ORIGINAL RESEARCH

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Improved wound healing after oral application of specific bioactive collagen peptides

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ABSTRACT

Wound healing is very important after surgery and undisturbed closure of wounds is sometimes a major problem. Intensive efforts are made to improve wound healing using numerous approaches. In recent years, the oral application of specific bioactive collagen peptides has demonstrated positive effects on matrix synthesis and skin physiology. In this observational trial, their impact on wound healing was investigated in a group of 22 (12 verum/10 placebo) patients with postsurgical wounds and a second group of 20 (10 verum/10 placebo) patients with badly healing wounds. In both groups, the patients treated with bioactive collagen peptides had a clearly better outcome regarding wound healing compared to the placebo groups who showed suboptimal or bad results in the majority of cases. No side effects or intolerance to the product were reported. The results of this investigation confirm the positive impact of collagen peptides on wound healing. These data suggest this product can be used to improve wound healing, even in cases where normal wound healing is expected, and to achieve a better aesthetic outcome.

Keywords

Bioactive collagen peptides
Nutritional supplement
Skin
Wound healing

Introduction

After surgical intervention, the primary focus of the surgeon and patient is efficient wound healing, particularly as regards the aesthetic result. Undisturbed closure of wounds is also important medically.

Wound healing is often prolonged or extremely difficult in patients with comorbidity (e.g., diabetes or vascular disease) and poses a challenge for the treating physician. There is also overall agreement in the surgical world that there is room for improvement in the general area of wound healing, for example as regards keloid.

In cases of initially normal wound healing, a change in the progress of wound closure is sometimes observed and often depends on individual circumstances. Topical applications are commonly used to treat badly healing wounds, with oral therapies also employed in recent years.

Animal studies have confirmed the positive effects of orally administered collagen peptides resulting in accelerated epithelialization and shortened wound healing time with improved angiogenesis, as well as enhanced wound healing in patients with diabetes [1, 2]. Recently, the favourable influence of specific bioactive collagen peptides on matrix synthesis and skin physiology has been demonstrated in several preclinical and clinical studies at a high scientific level. Experimental studies have also shown that collagen peptides are chemotactic for skin fibroblasts [3], increase the migration and growth of mouse skin fibroblasts [4], and enhance cell proliferation and hyaluronic acid synthesis [5].

Collagen peptides are absorbed in the gut, distributed by the blood stream, and accumulate in the skin where they stimulate fibroblasts to produce dermal extracellular matrix components. Clinical trials have demonstrated their positive effect on skin physiology [6, 7].

Clinical evidence on the efficacy of orally administered collagen peptides for wound healing has not been available to date. Therefore, the impact of specific bioactive collagen peptides on normal and disturbed wound healing was investigated in the current study.

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Material and methods

VERISOL® (GELITA AG, Germany) is a special collagen product for oral application and consists of pure bioactive

collagen peptides optimized for skin health. It is composed of different specific collagen peptides of porcine or bovine type I collagen obtained using a special hydrolysis method. The product is clearly defined by numerous specific collagen peptides with an average molecular weight of 2.0 kDa and a specific amino acid profile. It is absolutely safe and has been certified as GRAS (generally recognized as safe) by the FDA.

The present trial was divided into two parts. Enrolled patients were separated into a group which was due to undergo a surgical intervention and did not have any conditions that could affect wound healing (normal group, NG) and a second group which had undergone a surgical intervention and had conditions that could affect wound healing and a minimum of one badly healing wound (disturbed group, DG). Patients in both groups were then randomly assigned to a placebo or a verum group. A daily dose of either placebo or verum was taken by the patients for the entire healing period. The NG group received a maximum of 45 daily doses of 5.0 g VERISOL®, while the DG group received a maximum of 90 daily doses of a higher dose of 10.0 g VERISOL® on account of their worse tissue conditions. The placebo groups received equivalent doses of maltodextrin (5.0 g and 10.0 g). All patients provided informed consent to this study.

The NG group consisted of 22 female patients aged between 24 and 67. All had dermal alterations such as papillary dermal naevus or epidermal keratosis, mostly on the upper part of the body (head, neck, chest and abdomen), which were removed at a dermatological practice by a physician using excision or a scraping technique. Excisions were sutured while scraped wounds were left to secondary wound healing. No wound was larger than 5×2 cm. Photographs were taken before the intervention, directly after the procedure, and after 4–6 weeks (Figs. 1 and 2). The NG patients were then randomized to either a verum (n=12) or placebo (n=10) group. Intake of the daily dose of verum or placebo started on the day of surgery.

