



Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

The Result of Taking Mare's Milk for Nonalcoholic Steatohepatitis

Bakytzhan Bimbetov¹, Abay Zhangabylov², Saule Aitbaeva³, Marzhan Rakhimzhanova⁴, Abay Bakytzhanuly³

- 1. RSE "Hospital of the Medical Center" of the Department of Affairs President of the Republic of Kazakhstan, Nur-Sultan. Mangilik yel st. 80.
- 2. Kazakhstan-Russian Medical University, Almaty, N. Torekulov st. 71.
- 3. JSC "Medical University of Astana", Nur-Sultan, Beybitshilik st. 49A.
- 4. Corporate found of "University Medical Center", Nur-Sultan, Kerey, Ganibek khans st. 5/1, Kazakhstan.

Abstract

Nonalcoholic steatohepatitis (NASH) is a severe form of nonalcoholic fatty liver disease (NAFLD) and is linked to overweight, obesity and metabolic syndrome. The main role in treating NAFLD is attributed to leading a healthy lifestyle, keeping a healthy low-calorie diet and high physical activity. In dealing with issues of healthy diets of patients with NASH, mare's milk can be considered a pathogenically based, highly effective and affordable natural therapeutic dietary agent. The value of the product is defined by its similarity to the chemical components of women's breast milk. This article reports a case of a successful treatment of NASH with the help of monotherapy using sublimated mare's milk within a relatively short period of time, devoid of laborious dieting, physical activity or any side effects.

Keywords: Non-alcoholic fatty liver diseases, Non-alcoholic steatohepatitis, Mare's milk, Sublimated mare's milk, Medical and dietary properties of mare's milk.

Introduction

Nonalcoholic steatohepatitis (NASH) is an active form of nonalcoholic fatty liver disease (NAFLD) which often causes chronic liver diseases in the developed countries. NASH is associated with the rapid progression, which includes necrosis, inflammation and damage of liver tissues within the development of fibrosis, cirrhosis and even the development of hepatocellular carcinoma [1, 2].

According to the results of the all-Russian epidemiological research DIREG-2 the prevalence of NAFLD is accounted for 27,0%. Among them 16, 8% of patients had steatohepatitis, the rest 83,2% was made up by steatosis (80,3%) and liver cirrhosis (2,9%) as a result of steatohepatitis [3].

Unhealthy lifestyle, poor high-calorie diet and low physical activity play a significant role in the progression of NAFLD. As a result, the level of the free fatty acids (FFA) increases, which leads to the excessive accumulation of triglycerides in hepatocytes. Besides, FFA, combined with resistance to insulin, is responsible for lipotoxity, oxidative stress and inflammatory response that are a predisposing factor for progressing liver damage [4]. Also a genetic factor (PNPLA3 and TM6SF2) is worth mentioning, as people with those genes are at a bigger risk of having a higher level of liver fat and developing NASH [3, 6].

In the treatment of NAFLD the core role is attributed to leading a healthy lifestyle, keeping a healthy low-calorie diet with and high physical activity. In dealing with issues of healthy diets of patients with NASH, mare's milk (saumal) can be considered a pathogenically based, highly effective and affordable natural therapeutic dietary agent.

Therapeutic properties of mare's milk have been known for a long time. In various countries around the world mare's milk has been advertised as an effective treatment for problems with digestion and liver [7]. The value of the product is defined, particularly, by its similarity to the chemical components of women's breast milk which has a well-balanced and optimal composition of protein, fatty acids, carbohydrates and vitamins and minerals [7, 10]. Thanks to the high-quality compounds that mare's milk (saumal) is rich in, it has an antiinflammatory, antibacterial, antioxidant, and prebiotic alsoantiviral, immunestimulating and anti-cancer effect [8]. In the given article we have demonstrated a case of a successful treatment of NASH with the

help of using sublimated mare's milk (SMM).

Case Presentation

A man, aged 32, presented himself for gastroenterologist's, complaining about bloating and epigastric discomfort, a bitter taste in his mouth, abdominal distention and upset stomach, overall weakness, sickness and prompt fatigability. Besides, the patient mentioned having skin rash that caused dermal pruritus of his forearm and thighs, nasal stuffiness and distinct night snore (Table.1).

