KOUMISS THERAPY CAN IMPROVE THE INTESTINAL FLORA IMBALANCE IN PATIENTS WITH HYPERLIPIDEMIA IN A SHORT TIME

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ABSTRACT

Objective: *To investigate the changes in the structure and function of intestinal flora in patients with hyperlipidemia after the intervention of Koumiss.*

Methods: *the fecal samples of hyperlipidemia patients were collected at 0, 7, and 14 days after the treatment of Koumiss. The V3 + V4 region of 16S rRNA gene was amplified and analyzed by high-throughput sequencing α Diversity β Diversity analysis, species composition analysis at the phylum level, family level, and genus level, significance analysis of group differences, and functional gene prediction analysis.*

Results: *the abundance and diversity of intestinal flora in hyperlipidemia patients increased after 14 days of treatment with koumiss. The ace index and Chao index of the 0-day group were significantly lower than those of the 7-day group and 14-day group (P<0.01); The ace index and Chao index of the 14-day group were significantly higher than those of the 7-day group (P<0.01); At the phylum level, the relative abundance ratio of Firmicutes to Bacteroidetes (Firmicutes / Bacteroidetes) increased from 1.36 (units) to 3.36 (units) before drinking. At the family level, the number of Trichospirillum increased significantly after 14 days of treatment. At the genus level, agathobacter, subdoligranulum, Enterobacter, and Bacteroides accounted for the highest proportion.*

Conclusion: *the results of this study show that koumiss therapy can affect the structure of intestinal flora in patients with hyperlipidemia in a short time, regulate the balance of intestinal flora, improve intestinal immune function, and reduce high cholesterol and high triglyceride, which can be widely used in the clinic.*

Keywords: *Koumiss therapy, hyperlipidemia, intestinal flora.*

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Introduction

Hyperlipidemia is a common disease, which is caused by dyslipidemia. It mainly refers to the high or low levels of serum total cholesterol, triglyceride and, low-density lipoprotein. Hyperlipidemia has no obvious clinical symptoms in the early stage, and its damage to the body is occult, progressive, and systemic. Hyperlipidemia leads to liver overload, vascular thrombosis, atherosclerosis, diabetes, and other complications. Hyperlipidemia can also be divided into primary and secondary[1, 2]. The former is related to environment and family heredity. The latter is caused by diabetes, hypothyroidism, obesity, and pancreatic disease. Especially in the elderly, according to statistics, the number of people with hyperlipidemia has reached 200 million, and because there are no obvious symptoms in the early stage of hyperlipidemia, it is easy to be ignored by patients, and they all happen unconsciously. Finally, they can only be found in the physical examination, so they are also known as the silent killer[3, 4].

A large number of studies have shown that the reduction of fat deposition during weight loss is related to the changes in intestinal flora. The number of firmicum decreased and Bacteroides increased in obese patients after weight loss. Abnormal lipid metabolism led to the change of intestinal flora distribution, mainly involving Escherichia coli, Lactobacillus, Bifidobacterium, and other dominant bacteria showed a downward trend, while the abundance of Bacteroides, Enterococcus, and other non-dominant bacteria increased, and the number of bacteria showed an increasing and polymorphic trend. Recent studies have shown that intestinal microorganisms may be related to fat deposition[5]. Intestinal microbes help the host obtain extra energy from undigestable polysaccharides such as resistant starch and fiber. This is because the microbial flora can secrete a variety of glycopicritic enzymes and polysaccharide decomposing enzymes that cannot be encoded in human and animal genomes. In hindgut, microbial fermentation of resistant starch and food fiber, the main products are monosaccharide and short-chain fatty acids (SCFAs), acetic acid, propionic acid, and butyric acid, which are absorbed to promote the de novo synthesis of liver triglyceride[6, 7].

Bile acids and short-chain fatty acids (SCFAs), as important mediators of intestinal flora and lipid metabolism, participate in the process of lipid metabolism. It is found that beneficial bacteria such as Lactobacillus and Bifidobacterium can produce bile salt hydrolases (bshs) in the intestinal flora. Bshs combine bile salt to form free bile acids, which are not easily absorbed by intestinal epithelial cells and directly excreted out of the body after entering the large intestine, affecting the enterohepatic circulation of bile acids, Due to the feedback regulation, cholesterol is further decomposed into new bile acids in the liver, which promotes cholesterol decomposition and achieves the effect of lowering blood lipid[8-11].

