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The Effect of GeriLact on Non-Alcoholic Fatty Liver Disease

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Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease which is correlated with overweight, obesity, and insulin resistance. Recently, the use of probiotics has been suggested for these patients as they have considerable outcomes. The aim of the present study is to evaluate the effect of GeriLact on patients with NAFLD.

Method: In this randomized clinical trial, 61 patients with NAFLD were recruited and randomly assigned to groups receiving GeriLact, 500 mg, twice per day, or placebo (with the same dose) for sixty days. Weight, body mass index (BMI), lipid profile, fasting blood sugar (FBS), Alanine aminotransferase (ALT), Aspartate Aminotransferase (AST), and sonographic grading were evaluated before and at the end of the study.

Results: In the GeriLact group, there was a significant decrease in ALT ($p=0.002$) and AST ($p<0.001$) levels, while the placebo group showed a significant decrease only in ALT level ($p=0.01$). There was a significant decrease in cholesterol levels in the intervention group compared to the placebo group ($p=0.01$), but there were no significant changes in FBS, triglycerides, LDL, and HDL levels between the two groups. The fatty liver grade was improved by 63.6% in the intervention group and by 46.4% in the placebo group.

Conclusion: The results showed that probiotics caused significant improvement in ALT, AST, and cholesterol levels but had no effects on FBS, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL). Overall, treatment with GeriLact was found to be effective, safe, with low cost and well-tolerated in the long term use by the patients.

Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in children and adults leading to overweight, obesity, and insulin resistance (1). NAFLD includes a wide range of illnesses associated with excessive fat accumulation in people who have no alcohol abuse. Its severity varies from Steatosis to nonalcoholic steatohepatitis and, ultimately, it can lead to cirrhosis and liver cell cancer (2). About 14% to 30 % of people living in western societies are affected by NAFLD (3).

Obesity has a strong correlation with NAFLD and is a predictor of the advanced stages of the disease. The outbreak of obesity is expected to increase in Iran and the world (4,5). Despite widespread researches about probiotics, there are limited clinical trials on their effects on liver chronic disease and probiotics have been suggested as being effective in improving the metabolic complications of NAFLD by various mechanisms (6,7). So far, limited studies have investigated the effects of probiotics on the treatment of NAFLD in humans.. In a study, the daily consumption of probiotic supplementation

for two months reduced serum levels of liver enzymes such as ALT, GGT, and AST (8). Common NAFLD therapeutic modalities include lifestyle changes, increasing physical activity, and medication therapy (9-11). However, the possibility of long-term physical activity, and lifestyle changes are less likely, while most drugs have side effects that restrict their use. Therefore, new therapies with higher efficacy and fewer complications need to be developed in the future. The use of probiotics can be a convenient and cost-effective way to treat NAFLD and its effectiveness has been proved in some previous studies (8,12,13). However, all studies in this field did not yield consistent results. Previous studies showed that probiotics could improve the metabolic status of patients with NAFLD (14-16). However, a review by Tarantino and Finley found that due to the lack of or limited number of randomized studies with correct methodology, there is no definitive conclusion about the effect of probiotics on NAFLD and there is no definitive clinical decision on the treatment of the disease (17). Ma et al. showed that probiotic therapies can reduce liver aminotransferases, total-cholesterol, TNF-α, and improve insulin resistance in NAFLD patients (18). Therefore, more trials are needed to assess the effect of probiotics on the NAFLD accurately. The purpose of this study was to evaluate the effect of GeriLact on patients with NAFLD.

Materials and Methods

Study type and area

This randomized placebo-controlled trial was conducted on 61 patients with NAFLD who referred to the Gastroenterology Clinic of Ardabil Medical University.

Participants

All participants were divided into two groups; the intervention (n = 33) and placebo (n = 28) groups by random sampling method. All patients referred to a radiologist for performing liver ultrasonography. Fatty liver was diagnosed based on the ultrasonographic diagnostic criteria.

All the ultrasound reports were prepared by the same radiologist.

Inclusion and exclusion criteria

Patients older than 18 years, newly diagnosed NAFLD, Grade 2 and 3 of fatty liver, and treatment-naive patients were included in the study. The patients with digestive diseases, diabetes, rheumatoid arthritis and other rheumatologic diseases treated with immunosuppressive drugs, cholestatic liver disease, advanced liver disease, heart failure, thyroid and kidney diseases, any cause of chronic liver disease other than NAFLD such as positive test for hepatitis B, hepatitis C and autoimmune hepatitis, history of cancer and drug treatment, antibiotic use for two weeks before and during the study, using vitamin supplemental antioxidant, fiber and omega-3 in three weeks before and during the study, pregnancy or lactation, contraceptive use, liver transplantation, and alcohol consumption in the three months before the study were excluded from the sample.