Table 1: Baseline and control clinical parameters

N₂	Clinical parameters	Baseline	After 2 weeks	After months	After 2 months
1	1 Bloating and epigastric discomfort		-	-	-
2	Overall weakness, sickness and prompt fatigability	+	-	-	-
3	Bitter taste in patient's mouth	+ -	-	-	-
4	Dermal pruritus	+	-	-	=
5	Abdominal distention and upset stomach	++	+	-	-
6	Skin rash with dermal pruritus	++	+	-	-
7	Nasal stuffiness	++	+	-	=
8	Night snore	++	+	-	-
9	Weight/Height, kg/cm	92,5/175	91/175	89,7/175	88,5/175
10	Waist, cm	104	103	102	101
11	BMI, kg/m ²	29,8	29,4	28,9	28,5

The abovementioned complaints started bothering the patient 7 years ago when he for the first time noticed elevated transaminases (ALT, AST). He was previously diagnosed with «Nonalcoholic steatohepatitis» by a gastroenterologist 4 years ago. Thus, he was proscribed to take various hepatoprotectors (hepadiph, godex, ursosan) resulting in insignificant temporary improvements.

The patient notes that the latest health deterioration took place within a year and attributes it to his eating disorder. Moreover, according to his medical history, the patient suffers from seasonal grass pollen allergy (in August and September), the patient would occasionally have high blood pressure, with the maximum of 135/80 mm Hg. Also high

cholesterol and triglycerides were noted. An objective examination showed: weight 92,5kg. Height 175 cm, waist 104 cm. BMI=29, 8 kr/m² (Table.1). The cutaneous integument and observable mucous were of normal color. Forearms and thighs, affected by rash similar to urticaria. White coating on the tongue. Abdomen was soft, non-tender to palpation. The liver and spleen were not palpable.

A laboratory examination revealed elevated transaminases (ALT up to 2,6 times, AST up to 1,2 times), gamma glutamyl transpeptidase (GGT), triglycerides (TG) and glycated hemoglobin (Table.1), also such hormones as thyroid-stimulating hormone (TSH), antibodies to thyroid peroxidase (a/b to TPO) and prolactin (Table.2).

Table 2: Baseline and control laboratory parameters

N₂	Laboratory parameters	Baseline	After 2 weeks	After months	After 2 months	Reference range
1	ALT, unit/l	105,7	36,4	36,1	35,4	0,00-41,00
2	AST, unit/l	44,4	21,6	25,7	23,2	0,00-37,00
3	Bilirubin total, mkmol/l	9,0	6,3	4,2	5,2	< 21,0
4	GGT, unit/l	72,0	46,0	49,0	45,1	0,00-71,00
5	ALP, unit/l	119,0	103	100	101	0,00-129,00
6	Cholesterol, mmol/l	4,48	4,22	4,24	4,21	3,63-5,20
7	HDL, mmol/l	1,08	1,08	1,15	1,21	0,78-1,81
8	LDL, mmol/l	2,69	3,18	2,86	2,65	2,07-4,92
9	TG, mmol/l	2,35	1,37	2,19	1,75	0,00-2,30
10	Glucose, mmol/l	5,66	5,37	5,27	5,25	3,89-5,83
11	Glycated hemoglobin, %	5,78%	5,65	5,54	5,53	4,80-5,90

Ī	12	TSH, micro-IU/ml	3,8	1,72	-	-	0,40-3,77
Ī	13	a/b to TPO, IU/ml	66,13	33,12	-	-	0-34
ſ	14	Prolactin, ng/ml	36,6	5,24	-	-	4,60-21,40

 $Abbreviations: ALT-alanine\ aminotranspherase,\ AST-aspartate\ aminotranspherase,\ GGT-gamma\ glutamyl\ transpeptidase,\ ALP-alkaline\ phosphatase,\ TG-triglycerides,\ TSH-thyroid-stimulating\ hormone,\ a/b\ to\ TPO-antibodies\ to\ thyroid\ peroxidase$

An ultrasound scan revealed diffuse changes of liver and pancreas parenchyma (similar to steatosis), bile congestion in the gallbladder (Table.3). An elastometric examination with the «FibriScan 502 TOUCH» machine with a Controlled Attenuation Parameter (CAP) option revealed third degree liver steatosis (over 67% of fat in the liver) (Table.4).

Table 3: Baseline and control ultrasound parameters

No	Ultrasound parameters	Baseline	After 2 months	
1	Sizes	Right lobe -14.4 cm, Left lobe -7.6 cm,	Right lobe -13.7 cm, Left lobe -7.0 cm,	
2	Echostructure	Homogeneous	Homogeneous	
3	Density	High	High	
4	The condition of gallbladder and ducts	Anechoic contents	Anechoic contents	
5	Spleen Area – 38 cm2		Area – 27 cm2	
	Medical opinion	Diffuse changes of liver parenchyma similar to steatosis. Bile congestion in the gallbladder. Diffuse changes of pancreas parenchyma.	Diffuse changes of liver parenchyma similar to steatosis.	