Koumiss therapy is a Mongolian medical method to treat some diseases with Koumiss. Sour koumiss is a common health drink of Mongolian people, which is rich in probiotics. Sour Koumiss is a kind of health drink made from fresh koumiss after fermentation, and it is also thegood medicine for some diseases. As early as the 14th century, the content and indications of sour Koumiss therapy diet therapy were recorded in Yinshan Zhengzheng written by Hu Sihui, a famous Royal dietician of the Yuan Dynasty and a Mongolian nutritionist. At present, there are 47 genera of lactic acid bacteria, including 373 species and subspecies. Lactic acid bacteria are facultative anaerobes, some belong to specific anaerobes, which can use glucose to produce more than lactic acid, and most of them can not decompose protein. There are two types of lactic acid fermentation by lactic acid bacteria. One is homolactic acid fermentation which only produces lactic acid after glucose is decomposed; The other is heterolactic fermentation, which can produce acetic acid, ethanol, and other metabolites at the same time as lactic acid production after glucose decomposition[12-15]. SCFAs are beneficial metabolites of probiotics in yogurt, which mainly include acetic acid, propionic acid, and butyric acid. SCFAs participate in the lipid metabolism pathway in three aspects. SCFAs can activate the cyclic adenosine monophosphate (cAMP)/protein kinase A (PKA)/cAMP response element-binding protein pathway, enhance the body's oxidative metabolism, inhibit liver fat production, and improve the level of blood lipids. SCFAs can be used by colonic epithelial cells and enter the blood circulation through the hepatic portal vein, inhibit the synthesis of liver cholesterol, increase the excretion of bile acids in feces, and then reduce the level of body cholesterol. SCFAs can target adipocytes and increase lipolysis and leptin release. In addition, studies have found that intestinal flora can also affect lipid metabolism by increasing the sense of fullness of the host and controlling appetite[16-22].

In recent years, our research group has shown that drinking Koumiss, has a significant role in lowering blood lipids (total cholesterol decreased by 28% on average, triglyceride decreased by 31% on average). It has a significant effect on the myocardial strain, bradycardia, ventricular premature beat, and ventricular tachycardia, with a total effective rate of 48%, and a total effective rate of 93.7% for coronary heart disease. One of the reasons for the obvious decrease of blood lipid in patients after drinking Koumiss is that mare's milk is rich in unsaturated fatty acids and low molecular fatty acids. After drinking Koumiss, the systolic and diastolic blood pressure decreased by 24% and 29%, respectively.

Therefore, koumiss is a natural drug for coronary heart disease, hyperlipidemia, and coronary atherosclerosis. To explore the relationship between intestinal flora and hyperlipidemia is of great significance to further clarify the etiology and pathogenesis of the disease and optimize the treatment strategy.

Materials and methods

Ethics statement

All participants in this study provided written consent. All experiments and analyses in this study were approved by the ethics committee of Xilinguole Mongolian medical hospital.

Source of patients

Fresh stool samples and blood samples were collected from patients recruited for hyperlipidemia treatment in Xilingol League Mongolian Medical Hospital of Inner Mongolia Autonomous Region from 2018 to 2019. After harvest, it was immediately frozen in the refrigerator at - 80 °C. According to the Chinese guidelines for the prevention and treatment of dyslipidemia for adults (revised 2016), these patients were diagnosed with SLE by clinicians at least one year ago. The patient did not have other autoimmune diseases, as well as intestinal and metabolic diseases that affect the intestinal flora.

The patient did not receive any treatment affecting the intestinal flora for one month, including antibiotics, probiotics, and other microbial preparations. The clinical diagnosis and blood test reports of 10 SLE patients were all from the hospital. Ten healthy volunteers were given a routine physical examination. The healthy control group did not have a gastrointestinal disease and did not take any antibiotics within one month of this study. In addition, there were no significant differences in age, smoking history, alcohol, or dietary intake between the two groups. All subjects included in this study provided written informed consent, and the study protocol was approved by the First Affiliated Hospital of Harbin Medical University.

