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Assessment of the impact of comprehensive spa therapy with the use of radon and radon-sulfur therapeutic waters on the level of hemoglobin - preliminary studies

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ABSTRACT

Introduction: Comprehensive balneophysiotherapy improves health by reducing pain, enhancing physical fitness, and supporting immunity. Iron, essential for metabolic processes, is a key component of hemoglobin. This study aimed to assess the impact of spa therapy using radon and radon-sulfur waters on hemoglobin levels in patients with osteoarthritis. **Material and method:** The study included osteoarthritis patients undergoing 21-day spa therapy in two resorts (n=157). Both groups followed identical criteria and procedures. Treatment involved mud therapy, physiotherapy, kinesiotherapy, and radon or radon-sulfur waters. Hemoglobin levels were measured before therapy and after 18 days. **Results:** A statistically significant decrease in hemoglobin level was found in patients using radon-sulfur water therapy ($p < 0.001$). A statistically negligible increase in hemoglobin level occurred in patients using radon water ($p > 0.05$). **Conclusions:** The spa therapy with the use of radon-sulfur waters reduced the level of hemoglobin in patients with degenerative disease of the musculoskeletal system. The spa therapy with the use of radon waters slightly influenced the increase in the hemoglobin level in patients with degenerative disease of the musculoskeletal system. The hemoglobin level may, in the future, along with other blood test parameters, confirm the impact of the spa treatment and its effectiveness.

Keywords: radon therapeutic waters; radon-sulfur therapeutic waters; spa physiotherapy; osteoarthritis of the joints and spine; hemoglobin

1. INTRODUCTION

Hemoglobin (Hgb) is the fundamental protein of erythrocytes and is responsible for the transport of oxygen. Hgb carries oxygen from the pulmonary alveoli to the tissues, taking away carbon dioxide from the tissues to the lungs in the return pathway. In 100 ml of human blood, there are 13 to 16 grams of hemoglobin. Hemoglobin is produced in the red blood cells of the bone marrow. It belongs to the

class of chromoproteins, has a molecular mass of 65,000, and contains 0.34% iron. In the construction of hemoglobin, one can distinguish haem, which is composed of the protoporphyrin IX ring and iron, as well as of globin. The hemoglobin molecule consists of 4 protein polypeptide chains, i.e., two α and two β chains. The α and β chains differ in the number of amino acids in the molecule (Zapora and Jarocka, 2013; Herold and Röck, 2003; Kang et al., 2000).

In high doses, radon has an adverse impact on health, and its harmful effects are damaging to enzymes and nucleic acids, which leads to tumorigenesis. Therefore, when using radon as a therapeutic material, it should be given special consideration. The basis for the rationality of radon water's healing effect is the so-called radiation hormesis hypothesis. According to it, small doses of ionizing radiation activate life processes. Currently, there are no scientific reports explaining the mechanisms of radiation hormesis. Among the mechanisms at the level of cellular control systems are mentioned: stimulation of DNA repair processes, protein synthesis, activation of genes, production of stress proteins, oxygen radical detoxification, activation of membrane receptors, multiplication of splenocytes, and stimulation of the immune system, which in turn reduces the risk of mutation or carcinogenesis. Changes in the system result from ionization. The effects of radiation in a living cell depend on what molecules in its composition have been damaged, and so they rely on the disruption of various functions of a given cell. In somatic cells, repair mechanism's function; over time, damaged particles can be removed and replaced with new molecules. Perhaps this mechanism is the essence of radiation hormesis (Kraska and Bilski, 2012; Feinendegen, 2005; Widel et al., 2009).

Radon (radium) waters are specific waters containing small amounts of unstable radioactive radon and products of its decay. These waters are used in medicine if the radon content exceeds 74 Bq/L (2 nCi/L) and if they meet the operational and hygienic requirements. Radon is a chemical element formed in the radioactive decay of uranium and thorium. It is a colorless, odorless noble gas that dissolves well in water, especially when the water is slightly mineralized or acidified. It exists in the form of many isotopes, among which the precursor is radon-222, arising directly from radium-226 as a result of alpha decay. The emitted alpha particles have low penetration depth but high ionizing capacity. The half-life is 3.8 days. The concentration of radon in natural conditions varies throughout the day and seasonally due to atmospheric precipitation. During the therapy, radon losses were also observed due to technical factors, including water accumulation in reservoirs, pipe transfers, heating and cooling, and intensive exploitation (a 40-80% drop in radon content). The high variability in radon concentration at the collection site makes it impossible to calculate the dose, and this practice is not followed (Kochański et al., 2004; Dadel and Trościanko-Wilk, 2014). Radon absorption occurs primarily through the lungs; 90% of excretion from the body occurs through the lungs, and the remaining 10% through the kidneys and skin. During the bath, absorption mainly occurs through the respiratory tract because radon and its decay products accumulate in large quantities above the water surface. The lungs are particularly vulnerable to radon because its decay products sediment in the pulmonary alveoli. The radioactive sediment settles quite firmly on the skin and remains for several hours.