The DG group consisted of both male and female patients aged between 28 and 82. All had badly healing wounds after surgical interventions, injuries or vascular problems associated with common conditions such as diabetes or arterial occlusive disease (AOD), and were randomized to a verum (n=10) or placebo (n=10) group at a surgical practice. The wounds were located mostly on the lower body (abdomen, legs and lower back). Successful healing required a germ-free wound and constant dressing changes for a dry wound. Thus, the first step was debridement and decontamination of the wound surface by the physician. In case of accompanying inflammation, oral antibiotic therapy was initiated and continued until all signs of inflammation had resolved. Photographs were taken before debridement and at the end of the healing period (6–12 weeks) (Figs. 3 and 4). Intake of the daily dose of verum or placebo started at the first visit.

Referring to the photographs, four physicians experienced in the field of wound healing evaluated aesthetic outcome and wound healing in the NG and DG groups as very good, good, suboptimal or bad according to:

- Signs of inflammation (redness, hyperthermia and purulence)
- Surface condition (waviness, roughness, rosy or pale skin colour, elasticity and moisture)
- Scarring or keloid
- Haematoma
- Skin perfusion
- Internal skin discoloration.

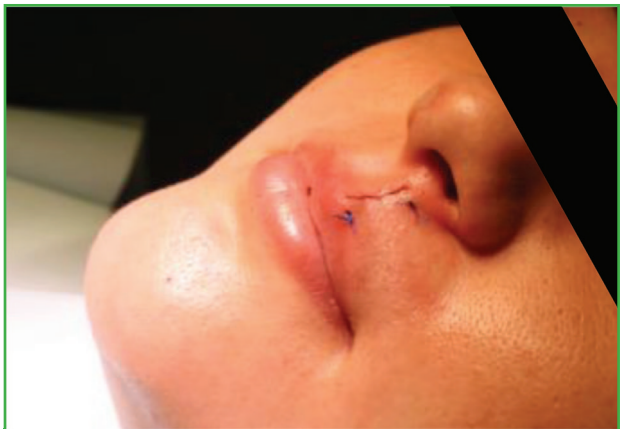

Figure 1 - Upper lip after naevus removal in a patient in the NG group

Figure 2 - Excellent result following naevus removal after 4 weeks of VERISOL® treatment in the patient shown in Fig. 1

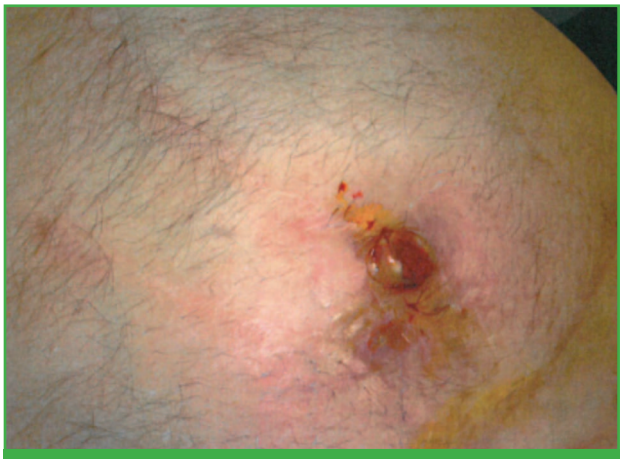

Figure 3 - Dehiscence after hernia operation in a patient in the DG group

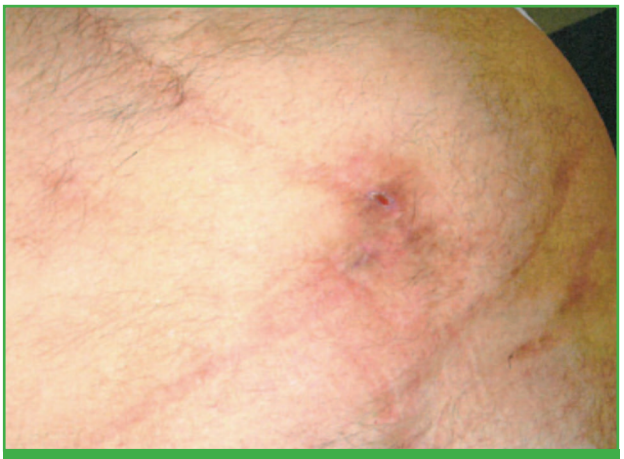

Figure 4 - Very good result following hernia operation after 6 weeks of VERISOL® treatment in the patient shown in Fig. 3

Results

No side effects or intolerance to the collagen product were reported. Patients complied with the physician instructions given at the first visit before the intervention or wound debridement.