Treatment and sample collection of Koumiss

In this study, we recruited 10 patients with hyperlipidemia and 10 matched normal controls. After treatment for 14 days, fecal samples and blood samples of normal people and patients were collected 0 days (before drinking), 7 days, and 14 days after treatment. 10 g fecal samples were collected with a sterile sampling scoop and put into a 50 ml enzyme-free sterile centrifuge tube. The same volume of DNA protection solution was added and mixed. The samples were stored and transported at low temperature and stored in the laboratory - 80 °C refrigerators as soon as possible. The source of Koumiss was provided by the Mongolian Medical Hospital of Xilin Gol League.

16S rDNA amplicon sequencing

DNA samples were extracted from feces, and total DNA was extracted from thawed fecal samples according to the manufacturer's agreement using qiaamp rapid DNA fecal Mini Kit (Qiagen, Hilden, Germany). Then the 16S rDNA amplicon was sequenced. Raw data obtained by sequencing needs to be spliced and filtered to eliminate the interference and error in the process of experiment and sequencing, so as to make the information analysis results more accurate and reliable. Then OTUs (operational taxonomic units) clustering and species annotation analysis were carried out based on the available data (1) The information of hypervariable region and common primers: 338f-806r (v3-v4) or 515f-907r (v4-v5).

Primers: (1) PCR primers: 515f (5 '- gtgccagcmg-cggtaa-3') and 806r (5 '- ggactachvggggtwtctaat-3'). 16S rRNA gene was amplified by specific primers with 12nt unique barcode.

Species diversity and diversity analysis

On the basis of species annotation, the abundance histogram of each group of samples at phylum, class, order, family, genus classification level was calculated by a sparse curve; According to the results of species annotation, OTUs of each sample or group with the largest abundance ranking in the top 10 at each taxonomic level (phylum, class, order, family, genus, specifications) were selected to generate a relative abundance column accumulation chart to observe the abundance of each sample at different taxonomic levels and compare the OTUs, microbial diversity and richness of the three groups. At the level of 97% similarity, the sequences were clustered (use arch, version 10.0), and 0.005% of the number of sequenced sequences was used as the threshold to filter out[9].

Species annotation and function prediction of intestinal flora

We used PICRUSt (biological investigation of communities by reconstruction of unobserved states) tool to analyze the differences between the two groups through KEGG (Kyoto Encyclopedia of genes and genes) metabolic pathway and analyzed the protein functional classification through COG (clusters of original groups of proteins). The OTU abundance table was standardized by PICRUSt, and the homologous clusters of protein family information and KEGG homologous information were obtained by the corresponding green gene ID of each OTU.

Then the abundance and Ko abundance of each cog were calculated. We compared the abundance of COG and Ko in patients with hyperlipidemia and healthy controls to predict the changes in intestinal flora function in patients with hyperlipidemia.

Statistical analysis

SPSS version 17.0 was used for all statistical analyses. A Single-sample t-test was used to compare the blood index of SLE patients with the population average. Microbial phylum family and genera concentrations between SLE patients and healthy controls were compared using a Welch T-test.

Results and discussion

Clinical characteristics of patients with hyperlipidemia

Clinical data including gender, age, course of the disease, triglyceride, total cholesterol, low-density lipoprotein, and high-density lipoprotein concentrations are shown in Table 1. The ESR of patients with hyperlipidemia was significantly higher than that of the healthy control group (P<0.01). The levels of TC, TG, and LDL-C in patients with hyperlipidemia were significantly decreased (P<0.05).

