: protein (hypoproteinemia and/or hypoalbuminemia) in 59 out of 66 patients, vitamin (groups B, D, E, A, etc.) in all patients, minerals (Ca, Mg, F, many trace elements) also in all patients.

Endoscopic examinations in all 66 patients revealed pathological changes in the mucous membrane of the small intestine of varying severity in the form of narrowing of the intestinal lumen, smoothness of folds, as well as the presence of erosive and ulcerative lesions. Especially pronounced changes were observed in patients after gastric resection and in chronic pancreatitis with excretory insufficiency in the presence of malabsorption syndrome of II severity.

The pathomorphology of the small intestine mucosa in patients with malabsorption syndrome in our study depended on the genesis of the formation of this process. Minimal phenomena were detected in patients with progressive chronic gastritis, chronic pancreatitis, irritable bowel syndrome. They were manifested by a weakly expressed picture of a decrease in the height of the villi, some deepening of the crypts, moderate infiltration of the own plate of the mucous membrane by lymphocytes, plasmocytes. More significant morphological manifestations of atrophy of the mucous membrane of the small intestine were observed with grade II malabsorption in patients with gluten enteropathy, with radiation damage to the small intestine. Thus, in celiac disease, we found an increase in the number of intraepithelial lymphocytes and crypt hyperplasia in 6 out of 9 examined patients, and a different degree of villous atrophy in 8 of them. In cases of enteropathy of radiation genesis, an increase in the number of intraepithelial lymphocytes and a different degree of villous atrophy were revealed in 7 out of 8 cases.

The most significant clinical and laboratory manifestations of malabsorption syndrome were revealed in patients with chronic pancreatitis with symptoms of external secretory insufficiency, in patients after gastric resection, with enteropathy associated with celiac disease and radiation damage to the small intestine in the anamnesis.

All 66 patients were randomly divided into 2 groups: the study group (40 patients) and the control group (26 patients). Patients of the study group and the control group underwent comprehensive etiopathogenetic and symptomatic treatment according to the profile of their underlying disease. All patients were prescribed therapeutic nutrition (a variant of the standard diet according to the profile of the underlying disease) according to the Order of the Ministry of Health of the Russian Federation no. 330, dated 05.08.2003, "On measures to improve medical nutrition in medical and preventive institutions of the Russian Federation" (with amendments and additions). Patients of both groups received a variant of the standard diet [3], according to the content and clinical and hygienic characteristics that corresponded to the norms of therapeutic nutrition according to the order of the Ministry of Health of the Russian Federation no. 395n, dated 21.06.2013, "On approval of the norms of therapeutic nutrition". In accordance with this order, 27 g of SBCS enriched with calcium of dairy origin were introduced into the daily diet of patients of this study group. 26 patients of the control subgroup received a similar sparing diet indicated in the above-mentioned order of the Ministry of Health of Russia with the inclusion of SBCS, but not enriched with calcium.

A specialized SBKS product enriched with calcium of dairy origin has the following indicators of nutritional value per 100 g of the product: protein — 40 g, fat (vegetable) — 20 g, total carbohydrates — 30 g, which include dietary fiber in the amount of 4 g; calcium — 1.85 g. The energy value is 452 kcal per 100 g. The SBKS product is a component of the preparation of ready meals (an integral part of the recipe of dairy and dairy-free porridges, slimy soups, dough dishes, omelets, vegetable dishes, desserts, drinks), was introduced into the dish in accordance with the technology of its preparation<sup>1</sup> [4].

The present clinical studies to evaluate the effectiveness of a specialized dietary therapeutic and dietary preventive nutrition product of a dry protein composite mixture enriched with calcium of dairy origin were conducted for 12 weeks and met the requirements of the Methodological Guidelines of the Ministry of Health of the Russian Federation no. 28-1/2406, dated 01.09.2016, "Procedure for conducting studies of the effectiveness of specialized dietary therapeutic and dietary preventive food products".

Before the study, all patients signed a voluntary informed consent to conduct the study with the researchers' guarantee of non-disclosure of patients' personal data.

Statistical processing of the results of the study was carried out using a single-factor analysis of ANOVA. There were significant ( $p < 0.05$ ) differences in the indicators (average values) of the study group and the control group.

## Results and their discussion

The dynamics of clinical manifestations of malabsorption syndrome in patients with certain diseases of the digestive organs included in the study group and the control group during all 12 weeks of this work indicates the priority of results in patients of the study group.