All wounds closed and healed in an adequate time frame. None of the participants had any problems regarding secondary bleeding, infection or purulence. Thus, the only objective assessment criterion was the appearance of the healed wound in the photographs evaluated by an expert who was blinded to the treatment received by the patient.

In both the NG and DG groups, patients who had been treated with the specific collagen peptides showed clearly better results than those who had received placebo.

NG group

Six of the 12 patients in the NG verum group had very good results, while the other six had good results as evaluated by the physicians. The patients themselves were very satisfied with their healed wounds and none had a suboptimal or bad result. These findings demonstrate that 100% of the patients in the verum group had a good or very good outcome (Fig. 5).

In contrast, none of the 10 patients in the placebo group was rated as having a very good outcome. Five of the patients had good results (50%), while three had suboptimal results and two had bad results. These findings demonstrate that 50% of the patients in the placebo group had a bad or suboptimal aesthetic outcome (Fig. 6).

DG group

Three of the 10 patients in the DG verum group were evaluated by the physicians as having very good results, while the other 7 patients had good results. The patients in this group

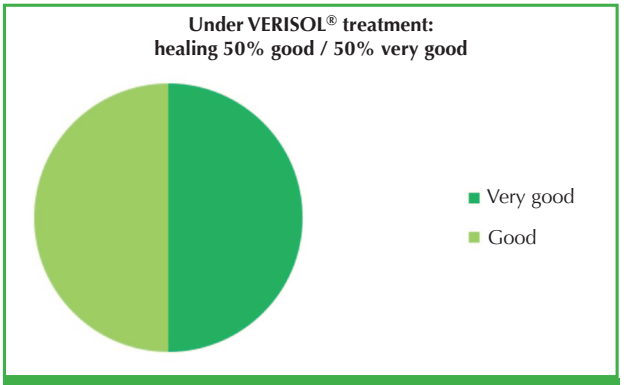

Figure 5 - Results in the NG verum group (n=12 patients)

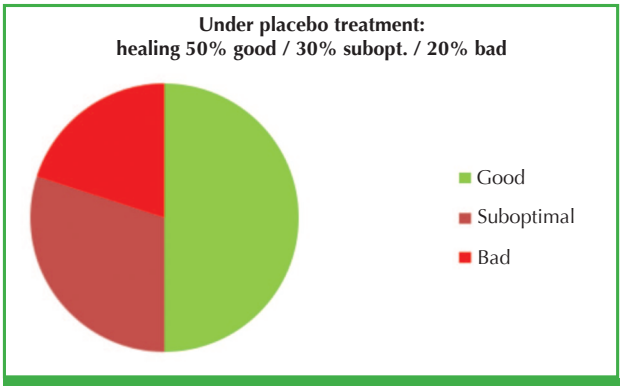

Figure 6 - Results in the NG placebo group (n=10 patients)

were very satisfied with the outcome of their wound healing and none had suboptimal or bad results. These findings show that 100% of the patients in the verum group had a good or very good outcome (Fig. 7).

In contrast, none of the 10 patients in the placebo group was rated as having a very good outcome. Two of the patients had good results (20%), while five had suboptimal results and three had bad results. These findings show that 80% of the patients receiving placebo had a bad or suboptimal outcome (Fig. 8).

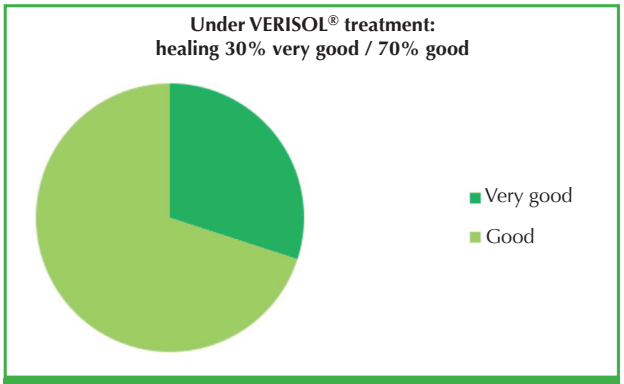

Figure 7 - Results in the DG verum group (n=10 patients)