Characteristics	Healthy controls	disease	treat	p value
Sample numbers (female+male)	10 (9+1)	10 (9+1)	10 (9+1)	
Age mean±SD	40.71±13.85	38.63±14.50	38.63±14.50	>0.05
TG（mmol/L）	3.68±1.20	3.36± 1.21	1.18± 0.46*#	<0.0001
TC（mmol/L）	0.80±0.61	6.38± 1.33	4.97± 0.91*	<0.0001
HDL-C（mmol/L）	1.57±0.34	0.95± 0.17	1.72± 0.37*#	<0.0001
LDL-C（mmol/L）	1.68±0.71	4.32± 1.10	2.79± 0.80*#	<0.0001
Disease duration (years) ± SD		4.86±2.21		
Whole blood viscosity（mpa · s）	5.20± 0.63	5.32± 0.67	4.22± 0.46*#	<0.0001
PCV（%）	46.76± 3.66	47.13± 4.57	40.91± 3.77*#	<0.0001
Fib	3.88± 0.57	3.91± 0.57	3.32± 0.43*#	<0.0001

PCV :packed cell volume; Fib: Fibrinogen

Table 1: Demographic and clinical characteristics of human subject.

Structure and composition of intestinal flora in patients with hyperlipidemia

Fecal samples were collected from 10 normal people and 10 patients with hyperlipidemia at 0, 7, and 14 days after drinking koumiss. Pacbio SMRT sequencing technology was used to analyze the microorganisms in feces. A total of 3006612 high-quality 16S rRNA gene sequences were obtained from 40 fecal samples, with an average of 75165 sequences per sample. According to the 97% similarity level of sequences, 8178 representatives OTUs were obtained. The results of the dilution curve and Shannon index curve (Figure 1) showed that the curve gradually flattened with the increase of sequencing quantity, and the number of species (SOBs) or Shannon index (Shannon) of each sample did not increase significantly with the increase of sequencing quantity, indicating that the sequencing depth has basically covered all species in the sample, and the obtained data can be used for analysis.

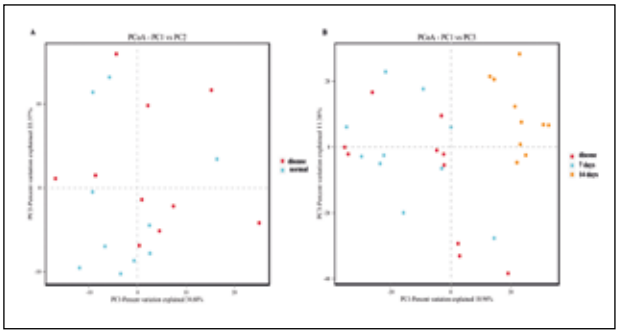

Figure 1: Alpha diversity of intestinal flora before administration.

a: Ace abundance index, B: Shannon diversity index, C: Chao abundance index, D: Simpson diversity index. A: Normal group B: drinking koumiss therapy for 0 days.

Effect of Koumiss on the structure of intestinal flora in patients with hyperlipidemia

Alpha diversity analysis of intestinal flora: after alpha diversity analysis, abundance index ACE, Chao1, diversity index Shannon, Simpson, coverage index were obtained. Results as shown in Figure 2 the coverage of each group was good, and the comparison among groups showed that the 0-day group, 7-day group, and 14-day group were significantly reduced (P<0.01); The ACE index and Chao index of the 14-day group were significantly higher than those of 7 day group (P<0.01).

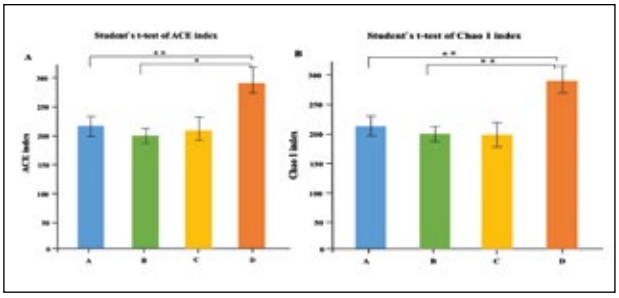

Figure 2: Alpha diversity of intestinal flora after administration.