Table 4: Baseline and control elastometric parameters

N₀	Elastometric parameters	Baseline	After 2 months	
1	Degree of fibrosis	stage of fibrosis F_0 (kPa=4,5),	stage of fibrosis F_0 (kPa=4,4),	
2	Degree of steatosis	stage of steatosis S_3 (CAP-381) – over 67%	stage of steatosis S_3 (CAP-345) – over 67%	
		of fat in the liver.	of fat in the liver.	

Besides, due to the medical history and the changes in improvement indicators of the hormones of the thyroid, the patient was also consulted by an endocrinologist and allergist. Based on the results of the abovementioned research, a lack of any additional etiological agents of liver damage (alcohol, medication, poisons) in the medical history, a lack of viral hepatitis markers and autoimmune liver damage and also, based on the medical opinions of the endocrinologist and an allergist, the patient was finally diagnosed with «Nonalcoholic steatohepatitis of minimal degree of minimal activity steatohepatitis. Hypotonic type of gallbladder dysfunction. Excess body mass. Hypertriglyceridemia. Glucose tolerance dysfunction. Hyperprolactinemia. Urticaria. Seasonal grass pollen allergy».

After that, according to the research protocol, as a result of randomization, the patient was proscribed with taking sublimated mare's milk (SMM) «Saumal» dissolved in 100-150 ml of warm water in a dose of 20 mg 3 times a day during 2 months. In addition, the patient was recommended to lead a healthier lifestyle and keep a low-calorie diet with the limited intake of fried food. As a result of taking «Saumal» for 2 weeks, the patient recovered from such symptoms as bloating

and epigastric discomfort, overall weakness and sickness. Also abdominal distention and upset stomach, skin rash, dermal pruritus, nasal and night snore were significantly alleviated. In one month the patient noted suffering from none of the initial clinical symptoms (table.1). Besides, the patient noted improvements in his overall health condition and sleep, felt a raise in his tone and stamina. Taking the product had a positive influence on lowering the amount of the food intake. At the beginning of the treatment the patient noted having slight diarrhea after drinking the milk which came back to normal within 5 days.

A dynamic observation of laboratory based indicators of taking «Saumal» by the patient was conducted in 2 weeks, in a month and at the end of the treatment. An ultrasound scan and elastometric parameters were conducted 2 weeks after the beginning of the treatment. Biochemical research of taking «Saumal» by the patient, conducted in 2 weeks, revealed the normalization of all indicators, including transaminases, GGT, TG and glycated hemoglobin.

Furthermore, enzyme immunoassay showed the normalization of thyroid indicators (TSH, a/b to TPO) as well as the normalization of prolactin. The further biochemical research took place in 1 and 2 months and found the same normalized indicators (table.2). An ultrasound scan of the patient's liver and spleen while taking mare's milk which took place at the end of the treatment, showed slightly reduced sizes of the patient's liver and spleen and absence of bile congestion in the gallbladder. (table.3).

From our point of view, aside from the normalization of the patient's biochemical liver functions, a significant result of treating the patient with mare's milk was the lowered stage of liver steatosis from 381 to 345 dB/m, which was revealed with the «FibriScan 502 TOUCH» machine with a CAP option (table.4). Besides, as a result of the twomonth treatment with mare's milk «Saumal» the clinical symptoms of the disease were significantly alleviated: bloating epigastric discomfort, a bitter taste in the patient's mouth, overall weakness, sickness, fatigability, nasal stuffiness, urticaria and night snore disappeared. He lost some weight (4 kg) and his waist became 3 cm thinner (table.1).

Discussion

Pathogenesis of NAFLD is considered to be a multifactor process that genetically inclined people develop. NAFLD is believed to be connected with resistance to insulin, lipid accumulation the liver. in intestinal microbiota, sedentary lifestyle, high-fat diet and obesity [11]. The key focus of treating NAFLD is leading a healthy lifestyle, increasing physical activity and keeping a low-calorie diet. The effectiveness and safety of lowering the calorie intake up to 450-1000 kcal per day for patients with NAFLD has been proven [12, 13].

Besides, the usage of prebiotics and probiotics demonstrated positive results in NASH patients in comparison with placebo: lower levels of cholesterol, ALT and AST were observed [14].Nowadays the European Medicines Agency does not provide a clear recommended scheme for treating NASH [15].

