#### **ORIGINAL ARTICLE**



# Lipid-Reducing Effects of Sulphate-Sulphide Mineral Water in Patients With Knee Osteoarthritis

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#### **Abstract**

**Background / Aim:** The positive effect of thermal mineral waters on human health has been known for a long time. Many pathophysiological mechanisms of action of balneotherapy are not specified. Patients with gonarthrosis often have elevated values of serum lipids. This study aimed to examine the effect of drinking sulphate-sulphide thermo mineral water on the lipid status of patients with gonarthrosis.

**Methods:** A prospective clinical study followed 60 patients, both sexes, mean age  $65.02 \pm 1.03$ , with gonarthrosis. All inpatient underwent physical treatment with topical application of sulphate-sulphide mineral water. Patients of group A (N = 30) had the use of this mineral water as an additional therapy by drinking, unlike patients of group B (N = 30) who drank plain water. The level of serum lipids of these patients was monitored at admission and 4 weeks after. The variance analysis test (ANOVA) with a level of statistical significance p < 0.001 was used for statistical analysis.

**Results:** A significant reduction in the levels of all lipid fractions in the serum of patients with gonarthrosis was found 4 weeks after the completion of inpatient physical treatment in both study groups. This decrease was statistically significant in patients of group A (p < 0.001).

**Conclusion:** Drinking sulphate-sulphide mineral water in patients with gonarthrosis shows a positive effect on the reduction of serum lipid levels in the short-term follow-up period.

**Key words:** Balneotherapy; Serum; Lipids; Osteoarthritis; Knee.

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## Introduction

Osteoarthritis (OA) is the most common joint disease and one of the main causes of pain and disability. It is a mildly progressive, degenerative and chronic disease that occurs as a result of joint cartilage damage. There is growing evidence that OA is also a "metabolic disorder" associated with insulin resistance, abdominal obesity, high cholesterol, high blood pressure and coagulation disorders. The level of total fatty acids and arachidonic acid within chondrocytes noticeably increases with severe cartilage damage. In addition, the expression of genes that regulate cho-

lesterol uptake into chondrocytes of damaged cartilage is reduced, which also contributes to lipid deposition.<sup>5</sup> Some studies have linked elevated blood lipids and osteoarthritic changes.<sup>6</sup> The use of bicarbonate and sulphate-sulphide mineral water by drinking under controlled conditions could lower blood lipid levels.<sup>7-9</sup> The exact mechanism of antilipemic action of these mineral waters is unknown. The increase in bile acid excretion is related to the alkaline nature of mineral waters and the osmotic effect. The release of pancreatic enzymes and bile acids increases with

increasing pH under the influence of mineral water, which leads to reduced uptake of cholesterol in the small intestine and its increased excretion in the faeces. The loss of bile acids through faeces is increased which could stimulate the liver to produce more bile acids from cholesterol. Consequently, the number of hepatic LDL cholesterol receptors increases, leading to a decrease in serum LDL cholesterol. This study aimed to examine the effect of internal application (drinking) of sulphide-sulphate mineral water on the lipid status of patients with gonarthrosis.

Table 1: Physical-chemical analysis of sulphurous mineral water "Mlječanica"

Compound		mg/L	mmol/L	m/val/L	m. val %			
Anions	Hydrocarbon	577.06	9.460	9.460	18			
	Chloride	15.80	0.440	0.440	1			
	Sulfate	2840.00	21.250	42.500	81			
	Phosphate	0.01	0.000	0.000	0			
Total mineralisation (mg/L) 2932.87								
Cations	Sodium	165.00	7.174	7.174	14			
	Potassium	7.20	0.185	0.185	0			
	Calcium	436.86	10.900	21.800	41			
	Magnesium	257.79	10.600	21.200	40			
	Strontium	11.20	0.127	0.225	1			
	Ammonium	35.00	2	1.940	4			
Total mineralisation (mg/L) 913.06; m. val: mineral value								