*a: Ace abundance index, B: Shannon diversity index. B: They drank sour milk for 0 days, C for 7 days, D for 14 days *P<0.05, **P<0.01.*

A total of 11 phyla were detected in all samples. Bacteroidetes, Firmicutes, Actinobacteria, and Proteobacteria were the main components of the flora. The proportion of Bacteroidetes / Bacteroidetes increased and the relative abundance of actinobacteria increased in the 0-day group compared with the

normal group. The relative abundance of Firmicutes and actinomycetes decreased, while the relative abundance of Bacteroides and Proteus increased in the 0-day group compared with the 7-day and 14-day groups. At the family level, 62 families of bacteria were detected. Figure 3 shows the top ten species at the abundance level. The abundance of four genera, Viillonellaceae, Lachnospiraceae, Ruminococcaceae and Bacteroidaceae, accounted for 82.0%. It can be seen from Figure 2 that: the abundance of Veillonella CEAE and Lachnospiraceae in the intestinal tract of the 0-day group was 10.1% and 2.2% lower than that of the normal group, and the abundance of Ruminococcaceae and Bacteroidaceae in the 0-day group was 4.75% and 3.45% higher than that of the normal group. The abundances of Veillonella CEAE, Lachnospiraceae, and Bacteroidaceae in the intestinal tract of the 0-day group were 0.97%, 3.49% and 0.12% lower than those of the 7-day group, and the abundances of Ruminococcaceae in the 0-day group were 5.87% higher than those of the 7-day group. The abundances of Veillonella CEAE, Bacteroidaceae and Ruminococcaceae in the intestine of the 0-day group were 1.47%, 14.19%, and 1.61% higher than those of the 14-day group, and the abundances of Lachnospiraceae in the 0-day group were 17.51% lower than those of the 14-day group (Table 2).

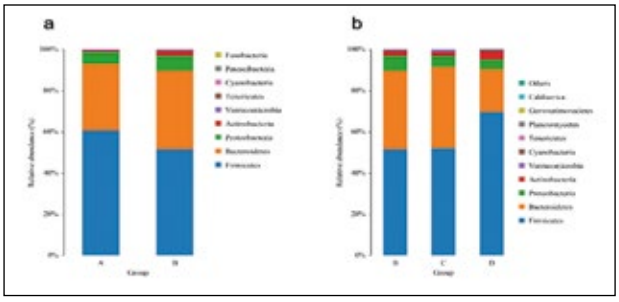

Figure 3: Abundance changes of intestinal microflora before and after administration, and abundance changes of intestinal microflora in group a compared with group B. b: The abundance of intestinal flora in groups B, C and d before and after treatment.
A: Normal group, B: 0 day, C: 7 days, D: 14 days. The abscissa is the name of the sample group; The ordinate is the relative abundance percentage.

Alpha diversity	Group A	Group B	Group C	Group D	P
Shannon	3.10±1.29	3.19±1.1	3.23±1.24	3.41±0.54	1.10E-15[b], 1.12E-15[c], 2.043E-15[d]
Simpson	0.11±0.1	0.07±0.05	0.07±0.07	0.08±0.1	0.20[b], 0.17[c], 0.14[d]
ACE	214.44±22.14	200.50±25.94	203.09±17.61	280.08±15.23	0.04[b], 0.07[c], 1.25E-09[d]
Chao1	221.32±29.36	206.05±21.92	204.72±24.76	282.20±11.85	0.04[b], 0.04[c], 5.536E-07[d]

P refers to the comparison between group A and group B; *P* refers to the comparison between group A and group C; *P* refers to the comparison between group B and group C.

Table 2: Comparision of the index of dataset diversity among the 4 groups (Mean±SD).

Performance evaluation of bacteria with significant changes after drinking Koumiss

The bacteria in fecal samples were further differentiated to genus level, and the abundance of 5 genera (other, Agathobacter, Subdoligranulum, Faecalibacterium, and Bacteroides) accounted for 80.3%. The abundances of Bacteroides, Faecalibacterium and Subdoligranulum in the intestinal tract of the 0-day group were 3.45%, 0.85%, and 3.81% higher than those of the normal group, and the abundances of agathobacter in the intestinal tract of the 0-day group were 4.94% lower than those of the normal group.

The abundances of Bacteroides and Agathobacter in the 0-day group were 0.12% and 1.75% lower than those in the 7-day group, and the abundances of Faecalibacterium and Subdoligranulum in the 0-day group were 10.876% and 0.19% higher than those in the 7-day group. The abundances of Faecalibacterium and Agathobacter in the intestine of 0-day group were 7.22% and 7.06% lower than that of the 14-day group. The abundances of Bacteroides and Subdoligranulum in 0-day group were higher than 14.19% and 7.12% in the14-day group (Figure 4).