The development of new medication faces difficulties due to the slow progression of the disease without clinically significant symptoms of NASH and a sufficient observation period [15]. Therefore, lifestyle modification and keeping a low-calorie diet

remain the main priority in treating NAFLD, including NASH. In this regard, in our opinion, using mare's milk in treating NASH is an interesting aid, as a natural low-calorie which dietary product has inflammatory, antibacterial, antioxidant, prebiotic and immune-stimulating effect. Despite the fact that mare's milk is considered to be a dietary product with therapeutic and protective properties all around the world, these days there is no large-scale clinical and scientific research on studying therapeutic properties of mare's milk.

There is absolutely no research on the possibilities of using mare's milk in diet therapy of definite nosological forms, in particular, the hepatobiliary system pathology. There are only occasional research papers which demonstrate its positive effect on intestinal microflora and immunologic indicators.

Additionally, the level of nonpathogenic bacteria in patient's feces became 8 times as higher. Besides, patients with intestinal and liver diseases have improved their sleep and wellbeing as a result of taking mare's milk. The patients significantly decreased or even stopped the intake of medication proscribed for their main illnesses [16, 18].

Clinical research conducted in 2009 at the University of Jena in Germany that studied patients with Crohn's disease and ulcerative colitis is being described. The placebocontrolled study lasted 8 weeks during which young participants took 250 ml of mare's milk twice a day. As a result, mare's milk helped with alleviating pain, decreasing the amount of blood in patients' stool and also with reducing doses of necessary medication intake [19].

As a result of an anonymous poll on taking mare's milk, doctors confirmed the effectiveness of taking mare's milk for skin and intestinal diseases in 500 respondents who regularly took saumal during a long period of time. In 91% of cases of milk consumers with skin diseases, there were improvements in their condition, such as alleviated inflammations and dermal pruritus and better sleep.

Positive effects could also be observed in 74% of patients with intestinal, respiratory and liver diseases, cancer, cardiovascular and

other diseases [16]. Based on the study, European researchers claim that «Mare's milk is a healthy therapeutic product, one of the most nutritious and healthy beverages which can be offered to us by the nature. » [16,17,18,19]. As fresh mare's milk is an unstable perishable product (it can be consumed only within 3 hours after milking), conducting clinical research on studying therapeutic properties of fresh mare's milk used to be impossible.

Consequently, patients were unable to take a necessary dose timely during a long period of time. Such an opportunity arose only after a sublimated form of mare's milk had been developed. Moreover, its storing period stays long even at room temperature. Sublimated mare's milk «Saumal» is produced at LLC «Eurasia Invest Ltd» (Karaganda, Kazakhstan) in collaboration with a large German horse-breeding farm in Europe «HOHER Odenwald» (Hans Zollmann), where innovative technology an implemented, all the processes of bio-milk production are certified and all production completely meets European quality standards.

Furthermore, this milk has been tested by independent laboratories of Russia (a test laboratory center of the Main hygiene and epidemiology center of Russia, Moscow) and China (SGS-CSTC Standards Technical Services Co., Ltd. Shanghai), where the high-quality compounds of the milk, absence of any toxic agents in it and its similarity to fresh mare's milk have been revealed [20].

References

- 1. Calzadilla Bertot L, Adams LA (2016) The natural course of non-alcoholic fatty liver disease. Int. J. Mol. Sci., 17: 774.
- 2. Sayiner M, Koenig A, Henry L, et al (2016) Epidemiology of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis in the United States and the rest of the world. //Clin Liver Dis., 20: 205-214.
- 3. Ivashkin VT, Mayevskaya MV, Pavlov Ch P et al (2016) Clinical recommendations on diagnosis and treatment of nonalcoholic fatty liver disease by the Russian liver research society and the Russian gastroenterology association. //The Russian magazine of gastroenterology, hepatology and coloproctology, 2: 24-42.

The clinical case, demonstrated in the article, showed the effectiveness of taking mare's milk for NASH in the form of monotherapy within a relatively short period of time. We result to attribute this mare's therapeutic potential, as it has an antiantibacterial, inflammatory, antioxidant, prebiotic and immune-stimulating effect. This property of mare's milk is a result of its optimally well-balanced composition biological components which makes this product a significant comprehensive part of the prevention and treatment of a wide range of digestive organs diseases, NAFLD and NASH.