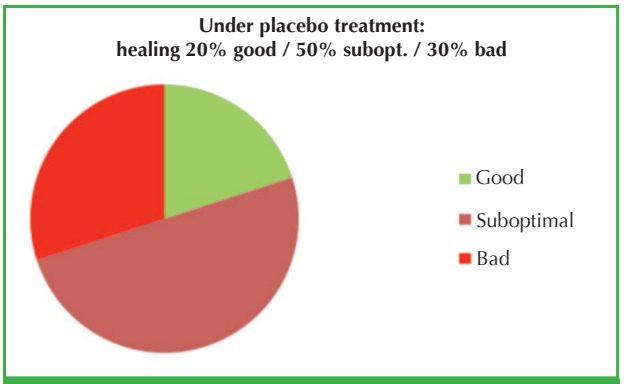

Figure 8 - Results in the DG placebo group (n=10 patients)

Conclusion

The results of this observational trial showed positive effects on wound healing after the oral application of bioactive collagen peptides. In the NG placebo group, none of the patients had a very good result, while 50% had a suboptimal or bad aesthetic outcome. Likewise, none of the patients in the DG placebo group showed a very good result, while more than 75% had a suboptimal or bad outcome.

The pronounced effect of bioactive collagen peptides on connective tissue has been demonstrated in several clinical studies. The positive effect on the skin is mainly due to a direct impact on dermal extracellular matrix turnover with a subsequent significant increase in collagen and elastin synthesis [7]. Accelerated epithelialization and shortened wound healing with improved angiogenesis, even in diabetic rats, has been observed in animal experiments [1, 2]. Other studies on humans have also confirmed stimulation of granulation tissue and proteases, a decrease in inflammation parameters, and improved perfusion especially with regard to microcirculation [8, 9]. These findings might explain the striking results for wound healing seen in this trial.

In summary, these findings show that these specific collagen peptides have a positive impact on wound healing, and suggest that these bioactive collagen peptides should be administered for better results even in cases where wound healing is expected to be normal. However, it must be noted that these results are only valid for VERISOL®, as other collagen hydrolysates or collagen peptides might show different outcomes.

Additional studies on larger populations, including patients with wound healing disorders, will be conducted and hopefully confirm these initial results.

Conflict of interest

Hans-Christoph Knefeli is an employee of GELITA AG, Uferstrasse 7, Eberbach, Germany. Benjamin Durani declares that he has no conflicts of interest.

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Trophological status and quality of life in infants administered probiotic enterococci

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ABSTRACT

This article presents the results of a study on the effectiveness of oral administration of the probiotic *Enterococcus faecium* L3 on the trophological status of infants and their quality of life. Over 10 weeks during autumn and winter, we observed 26 children aged 2–12 months in a specialized (psychoneurological) children's orphanage. Children were randomly divided into a main group (n=15) and a comparison group (n=11). The groups were similar regarding sex (p=0.62) and trophological status (body weight, Chulitskaya index and body mass index). The average ages of the children in the main and comparison groups were 4.3±0.4 and 6.4±0.18 months, respectively (p=0.02). In addition to their regular food, children in the main group received 5 ml of a liquid probiotic form of *E. faecium* L3 10^8 CFU/ml twice a day. Indicators of trophological status were assessed every 2 weeks, change in quality of life according to the QUALIN questionnaire at baseline and at study completion, incidence of acute respiratory infections, and completion of planned vaccinations. Children in the main group showed increased growth rates during the first 4 weeks of the study and also an improved Chulitskaya index during the first 8 weeks of the study. Children in the main group had fewer acute respiratory infections, improved quality of life and more planned vaccinations.

Keywords

Infants
Trophological status
Quality of life
Probiotic strain of Enterococcus
Incidence
Acute respiratory infection
Planned vaccination

Introduction

The trophological status of a person describes their state of health and physical development in relation to the optimal assimilation of nutrients. In the trophological approach, nutritional values are assessed as the consumption of a particular set of essential nutrients together with the complex interaction of nutrients with the digestive system and the body as a whole, including metabolic parameters and adaptation reserves. Disturbance of the internal environment of human systems can have negative consequences with a decline in nutrient absorption and an increase in the production of toxic biologically active substances [1].