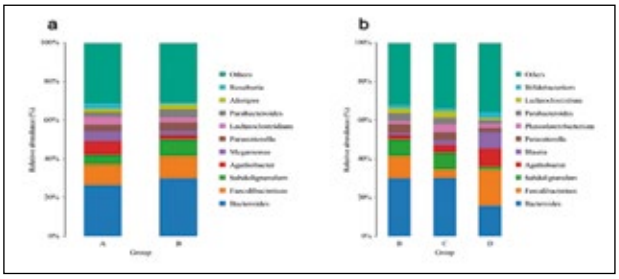

Figure 4: The abundance changes of intestinal flora before and after treatment were compared between group A and group B. b: The abundance of intestinal flora in groups B, C and d before and after treatment.
A: Normal group, B: 0 day, C: 7 days, D: 14 days. The abscissa is the name of the sample group; The ordinate is the relative abundance percentage.

Analysis of intestinal microbial function in patients with hyperlipidemia

To describe the functional changes of intestinal microbiota in PBC, we used piecrust to predict the functional composition of 16S rRNA sequencing data from patients with hyperlipoidemia and healthy controls. Cog analysis data showed that the abundance of samples from patients with hyperlipidemia was significantly different from that of healthy controls. Compared with the normal control group, the cellular pathways that significantly increase the abundance of COG samples in patients with hyperlipoidemia

include coenzyme transport and metabolism, cell wall, inorganic in transport and metabolism, signal transduction, cell motility, and so on Only by gene function prediction only.

The signal transduction mechanisms, cell cycle control, function unknown, transcription, and defense mechanisms were significantly different in the 14 day group however, KEGG analysis data showed that compared with the normal group, the cellular pathways with significant differences were amino acid metabolism, membrane transport, signal transduction and cell motility. There were significant differences in amino acid metabolism, global and review maps, translation and membrane transport in the 14-day group (Figure 5).

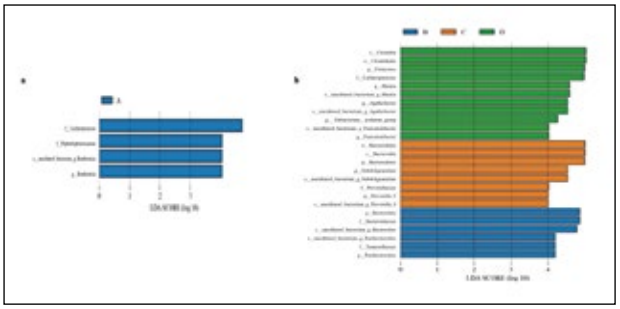

Figure 5: Histogram of LDASCORE distribution.

Discussion

Hyperlipidemia is the symptom that one or more of the blood lipid levels are higher than the normal range in the process of fat metabolism and transportation. After the onset of hyperlipidemia, most of them have no obvious clinical symptoms, leading to its often ignored. When it is found, there are often more serious cardiovascular and cerebrovascular diseases[1-5]. The abnormal blood lipid level has increased the incidence rate and mortality of cardiovascular and cerebrovascular diseases to a large extent. With the increase of body age, bad habits and habits have increased significantly, which also has a great impact on the body's blood lipid metabolism to a large extent[4]. The occurrence, development, and outcome of hyperlipidemia are closely related to intestinal microecology. Hyperlipidemia induced by a long-term high-fat diet will lead to an imbalance of intestinal flora. Under the influence of hyperlipidemia, the pH of intestinal contents, the composition of intestinal flora, and the characteristics of metabolites will change, and intractable diarrhea or alternating diarrhea and constipation will also appear[23]. The change of intestinal flora distribution structure further aggravates the imbalance of lipid metabolism and energy metabolism, leading to a vicious circle. In the process of hyperlipidemia, the abundance of spoilage bacteria such as Enterobacter and Enterococcus increased, the abundance of probiotics decreased, the activity of intestinal flora decreased, the level of free ammonia decreased, and the pH of intestinal contents increased, which further promoted the excessive growth of harmful bacteria[24, 25].