Thus, recovery or improvement of appetite in patients in the study group was observed by the planned end of work in 37 out of 40 people (in the control group — 15 out of 26 patients). Laboratory-recorded improvement of impaired absorption in the small

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<sup>1</sup> Interstate Standard. GOST 33933-2016. "Products for diet therapeutic and diet preventive nutrition. Dry complex protein blends. General specifications". Moscow, 2019. (In Russian)

intestine according to coprological studies, biochemical indicators of the content of total protein, albumin, vitamins, minerals in the blood was determined in the study group in 36 out of 40, in the control group in 19 out of 26 patients. Positive dynamics of body weight of patients was observed in all patients of the study group and the control group. At the same time, the reduction in the number of patients with protein-energy deficiency in the study group for 12 weeks of the study decreased from 18 to 12, in the control group from 13 to 11. The number of patients with detected steatorrhea and creatorrhea decreased in the study group from 35 to 24 patients, in the control group from 24 to 20 patients. Improvement of well-being as a result of complex treatment carried out during 12 weeks was observed in all 66 patients included in the study, however, according to the criteria of the SF-36 quality of life questionnaire [6], the average increase in physical functioning indicators in the study group was  $+21.3 \pm 6.8\%$ , in the control group  $+15.7 \pm 6.0\%$ , general health in the study group was  $+8.3 \pm 0.8\%$ , in the control group  $+7.0 \pm 6.6\%$ , viability, respectively  $+12.7 \pm 4.1\%$  and  $9.6 \pm 0.8\%$ , mental health, respectively  $+18.8 \pm 5.6\%$  and  $+13.8 \pm 8.7\%$ . All comparisons between the groups are statistically significant ( $p > 0.05$ ).

The positive effect of therapeutic nutrition, enhanced with a mixture of protein composite dry, enriched with calcium of dairy origin, on the main pathogenetic mechanisms of metabolic disorders in malabsorption syndrome in the examined patients is proved, first of all, by the restorative dynamics of the indicators of protein supply of the body. Thus, the increase in the provision of the body with a common pool of protein and, moreover, its main fraction for metabolism — albumin is especially noticeable (see Table). In patients of the study group, the increase in the concentration of proteins in the blood is significantly ( $p > 0.05$ ) ahead of this process in patients of the control group. Although it is necessary to objectively positively evaluate the dynamics under consideration in patients of the control group, whose diet, as well as in the control group, is enhanced with protein, but without combination with calcium.

The increased protein-calcium metabolism in patients with malabsorption syndrome, shown in this work, of course, contributed to the improvement of the functional viability of enterocytes for the absorption of many nutrients, including vitamins and minerals, the deficiency of which is directly involved in the formation of many clinical manifestations of malabsorption syndrome in patients with digestive diseases [6]. The following materials are proof of the above provisions.

Considering that a significant number of patients with malabsorption syndrome showed signs of protein deficiency at the beginning of the study, including hypoalbuminemia, which forms the development of many clinical manifestations of malabsorption syndrome. This to a certain extent explains, along with a decrease in the iron content in the body of patients, the pathogenesis of anemia in 34 out of 66 examined patients. Complex therapy with the inclusion of a specialized SBCS product, of dairy origin, should be considered in patients not only in the study group, but also in the control group, as the leading therapeutic factor of membrane-stabilizing action to improve many absorption processes in the small intestine, including iron absorption. It is important to note that we observed more noticeable positive trends in restoring serum iron deficiency in women of both groups in our study. This, perhaps, can probably speak of higher phylogenetically determined adaptive abilities of the female body, especially middle-aged and elderly, who experience regular blood loss during life, and, accordingly, iron loss [7]. In malabsorption

Some laboratory indicators of metabolic processes in the study and control groups of patients (blood tests)