As children's pathological conditions are often associated with malnutrition, it is very important that malnutrition is diagnosed and treated at an early age [2]. Timely diagnosis, treatment strategy and prognosis are based on the results of dynamic assessment of trophological status [3]. Correction of malnutrition, depending on aetiology, can be achieved by various approaches. Where breastfeeding is not possible, infant formula and food for artificial feeding provide the growing body with essential nutrients [4]. Inclusion of probiotic strains into the infant formula or supplementation of their diets with probiotic bacteria optimizes metabolism and increases resistance to infection due to the actions of probiotics as biocatalysts of many vital processes in the body [5]. Differences in the effectiveness of probiotic agents used to prevent or treat infectious and somatic diseases are determined by the characteristics of the probiotic strains [6, 7]. Numerous investigations have demonstrated the therapeutic

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and prophylactic effectiveness of probiotic strain *Enterococcus faecium* L3 in paediatrics [8, 9]. The aim of this study was to investigate the effect of a liquid form of the probiotic *E. faecium* L3 on trophological status and quality of life (QoL) in infants.

Materials and methods

A total of 26 children in the first year of life were observed in St. Petersburg specialized orphanage No. 16 for 10 weeks from November 2014 to February 2015. This orphanage cares for the children of socially disadvantaged parents. During pregnancy, most of the mothers consumed inappropriate drugs, alcohol and nicotine, and had various illnesses including sexually transmitted diseases (including HIV, hepatitis C and syphilis) and in some cases tuberculosis. The physical development indicators of the children at birth were characterized by low values due to the high incidence of prematurity, drug withdrawal syndrome at birth and intrauterine growth retardation. In the first months of life, these children received antibiotic treatment (prophylactic treatment for syphilis), antiretroviral prophylaxis (Viramune, Epivir, Retrovir) and pneumocystis pneumonia prophylaxis (Biseptol). During the first year of life, the physical development of children with intoxication at birth is delayed and they are underweight and stunted [10].

The criteria for enrolment of children in the study were age 2–12 months and absence of chronic diseases, serious congenital malformations and functional insufficiency of organs or systems. The children were randomly divided into two groups. The main group (n=15) included eight boys and seven girls, while the control group (n=11) consisted of seven boys and four girls. The groups did not differ significantly by sex (p=0.62), initial average body weight (p=0.07), Chulitskaya index (used to determine the trophological status of infants) (p=0.98) or body mass index (BMI) (p=0.66) (Table 1). The mean age (±SD) of children in the main group was 4.3±0.4 months, and 6.4±0.18 months (p=0.02) in the comparison group.

Twice a day, children in the main group received 5 ml of a liquid form of the probiotic *E. faecium* L3 (No. RU. 77.99.26.009.E.002272.02.11) with a titre of bacteria of not less than 10^8 CFU/ml. The probiotic *E. faecium* L3 was added to the infant formula. Children in the comparison group received the normal diet for their age.

The effectiveness of the addition of *E. faecium* L3 was compared in the two groups of children by assessing: (1) trophological status (evaluated at baseline and every 2 weeks for 10 weeks): body weight, body length, arm circumference, chest circumference, hip circumference, lower leg circumference, BMI, Chulitskaya index and Erismann index; (2) QUALIN [11], a quality of life questionnaire for paediatricians (assessed at baseline and at study completion); (3) the number of cases of acute respiratory infections (ARIs) during the study (the absolute number and percentage of children affected in each group); and (4) the absolute number and percentage of vaccinated children in each group.

The trophological status of the children was based on assessment of the Chulitskaya index, Erismann index and BMI. The Chulitskaya index is traditionally used by paediatricians to evaluate the nutritional status of children in the first year of life. Normal values are in the range 20–25 with a decrease in the index indicating malnutrition [2]. The Chulitskaya index was calculated using the formula: Chulitskaya index=3×arm circumference+thigh circumference+tibia circumference–body length (cm). The Erismann index was calculated using the formula: Erismann index=chest circumference–(0.5×length) (cm). BMI was determined using the formula: BMI=weight (kg)/length $(m)^2$ [12].

The QUALIN questionnaire for evaluating the quality of the first year of life in children consisted of 33 questions on: (1) behaviour and communication (13 questions); (2) ability to stay alone (5 questions); (3) family surroundings (4 questions); and (4) neuropsychological development and physical health (11 questions). Each question included six possible answers: 'Definitely not' (1 point), 'Rather no than yes' (2 points), 'Yes and no' (3 points), 'More likely than not' (4 points), 'Definitely yes' (5 points) and 'I do not know' (0 points). The average of each of these four indicators of QoL and the average value of the sum of all 33 questions (average value) were calculated. We counted the total number of points for each child and the average number of points in both groups. QUALIN also provides an 'overall assessment' of the child's QoL by assigning numbers in the range from 1 ('very bad') to 10 ('excellent'). The results of the estimations were converted to a 0–5 scale where 1 and 2 corresponded to 1 point, 3 and 4 to 2 points, 5 and 6 to 3 points, 7 and 8 to 4 points, and 9 and 10 to 5 points. The result was called the 'approximate overall assessment' and the average value was determined in both groups of children. We analysed seven QoL indicators in total.