As early as the 14th century, the famous Yuan Dynasty imperial dietician, Hu Sihui, a Mongolian nutritionist, recorded the contents and indications of the therapy in “yin shan zheng yao”. In the secret history of Mongolia written more than 700 years ago, there are also records about the efficacy of sour Koumiss. It is widely used in lung diseases and has a significant curative effect. It has the effect of nourishing lung and moistening lung and has a significant curative effect on pulmonary tuberculosis, tuberculous pleurisy, emphysema, pulmonary abscess, and bronchitis. At present, there are many studies on probiotics of Koumiss, but few studies on functional efficacy. In the clinic, we mainly study the curative effect of tuberculosis, hyperlipidemia, gastritis, and allergic rhinitis, and the results show that the curative effect is significant. The low concentration of ethanol (1.9%) produced in the fermentation process of Koumiss can reduce the level of HDL and increase the level of HDL. The rich unsaturated fatty acids in Koumiss are also the effective components to reduce cholesterol. Its function is to promote the synthesis of lecithin, improve the activity of cholesterol acyl converting enzyme (LCAT), promote the formation of cholesterol lipids and transform them into high-density lipoprotein (HDL), and promote the metabolism of cholesterol.In this study, the V3 and V4 variable regions of the 16S rRNA gene were amplified and sequenced. It was found that there were significant differences in the intestinal flora structure of hyperlipidemia patients after 14 days of treatment with koumiss on the level of phylum, family, and genus. At the phylum level, Firmicutes increased significantly, while Bacteroides decreased significantly; The relative abundance ratio of Firmicutes to Bacteroides (Firmicutes/Bacteroides) increased from 1.36 to 3.36 before treatment.

After drinking koumiss, the ratio of Firmicutes/Bacteroides was higher than that of normal adults, suggesting that drinking koumiss can improve the intestinal microenvironment and have beneficial

physiological effects on the body. At the family level, Trichospirillaceae has increased significantly. Trichospirillaceae is the beneficial bacteria of the body, which can participate in the process of intestinal carbohydrate fermentation and decomposition into short-chain fatty acids, and the important nutritional source of the body's tissues and intestinal epithelial cells is short-chain fatty acids[14, 15].

At the genus level, Enterobacter and Bacteroides accounted for the highest proportion; Enterobacter is one of the most abundant butyrate-producing bacteria[16]. Butyrate plays a major role in intestinal physiology and produces multi-directional effects in the life cycle of intestinal cells. It can produce many beneficial effects on human health by preventing pathogen invasion, regulating the immune system, and reducing the occurrence of cancer[17]. Therefore, Enterobacteriaceae can produce butyric acid in the intestine, further affect the physiological function of the intestine and maintain the health of the body.

Alpha diversity analysis is generally used to analyze the richness and diversity of the microbial community, and the results are a series of statistical analysis indexes. The richness index included sobs, ACE, and Chao, and the diversity index included Shannon and Simpson. After statistical analysis, the ace index, Chao1 index, and Simpson of the 0-day group were lower than those of the normal group. The ace index and Chao index of the0-day group were significantly lower than those of the 7-day group and the 14-day group ($P<0.01$); The ace index and Chao index of the 14-day group were significantly higher than those of the7-day group ($P<0.01$). The results showed that koumiss significantly increased the abundance and diversity of intestinal flora.

To sum up, hyperlipidemia is one of the main factors leading to carotid atherosclerosis. The physical examination personnel should strengthen the detection of blood lipid level, and timely implement further detection and preventive treatment for the people with abnormal blood lipid levels, which can effectively reduce the occurrence of carotid atherosclerosis. There are many kinds of probiotics and probiotic metabolites in yogurt milk. After the 14-days of treatment, there are obvious differences in the structure of intestinal flora of patients with hyperlipidemia at the level of phylum, family, and genus. It can effectively reduce the levels of cholesterol, triglyceride, and low-density lipoprotein in blood, increase high-density lipoprotein and improve hemorheological indexes. Therefore, the curative effect of sour Koumiss therapy on hyperlipidemia is exact, which can affect the intestinal flora structure of patients in a short time and achieve the clinical curative effect, which can be widely used in the clinic.

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