Radioactive decay in the organism is highly variable and largely depends on adipose tissue mass. In this process, the adrenal cortex, liver, and muscles also play an important role. The anti-inflammatory, desensitizing, and analgesic effect of radon is explained by stimulation of the adrenal cortex and increased production of steroid hormones. Studies have shown increases in serum concentrations of luteinizing hormone and growth hormone, as well as in cortisol, testosterone, estradiol, and estriol. Radiation treatments affect: improvement of peripheral circulation, reduction of edema, joint and tendon-muscular pain, and improvement of motor performance. There is also a decrease in blood pressure, cholesterol, and triglyceride levels, a decrease in the rate of red blood cell decline, and an increase in the level of hemoglobin and red blood cells, an increase in ionized calcium, parathyroid hormone, and calcitonin, and acceleration of the removal of harmful metabolic products (Erickson 2007; Franke et al., 2000, 2007; Demczyszak et al., 2009; Zdrojewicz and Belowska-Bień, 2004a; Zdrojewicz and Belowska-Bień, 2004b).

Small doses of ionizing radiation are used in spa therapy in the Świeradów-Zdrój health resort. In the case of the radiant medicinal waters of Przerzeczyn-Zdrój, it should be emphasized that in addition to ionizing radiation, sulfur is a quite important therapeutic factor. One of the basic indications for the use of waters with sulfur content is degenerative-production changes in joints and the spine, with associated pain syndromes. As a result of isotopic tests, the presence of absorbed sulfur in many tissues, particularly connective tissue, bone tissue, and articular cartilage, was found in the joint itself. The sulfur introduced into the system during the procedure is used for the synthesis of chondroitin sulfate, a component of articular cartilage. In addition, sulfur is a part of the cartilage, bone, and granulation proteoglycans (Mika and Engel, 2004). Sulfur in therapeutic waters is usually present in the form of sulfide, hydrogen sulfide ions, as well as hydrogen sulfide. When bathing, hydrogen sulfide is also absorbed through the bronchial, gastrointestinal, and genital tracts (Kucharski et al., 2006).

Bivalent sulfur that passes through the skin affects immune responses by inhibiting Langerhans cells and neutralizing free radicals (ROS). Sulfur absorbed during the bath helps remove ROS from the body and inhibits inflammation. Sulfur ions that participate in the synthesis of nucleic acids form organic complexes with proteins and enzymes, i.e., oxidases, reductases, hydrolases, and transferases. It is especially necessary for glutathione synthesis, which indirectly contributes to the removal or neutralization of ROS and is also essential for normal cellular metabolism. It is believed that sulfur is incorporated into methionine, cysteine, and together with its oxidized form -s-s cystine it is responsible for the formation of an active oxide-reducing glutathione center (McBean, 2017).

As a part of comprehensive spa therapy, other forms of healing are also used: kinesitherapy, physical therapy in the field of light therapy, electrotherapy, ultrasonotherapy, cryotherapy, low and high frequency pulsed magnetic field, hydrotherapy with the use of various curative waters (salt, bicarbonate, radon), and peloidotherapy - mud wraps and baths. Muds are peat formed in an aqueous environment through decomposition under low oxygen conditions. It contains many minerals, hormones, proteins, fats, tannins, and so-called humic acids. The use of treatments in balneophysiotherapy at the spa induces non-specific changes in the reactivity of an adaptive organism. As part of spa medicine, there are also activities in prevention, health education, and psychotherapy (Woźniak-Holecka et al., 2017).

The aim of the study was to evaluate the impact of comprehensive spa therapy using radon and radon-sulfur water on hemoglobin levels in people with osteoarthritis.

2. MATERIAL AND METHODS

The research was carried out in two spas: Przerzeczyn-Zdrój and Świeradów-Zdrój. Before the therapy and after 18 days of treatment, patients had blood aspirated from the venous aspiration system (ulnar vein). Venous blood was collected in accordance with the Principles of Good Laboratory Practice. In full blood, complete morphology was performed along with the determination of hemoglobin concentration using a hematological analyzer.