### Methods

The study was conducted as an open, controlled, prospective study of 60 patients with gonarthrosis at the Hospital for Physical Medicine and Rehabilitation "Mlječanica" in Kozarska Dubica. All respondents gave their voluntary consent to participate in the trial and signed informed consent. The Ethics Committee of the "Mlječanica" Hospital has approved this study. The microbiological correctness of the mineral drinking water was confirmed by the PHI Institute of Public Health Banja Luka No M-3206-V-4-2015 (Table 1).<sup>11</sup> Criteria for inclusion in the study were knee pain most days of the previous month and radiological confirmation of knee osteoarthritis. The study non-inclusion criteria were: significant changes in blood pressure, cardiac arrhythmias, cardiac decompensation, neurological disorders, complications of the gastrointestinal tract (vomiting, diarrhoea, abdominal cramps) and personal reasons of the subjects. The sample was divided into two groups (group A and group B) of 30 respondents each. All patients were given balneo-physical treatment every day, six days a week (the seventh day is a break from treatment) for the 4 weeks. The total of 24 treatments included: transcutaneous electrical nerve stimulation (TENS) on the affected knee exercises to increase the range of motion in the knee and strengthen the quadriceps and hamstrings and locally applied baths of sulphate-sulphide mineral water temperature 31-33 ° C for 20 minutes. Subjects from group A drank 100 mL of sulphate-sulphide mineral water three times a day, just before meals and patients from group B drank three times 100 mL of plain tap water three times a day before meals. The outcome was evaluated on the first and 28th day of rehabilitation. The following serum laboratory parameters were measured on each subject: to-

tal cholesterol, triglycerides, HDL cholesterol and LDL-cholesterol. The concentration of total cholesterol and triglycerides in the serum was determined by standard enzymatic methods with the help of commercial tests from the company Human. The concentration of HDL-cholesterol was determined in the supernatant after precipitation of all other lipoproteins with the help of a precipitating agent for the semi-micro method PREC-b and the concentration of LDL-cholesterol by the precipitation method. The variance analysis test (ANOVA) with a level of p < 0.001 was considered statistically significant.

#### Results

A total of 60 patients (19 males and 41 females, mean age  $65.02 \pm 1.03$ ) participated in the study, 30 in each group. Both groups were homogenous regarding age, gender and affected knee (Table 2).

Table 2: Demographic characteristics of the subjects

Group	Group A	Group B		
No of subjects	30	30		
Mean age	65.70	66.50		
Sex	M = 9; F = 21	M = 10; F = 20		
Comorbidities		•		
Hypertension	22	24 *p = 0.542		
Varicose veins	3	4 *p = 1.000		
Affected knee	L = 16; R = 14	L = 18; R = 12		

Decrease of serum lipids had obtained in patients in both groups. This decrease was statistically significant in patients in group A (treated with sulphate-sulphide mineral water) p < 0.001 (Table 3).

\*Fisher test: p > 0.05; M = male; F = female; L = left; R = right;

Table 3: Differences in serum lipid values in patients of groups A and B (admission/discharge)