Indicators	Standard	Start of the study (study group / control group)	Week 8 (research group / control group)	Week 12 (study group / control group) (end of study)
Total protein	66–87 g/l	41.4±6.6 / 42.2±6.1	52.9±6.4 / 51.4±6.5	69.7±7.1/* 56.6±6.3
Albumins	55.8–66.1 %	32.7±5.9 / 33.0±5.2	40.4±5.3 / 41.7±5.5	53.8±6.1/* 45.72±5.4
Total calcium	2.15–2.5 mmol/l	1.0±0.2 / 1.1±0.5	1.6±0.5 / 1.3±0.5	2.4±0.4/* 1.3±0.4
Ionized calcium (free)	1.16–1.32 mmol/l	0.4±0.11 / 0.5±0.1	0.7±0.15 / 0.6±0.1	1.1±0.12 / 0.7±0.09
Calcium-creatinine coefficient (urine tests)	0.03–0.93 mmol/mmol	0.01±0.007 / 0.01±0.008	0.02±0.007 / 0.02±0.004	0.06±0.008/* 0.02±0.006
Magnesium	0.66–1.07 mmol/l	0.42±0.07 / 0.48±0.05	0.58±0.07 / 0.55±0.05	0.96±0.05/* 0.57±0.07
Iron	Male: 11–28 mmol/l Female: 6.6–26 mmol/l	7.6±0.04 / 7.9±0.07	9.2±0.08 / 8.9±0.1	10.8±0.2 / 9.7±0.1
Vitamin B1 (thiamine)	45–103 ng/ml	24.8±1.9 / 27.3±2.4	29.3±2.0 / 29.7±3.1	44.0±1.8/* 33.1±2.7
Vitamin B2 (riboflavin)	70–370 ng/ml	51.1±5.5 / 50.6±4.8	59.8±4.7 / 57.3±5.1	67.4±7.4 / 59.1±6.2
Vitamin D	25–80 ng/ml	6.8±0.6 / 7.2±0.5	8.4±1.1 / 8.8±0.9	18.2±3.6/* 10.8±4.0
Vitamin E (tocopherol)	5–18 mcg/ml	0.8±0.06 / 1.0±0.4	2.6±0.7 / 2.0±0.5	3.9±0.4/* 2.4±0.6
Vitamin A (retinol)	0.3–0.8 mcg/ml	0.06±0.004 / 0.07±0.007	0.16±0.06 / 0.11±0.007	0.34±0.008 / 0.29±0.008

Note: \* — comparison of the indicators of the study group and the control group are statistically significant (p > 0.05).



syndrome, this function is reactivated with additional intake of protein from a specialized SBCS product into the body.

The concentration of magnesium in the blood during the dietary treatment of patients with malabsorption syndrome significantly increased in patients of the study group ( $p > 0.05$ ). It is known that hypomagnesemia indicates a pronounced deficiency of magnesium in the body, as a factor that can cause multiple adverse processes in the body: deterioration of microcirculation in organs and tissues, impaired blood clotting, etc. [8]. This is especially significant in conditions of protein metabolism disorders, especially with hypoalbuminemia [9], which we observed in the development of malabsorption syndrome in the examined patients. Diet therapy with the inclusion of a specialized SBCS product enriched with calcium of dairy origin in the diet significantly “leveled” the indicators of protein metabolism, which, accordingly, had a favorable effect on the concentration of magnesium in the body of patients. Similar dynamics was not observed in patients of the control group.

Important for understanding the therapeutic effects of inclusion in the diet of patients with malabsorption syndrome of a specialized SBCS product enriched with calcium of dairy origin were the materials of the study of some vitamins in malabsorption syndrome, accompanied by a significant decrease in the concentration in the body of all of the vitamins studied by us (see Table). There is literature evidence that even with a mild violation of the absorption activity of the small intestine, hypovitaminosis develops in the “first rows” of metabolic dysfunctions [10]. We have seen this in this paper (see Table). However, the increased provision of the body with dietary protein in combination with calcium of dairy origin made it possible to achieve a noticeable positive dynamics of all studied vitamins in both groups of patients, but to a greater extent in patients of the study group. At the same time, it is important to note that statistically significant positive dynamics ( $p > 0.05$ ) in the study group compared with the control group was noted when the body of patients with malabsorption syndrome was replenished with vitamin B1 (thiamine), vitamin D and vitamin E (tocopherol). It is the deficiency of these vitamins that is, as it were, a catalyst in the metabolic reactions of the formation of pathological processes that form the malabsorption syndrome in the studied diseases of the digestive organs [10]. The combination of dietary protein and calcium of dairy origin, as studies show, reliably restore disorders and to a certain extent complement drug therapy in relieving the pathogenesis of malabsorption syndrome.

As can be seen from the results of the study, SBCS included in the diet of gastroenterological patients with malabsorption syndrome had a markedly beneficial effect on reducing the severity of malabsorption syndrome, both in clinical manifestations and according to the results of biochemical indicators of metabolic processes. At the same time, a comparative analysis of the dynamics of all the studied signs of malabsorption syndrome showed that the specialized SBCS food product enriched with calcium of dairy origin, as part of the daily diet of patients, was noticeably ahead in its therapeutic and restorative effect on the mechanisms of malabsorption syndrome formation in patients of the study group. It is known that Ca, as the most important mineral macronutrient involved in many metabolic reactions and physiological functions of the body, gives stability to cell membranes, including enterocytes [11] and, with its increased content in the diet, improves the functional viability of enterocytes faster, although it moderately inhibits the absorption of some nutrients, for example iron.

