



The Effect of Sulphate-Sulphide Mineral Baths on Blood Glucose Level in Patients With Knee Osteoarthritis

Tatjana Erceg-Rukavina,¹ Dragana Dragičević-Cvjetković,^{1, 2} Dragan M Djuric,³ Miloš P Stojiljković,^{4, 5} Ranko Škrbić^{4, 5}

Abstract

Background/Aim: Type 2 diabetes is a common comorbidity in patients with knee osteoarthritis. Bearing in mind that obesity and insulin resistance are risk factors for the development of knee osteoarthritis, physical therapy and balneotherapy containing hydrogen sulphide (H₂S) has a positive effect on the functional and metabolic status of these patients. This work was aimed to investigate the effect of sulphate-sulphide-rich mineral baths containing H₂S on the level of serum glucose in patients with knee osteoarthritis.

Methods: An open prospective randomised clinical trial included patients suffering from stage I and II of the knee osteoarthritis. Patients were divided into two groups of 40 subjects each: control group and experimental group. All subjects underwent inpatient physical treatment consisting of kinesitherapy and transcutaneous electrical nerve stimulation (TENS) 6 days a week. Patients from experimental group, in addition to all the mentioned treatments, also took sulphate-sulphide mineral water baths once a day for 30 minutes for 7 days, unlike the patients from control group who took tap water baths, according to the same schedule. The level of serum glucose was monitored in all patients on admission, after discharge and 6 months after the treatment. The Student t-test was used for statistical data processing and $p < 0.05$ was considered as statistically significant.

Results: Study included 80 patients of both sexes, with an average age of 67.00 ± 5.75 years. All patients had elevated serum glucose values on admission. The initial levels of glycaemia in the control and experimental groups were not significantly different (6.99 ± 1.95 and 7.88 ± 1.90 mmol/L, respectively). At discharge, patients who performed balneotherapy had a statistically significant decrease in serum glucose values compared to patients from the control group (by 1.84 vs 0.26 mmol/L, $p < 0.001$). This effect did not persist six months after the end of the treatment ($p > 0.05$).

Conclusion: The application of balneotherapy with sulphate-sulphide mineral baths containing H₂S as a potent gas transmitter significantly reduces serum glucose levels in patients with knee osteoarthritis.

Key words: Hydrogen sulphide; Balneology; Osteoarthritis; Knee.

1. Institute of Physical Medicine and Rehabilitation "Dr Miroslav Zotović", Banja Luka, the Republic of Srpska, Bosnia and Herzegovina.
2. Department of Physical Medicine and Rehabilitation, Faculty of Medicine, University of Banja Luka, the Republic of Srpska, Bosnia and Herzegovina.
3. Institute of Medical Physiology "Richard Burian", Faculty of Medicine, University of Belgrade, Belgrade, Serbia.
4. Department of Pharmacology, Toxicology and Clinical Pharmacology, Faculty of Medicine, University of Banja Luka, Banja Luka, the Republic of Srpska, Bosnia and Herzegovina.
5. Centre for Biomedical Research, Faculty of Medicine, University of Banja Luka, Banja Luka, the Republic of Srpska, Bosnia and Herzegovina.

Correspondence:

TATJANA ERCEG-RUKAVINA
E: dr.tanjaerceg@gmail.com
M: +387 65 737 936

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Introduction

Osteoarthritis (OA) is a slowly progressive, degenerative and chronic disease that occurs as a result of damaged joint cartilage.¹ According to

data from the World Health Organisation (WHO), 9.6 % of men and 18 % of women over the age of 60 have symptomatic OA.² Given that life expectancy