The results were subjected to statistical analysis using Student's t-test and Pearson's χ^2 test. Differences between the results obtained in the groups under study were considered significant at $p<0.05$.

Results

Comparison of the main indicators of trophological status (weight and body length) revealed a marked increase in the weight of children throughout the study and the absence of significant differences between the groups (Table 1). The body length of the children also increased. The baseline body length in the comparison group was higher than in the main group, but this difference later disappeared, indicating accelerated growth in children in the main group. The increase in the average body length of the comparison group early in the study was slower than in the main group of children (Table 1).

Trophological status criteria	Comparison group (n=11)	Main group (n=15)	Student's t	*p* Value
Baseline data				
Body mass (g)	6340±1402	5386±1168	1.89	0.07
Length (cm)	62.2±4.7	56.8±5.1	2.78	**0.01**
Body mass index (kg/m^2)	16.2±1.9	16.5±1.6	-0.44	0.66
Chulickaya index (cm)	15.5±5.6	15.4±4.2	0.03	0.98
Erismann index (cm)	10.2±1.5	12.2±2.1	-2.66	**0.02**
At 2 weeks				
Body mass (g)	6563±1387	5635±1170	1.85	0.08
Length (cm)	62.9±4.5	58.4±4.9	2.38	**0.03**
Body mass index (kg/m^2)	16.4±1.9	16.3±1.6	0.13	0.89
Chulickaya index (cm)	16.0±5.7	16.3± 4.6	-0.15	0.88
Erismann index (cm)	10.2±1.5	12.0±1.7	-2.82	**0.01**
At 4 weeks				
Body mass (g)	6717±1321	5874±1188	1.71	0.10
Length (cm)	63.4±4.4	60.0±4.8	1.85	0.08
Body mass index (kg/m^2)	16.6±1.8	16.2±1.6	0.64	0.53
Chulickaya index (cm)	16.3±5.9	16.6±4.4	-0.16	0.87
Erismann index (cm)	10.6±1.5	11.7±1.6	-1.64	0.11
At 6 weeks				
Body mass (g)	6871±1264	6094±1021	1.73	0.10
Length (cm)	64.2±4.4	61.2±3.8	1.83	0.08
Body mass index (kg/m^2)	16.6±1.6	16.1±1.4	0.75	0.46
Chulickaya index (cm)	17.1±6.4	17.8±3.9	-0.35	0.73
Erismann index (cm)	10.8±1.7	11.8±1.3	-1.67	0.11
At 8 weeks				
Body mass (g)	7072±1192	6349±1026	1.66	0.11
Length (cm)	65.0±4.0	62.2±3.8	1.79	0.09
Body mass index (kg/m^2)	16.6±1.4	16.3±1.4	0.59	0.56
Chulickaya index (cm)	17.1±6.1	19.3±3.3	-1.21	0.24
Erismann index (cm)	10.6±1.6	12.0±1.5	-2.26	**0.03**
At 10 weeks				
Body mass (g)	7246±1223	6485±1055	1.70	0.10
Length (cm)	66.0±4.0	63.3±4.0	1.75	0.09
Body mass index (kg/m^2)	16.5±1.5	16.1±1.2	0.77	0.45
Chulickaya index (cm)	18.2±6.5	19.7±3.1	-0.80	0.43
Erismann index (cm)	11.0±1.5	11.9±1.7	-1.41	0.17
Significant *p* values are shown in bold				

Table 1 - Average trophological status data (mean±SD) in two groups of children in the first year of life

Erismann index values were significantly higher in children in the main group at baseline, 2 weeks and 8 weeks (Table 1). There were no significant differences in BMI or the Chulitskaya index between the groups during the study. Chulitskaya index values were below normal throughout the study, reflecting the difficulties treating malnutrition in these patients.