Data collection procedure

All patients signed the written consent form. The general demographic questionnaire including age, sex, physical activity, and other diseases were completed by interviewing all the patients. The usual dietary and exercise recommendations were provided by a medical practitioner using a blind protocol for all patients by providing a written brochure for both groups. The participants' weight and height were measured and their BMI was calculated. The participants were randomly divided into intervention and control groups by nurses working in the

gastroenterology clinic. The patients received medication or placebo using a blind protocol.

Laboratory Measurements

Venous blood samples were taken at the baseline to measure TG, TC FBS, HDL, LDL, AST, and ALT. In addition to the diet and exercise recommendation for both groups, the subjects in the intervention group received daily 2 capsules of 500 mg of GeriLact and the control group received a placebo for 60 days in the same intervals. At the end of the intervention, US was performed again and serum levels of liver enzymes and Lipid profile and body mass index were measured and the results were compared between two intervention and control groups. Tests and sonography were performed free of charge at the beginning of the study by the same radiologist and in the same laboratory. GeriLact is a product of symbiotic drugs used as an oral capsule and it contains a high level of beneficial bacteria (lactobacilli, cassia, acidophilous, langburoum, bifidobacteria, and streptococcus) along with peribiotics fructolucosaccharide (contributing to the growth and activity of probiotics). Gerilact was used in this study as a symbiotic product in capsule form.

Statistical Analysis

The collected data were analyzed by SPSS 16 using the descriptive statistics (frequency, percentage, mean ±standard deviation). The Kolmogorov-Smirnov test was performed to determine the normality of the data. To compare the means in two groups, we used the independent samples t-test. Besides, the qualitative data were compared by using the Chi-square or Fisher exact test. In this study p-value less than 0.05 was considered significant. The CONSORT diagram of the trial is presented in Figure 1.

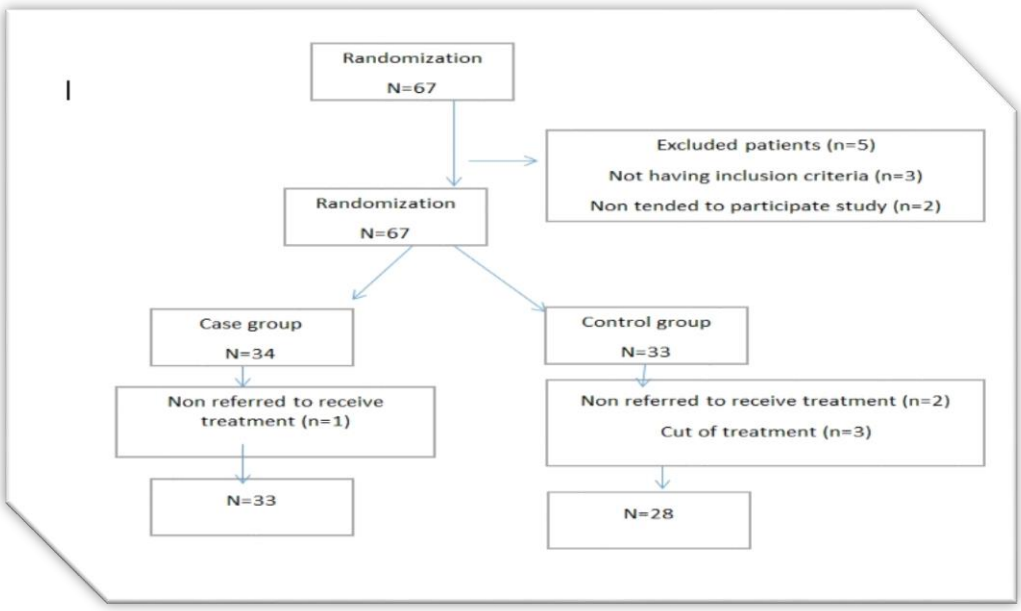

Figure 1. Study design

Results

There was no significant difference in age and sex between the two groups (Table 1). The liver enzyme levels were not significantly different between the two groups before the intervention. However, after the intervention, the medication group had a lower ALT level than the placebo group (Table 2). Compared to the levels of liver enzymes before and after the treatment in the intervention group, there was a significant improvement in ALT ($p = 0.002$) and AST ($p < 0.001$). In the placebo group, only a significant difference was observed in the level of ALT ($p = 0.01$), but the AST variations were not significant. There was no difference between the two groups before and after the intervention in terms of lipid and glucose profile, while the cholesterol level after the intervention was significantly lower in the intervention group than the control group (Table 2).