Strengthening the dietary intake of patients with malabsorption syndrome with an additional amount of milk-derived Ca in combination with high digestibility dietary protein, as can be seen, significantly increases the absorption activity of the small intestine mucosa for most of the food ingredients studied in this study. That is why the patients in the study group had an increase in the concentration of many indicators of impaired metabolism, including total protein, albumin, iron, magnesium, and vitamins, faster than in the control group of patients. The indicated processes served as sanogenetic conditions for the degradation of the symptoms of malabsorption syndrome, faster in the study group than in the control group.

In this regard, attention should be paid to the temporal characteristics of the relief of signs of malabsorption syndrome in the examined patients. We are talking about the fact that in the interim studies (after 8 weeks) we received minimally noticeable improvements in the studied indicators, but by the end of the established study time, i. e. by the end of the 12<sup>th</sup> week of treatment of patients, both clinical and laboratory dynamics of signs of malabsorption syndrome acquired positive reliable indicators in all 40 patients, however, not for all studied indicators, as noted above. But, at the same time, the results of the work give reason to believe that the continuation of over 12 weeks of dietary treatment of patients with diseases of the digestive system, accompanied by malabsorption syndrome, can provide a further beneficial effect of calcium-enriched SBCS of dairy origin on the recovery processes in the mucous membrane of the small intestine and the progressive normalization of tissue metabolism and, accordingly, the clinical condition of patients.

It is important to note that in 2020–2021, a large-scale scientific study was conducted to study the clinical efficacy of SBCS enriched with calcium of dairy origin in various non-communicable diseases. A small fragment of the indicated study was the “gastroenterological unit”, the results of which are presented in this publication. In a number of other diseases of the liver, lungs, cardiovascular system, kidneys, etc., in the therapeutic nutrition in which SBCS enriched with calcium of dairy origin were used, equally significant positive results were obtained.

## Conclusion

The use of SBCS enriched with calcium of dairy origin as part of the dietary program of complex therapy of patients with digestive diseases complicated by malabsorption syndrome was able to obtain a good clinical effect of the course of malabsorption syndrome, confirmed by the improvement of laboratory evidence of various disorders of metabolic processes accompanying malabsorption syndrome and determining a variety of unfavorable clinical prospects for this violation of the digestive conveyor. The widespread use in clinical practice of SBCS enriched with calcium of dairy origin can increase the therapeutic effectiveness of drug treatment of patients with gastrointestinal pathology complicated by malabsorption syndrome.

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### **Белковая композитная сухая смесь, обогащенная кальцием молочного происхождения, и ее использование в диетическом лечении некоторых заболеваний органов пищеварения, сопровождающихся синдромом мальабсорбции**

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Статья посвящена исследованию по оценке эффективности диетотерапии со включением специализированного пищевого продукта, смеси белковой композитной сухой, обогащенной кальцием молочного происхождения, у больных с синдромом мальаб-

сорбции. Обследовано 66 больных с различными заболеваниями органов пищеварения (хронический атрофический гастрит, состояние после резекции желудка, хронический панкреатит, энтеропатии различного генеза), осложненными синдромом мальабсорбции, в возрасте от 47 до 79 лет. Все больные были разделены на две группы: группа исследования (40 больных) и группа контроля (26 больных). Всем больным проводилось комплексное лечение по профилю их основного заболевания, а также назначалось лечебное питание со включением 27 г смеси белковой композитной сухой. Для больных группы исследования смесь была обогащена 1,85 г кальция молочного происхождения. Продолжительность лечения — 12 недель. У больных группы исследования в сравнении с группой контроля статистически достоверно улучшились все клинические признаки энтеральной недостаточности, активизировалась всасывательная функция энтероцитов, ускорилась динамика восстановления метаболических расстройств. Исследование впервые показало, что использование смеси белковой композитной сухой, обогащенной кальцием молочного происхождения, в составе диетической программы комплексной терапии больных с синдромом мальабсорбции достоверно улучшает функциональное состояние тонкой кишки, обеспечивает быструю динамику регресса клиники синдрома мальабсорбции и метаболических нарушений организма больных.

*Ключевые слова:* синдром мальабсорбции при заболеваниях органов пищеварения, диетотерапия, смесь белковая композитная сухая, обогащенная кальцием молочного происхождения.

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