Lipid values	Treatment	Water				n volue	
Lipiu values	(water)	Mean	SD	Median	Perc. 25	Perc. 75	p value
Total cholesterol (admission)	regular	7.01	1.11	6.75	6.12	7.97	0.700ª
	mineral	6.91	0.85	6.74	6.54	7.26	
Total cholesterol (discharge)	regular	6.00	0.87	5.91	5.43	6.43	< 0.001a
	mineral	5.20	0.62	5.30	4.80	5.80	< 0.001
Δ Total cholestrol	regular	-1.01	1.02	-0.71	-1.77	-0.27	0.001ª
	mineral	-1.70	1.02	-1.80	-2.35	-0.71	
Triglycerides (admission)	regular	2.67	1.33	2.76	1.82	2.97	0.539b
	mineral	2.84	1.21	2.52	1.97	3.30	
Triglycerides (discharge)	regular	2.41	1.13	2.37	1.74	2.72	0.007b
rrigiyoorides (disoridige)	mineral	1.80	0.88	1.77	1.50	1.98	
△ Triglycerides	regular	-0.27	0.85	-0.19	-0.40	0.06	< 0.001 <sup>b</sup>
Δ mgrycendes	mineral	-1.04	0.91	-1.04	-1.51	-0.27	
HDL (admission)	regular	1.43	0.60	1.37	1.02	1.78	0.703ª
TIDE (dullission)	mineral	1.49	0.67	1.29	1.00	1.85	
HDI (dicebargo)	regular	1.47	0.60	1.34	1.02	1.89	0.005ª
HDL (discharge)	mineral	1.94	0.64	1.90	1.40	2.45	
ΔHDL	regular	0.04	0.37	0.04	-0.07	0.20	0.001ª
ΔΠΙΙ	mineral	0.45	0.53	0.28	0.05	0.90	
LDL (admission)	regular	5.21	1.28	5.22	4.00	6.20	0.228ª
LDL (autilission)	mineral	4.83	1.18	4.53	3.70	5.71	
LDL (discharge)	regular	4.55	0.96	4.22	3.80	5.00	< 0.001 <sup>a</sup>
LDL (discridige)	mineral	3.56	0.48	3.52	3.10	3.91	
ΔLDL	regular	-0.66	1.08	-0.32	-0.98	-0.01	0.028ª
ΔLDL	mineral	-1.26	1.00	-1.15	-2.13	-0.32	

a - T test for independent samples; b - Mann Whitney U test; red colour: statistical significance; perc: percentile;

## Discussion

At first glance, patients with gonarthrosis would not be closely associated with elevated serum lipids. However, these patients are mostly older, less physically active and adipose, the connection of these clinical entities can be seen. Patients from both study groups had elevated serum lipid fractions at baseline. There are studies showing lipid deposition within damaged cartilage. The expression of genes that regulate the intake of cholesterol in chondrocytes is reduced, which in turn contributes to increased lipid deposition in chondrocytes.<sup>5</sup> In a 2009 study of 148 middle-aged women without clinical signs of gonarthrosis and with reference cholesterol and triglyceride values, Davies et al found an increased number of women with osteoarthritis who had low and elevated serum lipids after two years.<sup>6</sup> The treatment of patients with dyslipidaemias is complex and requires a multidisciplinary approach. Physiological treatment of patients with gonarthrosis can affect the level of reduction of serum lipids in several ways. One is the reduction of body weight, the other is the increase of physical activity through training, but the effect of balneotherapy is not reduced. 12-15 The mechanisms of action of sulphate-sulphide mineral waters on

the level of serum lipids have been insufficiently investigated. The mechanisms that could explain this effect are increased excretion of bile acids and pancreatic enzymes, alkalinity of mineral waters and osmotic effect. Cholesterol uptake in the small intestine is reduced and its excretion is increased. This leads to a decrease in the liver's cholesterol reserve which withdraws LDL cholesterol from the serum and thus leads to its reduction.<sup>16</sup>

Positive effects of sulphate-sulphide mineral water have been found in patients with constipation and gastritis.<sup>17</sup> Positive effects of local application of these mineral waters have also been reported in patients with hypertension and after cerebrovascular insult.<sup>18-20</sup>

Our research can undoubtedly be considered pioneering because no research has been done so far on the impact of mineral water in patients with dyslipidaemia. Balneotherapy as a cheap and affordable therapy could, if its positive effects are proven, be a significant modality of non-pharmacological treatment of these patients.

The results obtained in this study need to be interpreted from several angles. Namely, the effect of mineral water on BMI was not examined due to a short follow-up period of 4 weeks. The effect of drug therapy was minimised because all patients due to pain took only Paracetamol in a maximum dose of 3 g per day due to knee pain. Patients in the study groups did not receive statin therapy.

As all patients were on a reduction diet during all 28 days, the effect of the diet was reduced to a minimum. Therefore, a significant decrease in serum lipids in patients in group A can only be attributed to the effect of drinking sulphate-sulphide mineral water. However, a short follow-up period and a small sample are the disadvantages of this study.

#### Conclusion

Drinking sulphate-sulphide mineral water leads to a decrease in serum lipids in patients with gonarthrosis in the short-term follow-up period.

# Acknowledgements

None.

# Conflict of interest

None.

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