The AST, ALT and cholesterol variations in the intervention group were significantly higher than the placebo group. However, in other cases, the percentage of the changes was not statistically significant (Table 3).

Probiotics consumption in men significantly improved ALT and cholesterol levels compared to the placebo group but no significant changes were observed among women. The improvement in fatty liver grade in both male and female participants in the intervention group was higher than the placebo group but the difference wasn't significant. Also, comparing comparison of the men and women in the intervention group showed that the improvement in men was higher but no significant (Table 4).

Table 1. Baseline demographic and anthropometric data of the NAFLD patients

Groups		Gerilact		Placebo		p-value
Variables		n	%	n	%	
Sex	male	22	66.7	18	64.3	0.84
	female	11	33.3	10	35.7	
Age Mean ± SD		43.26±11.42		43.72±10.76		0.88
Weight	Before	88.15±14.6		90.75±10.1		0.43
Mean ± SD	After	86.42±13.8		86.7±10.3		0.93
BMI	Before	31.87±5.4		30.83±4.6		0.44
Mean ± SD	After	31.53±5.83		29.1±3.76		0.09

Table 2. Mean level of liver enzymes and lipid profile lipid among all patients in two groups

Groups Variables		Gerilact	Placebo	p-value
AST Mean ± SD	Pretreatment	28.8±9.6	29.8±21.8	0.82
	Post-treatment	23.84±7.5	27.8±19.1	0.28
ALT Mean ± SD	Pretreatment	48.93±33.64	49.2±35.3	0.97
	Post-treatment	31.4±12.7	42.9±29.6	0.04
FBS Mean ± SD	Pretreatment	92.4±12.3	92.4±8.1	0.99
	Post-treatment	90.6±9.4	90±10.1	0.78
TG Mean ± SD	Pretreatment	188.6±62.6	226.7±108.3	0.09
	Post-treatment	189.6±109.3	200.4±90	0.68
CHOL Mean ± SD	Pretreatment	189.2±32.6	190.4±45.1	0.9
	Post-treatment	173.8±37.9	200.7±55.5	0.03
LDL Mean ± SD	Pretreatment	105.43±25.8	106.1±25.1	0.92
	Post-treatment	103.9±29.3	111.03±24.8	0.32
HDL Mean ± SD	Pretreatment	45±12.9	40.2±8.3	0.11
	Post-treatment	41.5±7.4	39.7±10.6	0.44

Table 3. The difference mean of anthropometric indices among the patients in two groups

Groups Variables	Gerilact	Placebo	p-value
Weight	-2.81±2.8	-3.7±3.3	0.48
BMI`	-2.25±2.14	-3.3±3.1	0.38
AST	-14.9±21.3	55.3±3.9	0.02
ALT	-21.1±37.42	-4.9±40.32	0.01
FBS	-1.24±8.72	-2.5±9.9	0.58
TG	-0.11±33.9	-6.2±26.1	0.74
CHOL	-5.7±25.6	5.4±17.1	0.01
LDL	1.46±26.3	6.18±20.6	0.13
HDL	-2.14±17.7	2.1±24.2	0.15

Table 4. Changes in the grade of fatty liver in two groups by sex

Grade of fatty liver		Gerilact		Placebo		p-value
		n	%	n	%	
Male	Improved	16	72.7	10	55.6	0.35
	Non-change	6	27.3	7	38.9	
	Progressed	0	0	1	5.6	
Female	Improved	5	45.5	3	30	0.38
	Non-change	5	45.5	6	60	
	Progressed	5	9	1	10	
Total	Improved	21	63.6	13	46.4	0.33
	Non-change	11	33.3	14	50	
	Progressed	1	3	1	3.6	