Average growth values were compared throughout the study. There was a reduction in BMI gain in the main group compared to the comparison group. This difference was significant at 2 weeks (–0.15±0.51 kg/m^2; 0.25±0.38 kg/m^2; t=2.13; p=0.04) but not significant at 4 weeks (–0.19±0.59 kg/m^2; 0.13±0.48 kg/m^2; t=1.48; p=0.15), reflecting an overall increase in body length in the main group. Changes in the average increase in the Erismann index in children in the main group compared to the comparison group were characterized by their low values at 4 weeks (–0.33±1.09 cm; 0.46±0.69 cm; t=–2.11; p=0.05) and high values at 8 weeks (0.23±0.46 cm; –0.18±0.40; t=2.40; p=0.03). This indicated greater improvement in the nutritional status of children in the main group than in the comparison group. Changes in the Chulitskaya index indicated accelerated elimination of malnutrition in children in the main group as values from 2 to 8 weeks were higher in the main group than in the comparison group (Fig. 1). The average Chulitskaya index values in the main group significantly increased between the 6th and 8th weeks (1.53±1.77 cm) compared to no increase in the comparison group in the same age group (0.00±1.00 cm; t=2.58; p=0.02). The faster increase in the main group was the result of significantly higher increases in tibia cir-

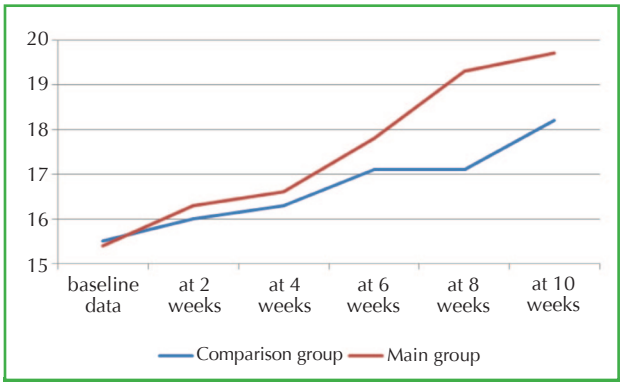

Figure 1 - Chulitskaya index in children of the main and comparison groups. The observation time points are shown on the x axis and index values on the y axis

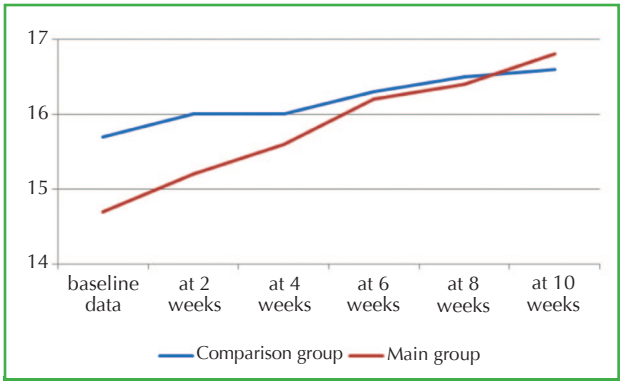

Figure 2 - Lower leg circumference values in children in the main and comparison groups. The observation time points are shown on the x axis and circumference values (cm) on the y axis

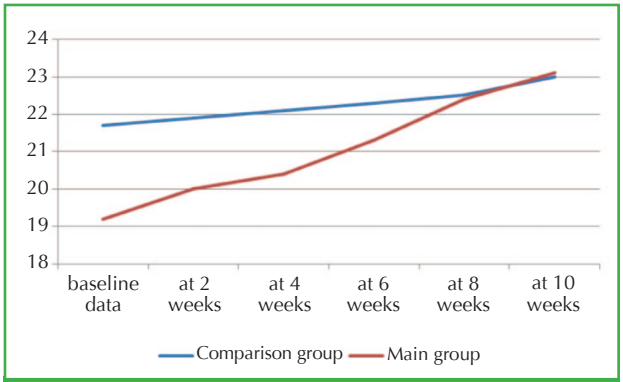

Figure 3 - Thigh circumference in children in the main and comparison groups. The observation time points are shown on the x axis and the thigh circumference values (cm) on the y axis

cumference (Fig. 2) at 4 weeks (0.40±0.47 cm; 0.0±0.0 cm; t=2.8; p=0.01) and 6 weeks (0.61±0.42 cm; 0.23±0.26 cm; t=2.67; p=0.01) and in thigh circumference (Fig. 3) at 2 weeks (0.80±0.62 cm; 0.18±0.25 cm; t=3.11; p=0.005), 6 weeks (0.87±0.69 cm; 0.20±0.33 cm; t=2.94; p=0.007) and 8 weeks (1.07±0.62 cm; 0.18±0.25 cm; t=4.43; p<0.0001). Similar changes were observed in chest and arm circumference values, with a higher gain seen in the main group than in the comparison group. Thus, addition of the probiotic strain *E. faecium* L3 to the diet of infants helped to improve their trophological status.