Funding

The work was conducted in the implementation of a research Grant (ID AP051355855) of the Committee of Science of the Ministry of Education and Science of Republic of Kazakhstan on the priority of "The Science of Living" after receiving the patient's consent with respect to the examination.

The scientific work studied therapeutic properties of pasteurized SMM «Saumal», produced at LLC «Eurasia Invest Ltd» (Karaganda, Kazakhstan) in collaboration with a large German horse-breeding farm in «HOHER Europe Odenwald» (Hans Zollmann), where an innovative technology of sublimation drying is implemented, while all production completely meets European quality standards. The research work has been registered in the Clinical Trials.gov database.

- 4. Mann JP, Raponi M, Nobili V, authors (2017) Clinical implications of understanding the association between oxidative stress and pediatric NAFLD. Expert Rev. Gastroenterol. Hepatol., 11: 371-382.
- 5. Liu YL, Reeves HL, Burt AD, Tiniakos D, McPherson S, Leathart JB, et al (2014) TM6SF2 rs58542926 influences hepatic fibrosis progression in patients with non-alcoholic fatty liver disease. //Nat. Commun., 5: 4309.
- 6. Dongiovanni P, Petta S, Maglio C, Fracanzani AL, Pipitone R, Mozzi E, et al (2015) Transmembrane 6 super family member 2 gene variant disentangles

- nonalcoholic steatohepatitis. //Hepatology, 61: 506-514.
- 7. Mare's milk (2007) New Scientist, UK. 02624079, 194 (2608): 6-16.
- 8. Mare's milk New Scientist, UK. 02624079, 6/16/2007, 194: 2608.
- 9. Zhangabylova AK (2018) «Saumal, koumiss – therapeutic effect». «LAP» Lambert Academia Puplishing, Brivibas gatve 197, LV-1039, Riga, Latvia, European Union, 182.
- 10. Malacarne M et al (2002) Protein and fat composition of mare's milk: some nutritional remarks with reference to human and cow's milk /International Dairy Journal, 12 (11): 869-877.
- 11. Markiewicz-Kęszycka Maria, Wójtowski Jacek, Czyżak-Runowska, Grażyna et al (2014) Concentration of selected fatty acids, fat-soluble vitamins and β-carotene in late lactation mares' milk. //International Dairy Journal, 38(1):31-36. DOI: 10.1016/j.idairyj.2014.04.003
- 12. Buzzetti E, Pinzani M, Tsochatzis EA (2016) The multiple-hit pathogenesis of non-alcoholic fatty liver disease (NAFLD). //Metab Clin Exp., 65: 1038-1048.
- 13. Ferolla SM, Silva LC, Ferrari MD, et al (2015) Dietary approach in the treatment of nonalcoholic fatty liver disease. //World J. Hepatol., 7: 2522-2534.
- 14. Kargulewicz A, Stankowiak-Kulpa H, Grzymisławski M (2014) Dietary recommendations for patients with nonalcoholic fatty liver disease. //Prz Gastroenterol., 9: 18-23.

- 15. Ma YY, Li L, Yu CH, et al (2013) Effects of probiotics on nonalcoholic fatty liver disease: a meta-analysis. //World J. Gastroenterol., 19: 6911-3618.
- 16. Christiana Lucas, Georgia Lucas, Nicholas Lucas et al (2018) A systematic review of the present and future of non-alcoholic fatty liver disease. //Clinical and Experimental Hepatology 3/2018, 3: 165-174.
- 17. Schubert Rainer Der Einsatz von Stutenmilch zur Therapieunterstützung-Ein Studienüberblick //Die Naturheilkunde. Sonderdruck aus Ausgabe., 1: 1-3.
- 18. Foekel C, Schubert R, Kaatz M et al (2009) Dietetic effects of oral intervention with mare's milk on SCORAD, faecal microbiota and immunological parameters in patients with atopic dermatitis. //Intern at J. Food Sci. Nutr., 60 (S7): 41-52.
- 19. Watanabe S, Narisawa Y, Arase S, et al (2003) Differences in fecal microflora between patients with atopic dermatitis and healthy control subjects. //J. Allergy Clin Immunol., 111 (3): 587-591.
- 20. Schubert R, Kahle C, Kauf E et al (2009) Dietetic efficacy of mare's milk for patients with chronic inflammatory bowel diseases clinical study. //Ernährung/nutrition, 33 (7/8): 314-321.
- 21. Bimbetov B, Zhangabylov A, Aitbaeva S et al (2019) The qualitative composition of sublimated mare's milk //Medicine, 6 (204): 23-28.