has increased due to the advancement of medicine and the improvement of living conditions, it is expected that an increasing number of people will have complaints related to OA. There is more and more evidence that OA is also a “metabolic disorder” associated with abdominal obesity, insulin resistance, high blood lipid levels and elevated blood pressure.³ Each of the factors mentioned is an important risk factor for the development of diabetes mellitus and cardiovascular diseases⁴⁻⁷ and the combination of these factors is associated with an increase in the risk on the occurrence and progressing of the knee OA.⁸ Elevated values of blood glucose disturb the homeostasis of chondrocytes by various mechanisms.⁹⁻¹¹ Balneotherapy and especially the hydrogen sulphide bath, takes an important place in the treatment of degenerative rheumatism. H₂S an important vasoprotective gas transmitter in those diseases where endothelial dysfunction is a central issue, such as hypertension, diabetes mellitus and atherosclerosis, which in the future provides an opportunity for H₂S donor compounds to take a place in the prevention and treatment of these pathological conditions and diseases.¹² Being a gas, H₂S can be absorbed by numerous routes. It is able to penetrate the skin and mucosae and can therefore act at the cell level both in the skin and in internal organs of our organism. This means that the topical application of sulphurous mineral waters rich in hydrogen sulphide has the potential to treat disorders of the internal organs such as high blood pressure, ischaemia and conditions affecting the kidneys or nervous system. Many authors have examined the mechanisms of action of mineral waters and their therapeutic effects and certain inorganic components have been linked to the effects of curing baths.¹³⁻¹⁷

This work was aimed to investigate the effect of sulphate-sulphide-rich mineral baths containing H₂S on the level of blood glucose in patients with knee OA.

Methods

This research was conducted as an open, controlled, prospective clinical trial at the Hospital for Physical Medicine and Rehabilitation “Mlječanica” from December 2017 to April 2019 and was approved by the Ethics Committee of the Hospital. It included 80 patients aged between 40 and 75 with radiographic confirmation of

gonarthrosis who gave written consent to participate in the study. Subjects were divided into two groups of 40 subjects each, experimental and control group.

All subjects were given the same physical treatment every day for a period of 4 weeks, six days a week, which consisted of the application of transcutaneous electrical nerve stimulation (TENS) to the affected knee for 30 minutes, an individual kinesiotherapy programme to increase the muscle strength of the quadriceps and exercises to increase the range of motion in the affected knee for 30 minutes. The experimental group was treated with baths of sulphate-sulphide mineral water¹⁸ at a temperature of 33-35 °C every day for 20 minutes and the control group with baths of tap water under the same conditions.

M 3.500 H₂S 136.0 T 14.0 °C

Figure 1a: Curl's formula of sulphate-sulphide mineral water “Mlječanica”

There was a 30-minute break between procedures.

The study did not include persons with contraindications for balneotherapy on behalf of the cardiovascular system, kidney and liver patients, persons with acute illness, recent trauma, surgery in the last three months before the study, insulin-dependent diabetics, persons suffering from neurological diseases, as well as people with communication disorders. The exclusion criteria were the worsening of the patient's general condition, as well as personal reasons. Blood glucose values were measured by standard enzyme techniques in all subjects at admission, after 4 weeks and after 6 months during which the patients stayed at home. All subjects had the same diabetic menu consisting of three meals and two snacks. A total of 4 patients were excluded from the study from the experimental group due to hypertensive crises that did not resolve with antihypertensive drugs during the second week after the start of the baths.

The Student t-test was used for statistical data processing. A level of $p < 0.05$ was considered statistically significant. Tests were performed on IBM SPSS v 16.0 software.

Results

A total of 80 patients (47 women and 33 men, average age 66.80 years) participated in the study, 40 in each group. Patients from the examined groups did not differ significantly in terms their gender or age (average age of patients in control and experimental groups were 67.5 ± 6.1 and 66.5 ± 5.4 , respectively) (Table 1).

Table 1: Demographic characteristics of the sample

Parameters	Control group	Experimental group	p-value
Sex			
Male N (%)	15 (40.5)	10 (28.6)	0.451 ^a
Female N (%)	22 (59.5)	25 (71.4)	
Age			
Mean \pm SD	67.5 \pm 6.1	66.5 \pm 5.4	0.790 ^b

^aChi-square test; ^bANOVA; SD: standard deviation;
Control group (treatment without sulphate-sulphide mineral water baths);
Experimental group (treatment with sulphate-sulphide mineral water baths);

Table 2: The values of serum glucose in patients with knee osteoarthritis on admission, discharge and 6 months after treatment with sulphate-sulphide mineral water baths