Analysis of QoL showed significantly higher values (mean±SD) for neuropsychological development and physical health (3.93±0.22; 3.41±0.50; t=3.18; p=0.04) and approximate overall assessment in the comparison group (3.64±0.81; 2.60±0.51; t=4.02; p=0.001) at the beginning of the study (Table 2). After 10 weeks of observation, the values of five of the seven parameters under study were higher in the comparison group than in the main group (Table 2). However, in the comparison group at 10 weeks, only neuropsychological development and physical health demonstrated significantly higher values as compared to baseline (3.93±0.22; 4.17±0.19; t=3.95; p=0.003). In the main group, significant increases were seen in the ability to stay alone (2.58±0.86; 3.28±0.78; t=3.40; p=0.004), neuropsychological development and physical health (3.41±0.50; 3.84±0.38; t=3.08; p=0.008) and approximate overall assessment (2.60±0.51; 4.00±0.00; t=10.70; p<0.001). These data demonstrated significantly better QoL indicators in children of the main group.

During the autumn–winter period, six (66.7%) cases of ARI were observed in the comparison group and only three in the main group (33.3%; p>0.05). Five (45.5%) children in the comparison group and two (13.3%) in the main group had ARIs (p>0.05). Thus, there was a lower incidence of ARI in the main group than in the comparison group.

Routine vaccination also indicated the general health of the children. Seven children (63.6%) in the control group and 11 (73.3%; p>0.05) in the main group were vaccinated during the observation period. Four (36.4%) children in the comparison group and eight (53.3%; p>0.05) in the main group received two or more vaccinations at the same time, indicating that probiotic *E. faecium* L3 improved health indicators in the main group, thus allowing more vaccinations.

Discussion

This work was a continuation of a study on the positive impact of 3-month administration of a liquid form of the probiotic *E. faecium* L3 on the health of infants [13].

The results of the present study confirm the beneficial effects of the administration of the probiotic *E. faecium* L3 on the trophological status of children during the autumn–winter period as a marked acceleration in growth and improvement in nutritional status was seen in the children in the main group (Chulitskaya index and Erismann index).

Quality of life parameters	Compared parameters	Comparison group (n=11)	Main group (n=15)	Student's t	*p* Value
Behaviour and communication	Baseline	3.99±0.51	3.78±0.74	0.82	0.42
	At 10 weeks	4.29±0.21	3.85±0.57	2.40	**0.02**
Ability to stay alone	Baseline	3.60±0.59	3.21±0.70	1.49	0.15
	At 10 weeks	3.62±0.57	3.04±0.70	2.25	**0.03**
Family surroundings	Baseline	3.20±0.74	2.58±0.86	1.93	0.07
	At 10 weeks	3.55±0.51	3.28±0.78	0.97	0.34
Neuropsychological development and physical health	Baseline	3.93±0.22	3.41±0.50	3.18	**0.004**
	At 10 weeks	4.17±0.19	3.84±0.38	2.64	**0.01**
Approximate overall assessment	Baseline	3.64±0.81	2.60±0.51	4.02	**0.001**
	At 10 weeks	4.00±0.00	4.00±0.00	0.0	1.0
Number of points	Baseline	125.9±9.2	113.1±19.3	2.04	0.053
	At 10 weeks	133.9±7.9	120.7±15.4	2.60	**0.02**
Average value	Baseline	3.82±0.28	3.43±0.59	2.04	0.053
	At 10 weeks	4.06±0.24	3.66±0.47	2.61	**0.02**

Significant *p* values are shown in bold

Table 2 - Quality of life (mean±SD) parameters assessed using the Qualin questionnaire in children in their first year of life

The intestinal microbiota responds dynamically to changes in the external environment, including food and weather conditions. Probiotic bacteria can produce hormones, growth factor analogues and neurotransmitters that affect metabolism [14]. The data obtained suggest that the qualitative and quantitative composition of the intestinal microbiota was improved in children of the main group receiving the probiotic. Although the initially higher QoL indicators in the comparison group were possibly explained by the difference in the age of the children in the two groups, during 10 weeks of observation only one of the seven QoL parameters studied in the comparison group improved compared to three of the seven parameters in the main group. Thus, the improved trophological status of the children in the first year of life in the main group indicates the prophylactic value of probiotic of *E. faecium* L3. We also noted a lower incidence of ARIs, increased routine immunization and a marked increase in QoL.

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