Discussion

This study investigated the effect of probiotic GeriLact on laboratory findings, weight, and ultrasound findings of the NAFLD patients and showed that the use of probiotics significantly improved liver enzymes and cholesterol levels in the intervention groups compared to placebo groups. There was also a significant reduction in body weight and BMI in both placebo and intervention groups but the difference between the two groups wasn't significant. This finding could be interpreted with reference to the fact that both of the groups had the same dietary and exercise recommendations provided by a single interviewer. Similar to the current study, Shavakhi et al. showed that BMI in both probiotic and placebo groups decreased significantly (19). Some studies found a significant reduction in weight and BMI in the probiotic group compared to the placebo group. Famouri et al. did not notice a significant change in weight and BMI after probiotic treatment in children with NAFLD (20). Wong et al. showed that there was no change in BMI and waist circumference of patients during the probiotic treatment (21). In a review study by Ma et al., BMI change was not statistically significant (18). It is observed that the results of various studies were inconsistent in terms of the efficacy of probiotics on the weight loss of these patients which can be due to differences in the type of selected groups, duration of the study, and the diet observance by the patients. So, further studies are recommended to obtain better results. In this study, GeriLact treatment led to a significant improvement in both AST and ALT, while as in the placebo group only a significant improvement was observed in ALT levels. It was also observed that AST and ALT changes in the post-treatment phase were more significant for the GeriLact group compared to the placebo group. The desired effect of the probiotic treatment on liver enzymes was supported by both this study and previous studies. In a study conducted by Nabavi et al., a significant decrease in AST, ALT was observed at the end of the study in the intervention group (22). Rafraf et al. also found that the consumption of probiotic yogurt reduced ALT and AST serum levels in patients with NAFLD and the intervention could be helpful in improving fatty liver disease (23). Aller et al. showed that ALT and AST in the intervention group were significantly lower following the treatment while in the placebo group, all liver parameters remained unchanged (8). Also, Wong et al. found that AST levels reduced significantly after the treatment in the probiotic group but there was no significant difference for the control group (21). Manzhalii et al. observed that, 12 weeks of treatment with probiotics lead to a significant improvement in liver enzymes in patients with NASH (24). Buss et al. showed that using probiotics along with a decrease in liver enzymes could be a promising treatment for NAFLD patients (25). Similarly, Nursalim et al. stated that the consumption of probiotic products reduces the inflammatory markers and the level of liver enzymes, and they, in turn, reduce liver inflammation in NAFLD patients (26). Finally, it can be said that the use of probiotics has a major impact on the reduction of liver enzymes which is followed by reduction of liver inflammation, which improves the condition of patients. Accordingly, NAFLD patients are recommended to use probiotic products. This study did not show the effect of probiotics on glucose level. Similarly, Nabavi et al found that the effect of administration of probiotic yogurt in NAFLD patients is not associated with significant changes in glucose levels (22). Furthermore, Wong et al. concluded that probiotics had no effect on blood glucose levels (21). In another study, Sepideh et al. showed that probiotic consumption significantly reduced

FBS, insulin and insulin resistance (27). Moreover, the present study showed that despite a better lipid profile in the intervention group, there was only a significant improvement in the cholesterol level in the intervention group compared to the placebo group and at the level of triglyceride, HDL and LDL did not significantly change. Various studies have also shown different results in this regard. Similar to the current study, Manzhalii et al. showed a significant reduction in cholesterol levels in patients treated with probiotic but there was no change in triglycerides, LDL, and HDL (24). Nabavi et al. demonstrated that the prescription of probiotic yogurt in NAFLD patients significantly decreased LDL levels at the end of the study but there was no significant change in triglyceride and HDL levels (22). Famouri et al. observed a significant reduction in the average cholesterol level, LDL-C, and triglycerides in the intervention group (20). However, Abdel Monem did not observe any significant changes in the level of lipid profile following the treatment with probiotics (13). In a study conducted by Wong et al., probiotic consumption had no significant effect on lipid profiles in patients (21). The reason for these differences in the effect on the lipid profile is probably due to the probiotic compounds and differences in colony counts and strains used, as well as their effect on levels of triglycerides, cholesterol, HDL, and LDL. Also, it is likely that the increased levels of HDL require long -term treatment and there are other mechanisms affecting the changes in the level of HDL in the NAFLD which are still not well evaluated. In this study, there was about 17% improvement in fatty liver grade in the intervention group and more progression in the placebo group, but there was no significant difference which can be related to the low sample size of the study. Shavakhi et al. observed that NASH's ultrasound grading was significantly reduced at the end of the treatment in the probiotic group (19). In Famouri et al. study following the treatment, normal liver ultrasound was reported in 53.1% of the intervention group and 16.5% of the control group (20).

Conclusion

The results of the present study showed that the use of probiotics could significantly improve ALT, AST, and total cholesterol levels but did not significantly alter the levels of FBS, triglycerides, HDL, and LDL. Moreover, a significant improvement was observed in ultrasound grading of the patients after the treatment. However, the observed difference was not significant. Overall, the results of this study indicated that treatment with probiotics is effective, safe, low cost and well-tolerated in the long-term use by patients. Thus, the use of these drugs in treating NAFLD patients is recommended. Besides, further research is recommended to explore the issue in larger sample sizes.

Acknowledgment

The results of this study were ethically approved by Ardabil University of Medical Sciences with code IR.ARUMS.REC.1396.109 and the consent form was completed for all participants in the study. Moreover, the study was registered in IRCT with code IRCT2017102537007N1.

Conflict of interest

None

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