Serum glucose	Control group		Experimental group		p-value
	Mean	SD	Mean	SD	
SGC 1	6.99	1.95	7.88	1.90	0.290
SGC 2	6.73	1.51	6.04	1.15	< 0.001 [†]
SGC 3	6.91	1.68	7.35	1.55	0.880
Δ SGC (1 month - admission)	-0.26	-0.26	-1.84	1.36	< 0.001 [†]
Δ SGC (6 month - admission)	-0.08	-0.08	-0.53	0.98	0.035

Control group (treatment without sulphate-sulphide mineral water baths);
Experimental group (treatment with sulphate-sulphide mineral water baths);
SGC: serum glucose concentration in mmol/L; SD: standard deviation;
Serum glucose concentration (SGC) 1 - value on admission;
Serum glucose concentration (SGC) 2 - value on discharge;
Serum glucose concentration (SGC) 3 - value after 6 months of treatment;
 Δ SGC (1 month - admission) – differences in value from SGC on admission and discharge;
 Δ SGC (6 month - discharge) - differences in value from SGC on discharge and 6 months after treatment;
[†] - Student t-test; $p < 0.05$;

Patients in both groups had similarly elevated average blood glucose values on admission. A significant decrease in blood glucose values was confirmed in the group that used sulphate-sulphide mineral water baths and not in the control group of patients (1.84 vs 0.26 mmol/L, $p < 0.001$), but these values were not maintained at the control measurement after 6 months (Table 2).

Discussion

Elevated blood glucose values lead to reduced expression on the membrane of the chondrocyte of the glucose transporter protein type 1 (GLUT1) carrier that takes up intracellular glucose, which leads to the accumulation of glucose in the chondrocyte, an increase in reactive oxygen species (ROS) and cell death. It was found that H₂S, a newly discovered gas transmitter, plays an important role in regulating the homeostasis of glucose metabolism.¹² H₂S can be produced endogenously in B cells, liver, adipose tissue, skeletal muscle and hypothalamus. H₂S is thought to regulate blood glucose metabolism by inhibiting insulin secretion in pancreatic islet B cells, inhibiting glucose uptake as well as glycogen storage. It plays an important role in the regulation of insulin sensitivity in insulin-responsive tissues. H₂S values were found to be lower in the plasma of individuals with diabetes mellitus, compared to the values in healthy individuals. Balneotherapy with sulphurous mineral water, thanks to the presence of H₂S, is the main responsible agent for antioxidant and hypoglycaemic effects. In a study that included patients with gastrointestinal complaints, the influence of the use of sulphur balneotherapy on blood glucose levels during a two-week treatment was examined. A statistically significant reduction in glycaemia was found in the group that received balneotherapy.¹³ However, many important questions related primarily to the concentration of H₂S are still unknown and the problem connected with the application of balneotherapy is also the definition of the balneotherapy dose.

This study showed that the exogenous application of H₂S through sulphate-sulphide mineral baths leads to a short-term decrease in glycaemic values in patients with knee OA. Considering the way of reabsorption and the endogenous effect of H₂S, this effect can be explained by the influence on H₂S ion channels, but also by its immunomodulatory role. The results obtained 6 months after the end of the treatment can be interpreted in the light of poor compliance with the applied therapeutic measure, in this case, H₂S. The effect did not persist due to the interruption of balneotherapy because the extract of exogenous H₂S was not constantly present and the level of endogenous H₂S was blocked by an elevated level of glucose in the blood.

A group of Italian authors also reported positive

short-term effects of H₂S on blood glucose reduction in patients with diabetes mellitus type 2.¹⁹ Authors found no studies that were negatively correlated with this research although most of them were done at the cellular and subcellular level and with different H₂S donors.

Understanding how H₂S levels change *in vivo* is crucial to understanding its role and thus its application. Whether H₂S acts as a promising new target for the treatment of diabetes mellitus deserves further investigation.²⁰

Conclusion

Sulphate-sulphide mineral water applied in the form of baths statistically significantly reduces blood glucose values in patients with gonarthrosis in the short-term follow-up period.

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Conflict of interest

None.

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