In Przerzeczyn-Zdrój, the group of respondents comprised 122 patients. The patients' ages ranged from 32 to 67 years. The average age of the patients was 53.5 years old. There were 91 women and 31 men. In Świeradów-Zdrój, the group of respondents was $n = 35$ patients. The patients' ages ranged from 47 to 63 years. The average age of the examined patients was 56.5 years old. Among the respondents, 24 were women, and 11 were men. Both groups were selected for treatment in spas due to osteoarthritis. The main criteria for patient selection were the presence of osteoarthritis of the joints and/or the spine, agreement to participate in the research, and the absence of contraindications to comprehensive therapy in the spa. The exclusion criteria were refusal to participate in the research and the presence of conditions that contraindicated therapy. Patients were on a basic diet or an easily digestible diet, with low-fat cooked meals prevailing. Both diets were normocaloric diets. Vitamin preparations were not used. Medicinal waters were accepted as the main healing factor. In Przerzeczyn-Zdrój, there are radon-sulfide waters at 12 °C and pH 7.62. In 1 dm³ of water, there is 1.96 mg H₂S, 289.6 mg HCO₃, 2.21 nCi/IRn (81.8 Bq / l). They belong to low-mineralization waters. In Świeradów-Zdrój, there are also low-mineralized waters, and the main therapeutic factor is radon content in the water - Rn 303,1-441,5 Bq/l. Differences in the concentration of radon are characteristic of individual spas and are a peculiar feature.

Comprehensive spa therapy included the use of radon-sulfur medicinal water (Przerzeczyn-Zdrój) and radium (Świeradów-Zdrój), peloid therapy (peloidotherapy), cryotherapy, therapeutic massage, physical therapy, and kinesitherapy. Characteristics of applied radon treatments: total radon baths - temperature 37°C, duration 15 minutes, treatments were performed every 2 days, radon inhalations through mouth, duration 15 min, temperature 37°C - treatments were performed every 2 days. Bathing and inhalation were alternated; the total number of radon treatments during the stay was 15. Characteristics of radon-sulfur treatments: radon-sulfur or partial baths, including covering upper and/or lower limbs - temperature 37-38°C, duration 20 min.

Patients were advised to undergo a series of 10 treatments for each type of therapy, depending on their physical condition and reported ailments. Doses and treatment durations were selected in accordance with applicable standards. An exemplary set of treatments used in the treatment is radon baths or inhalations, radon-sulfur baths, mud wraps, group and individual healing gymnastics, biostimulation with laser radiation, and interference currents.

Below are the types and doses of other treatments used:

- peloid treatments (peloidotherapy) - partial mud sediments, duration of the treatment 20 min, temp 40-42°C,
- therapeutic gymnastics in a pool with therapeutically inert water,
- individual gymnastics on instruments and group gymnastics, which were selected for each patient according to their individual fitness; the average duration of kinesitherapy was 30-45 minutes,

- terrain-walk, outdoor activities
- dry massage - depending on the needs that are related to cervical (CC), thoracic (TH), or lumbar spine (LS),
- laser therapy - parameters of the treatment: sweeping, continuous operation, wavelength 808 nm, power 12.0 J, 400 mV, duration 30s,
- low frequency magnetic field: duration: 20 minutes, rectangular pulse shape, 5 mT induction, 20-50Hz frequency,
- ultrasonotherapy - treatment parameters: 800kHz / 6cm² head, ultrasonic impulse wave 2ms-pulse, 9ms interval, in a dose of 0.5-0.6 W / cm² in 6 min,
- cryotherapy - supply, duration of the treatment: 2-3 minutes, temp. from -80 ° C to -1100 ° C,
- electrotherapy: Bernard's diadynamic currents - treatment parameters - DF1 CP4 LP4, Nemeca interference currents (frequency range 0-100Hz), percutaneous electrical stimulation (TENS) - rectangular pulsed current with a pulse duration of 0.2 ms, frequency 40 HZ and controlled intensity from 0-100 mA,
- light therapy: Sollux lamp with a blue filter, exposure distance 30-40 cm, duration 15 min., Biopton lamp - distance of exposure 10 cm, time of exposure 5-10 min.

The model of spa therapy, including radon therapy, is a tradition in Poland and Europe that dates back over a century. Of course, the therapeutic program was modified with the aid of actively developing hydrotherapy and then balneology. Radon therapy in Polish conditions can be prescribed only on a medical order, after consideration of indications and contraindications, in accordance with the established dosage standard. The number of treatments, duration, and type are determined - inhalations, baths, or mouthwash. Radon spas use water from natural sources, obtained from wells drilled in accordance with mining law, with the consent of the Ministry of Environmental Protection and under the supervision of the Ministry of Health. Each treatment water must meet certain criteria for balneochemical and bacteriological tests to be considered medicinal.

In the radium spas, dosimetry evaluation of treatment water and dosimetry assessment of treatment rooms are carried out. This assessment allows for determining the patient's exposure. The calculation of absorbed radiation dose is not carried out because it is variable and depends on body structure, especially fat content and the absorption surface (airways), co-existing diseases, and exploitation-related losses. Dosimetry measurements are carried out daily using certified detectors.

The approval of the Bioethical Commission of the Medical University of Wrocław was obtained for the tests - opinion No. KB-401/2008 and opinion No. 135/2015, written consent of the Presidents of both spas, individual written consent of patients prepared in accordance with the formula recommended by the Bioethical Commission.

Statistical analysis was performed using the Statistica 13 program (StatSoft, Inc., USA). For arithmetic variables, arithmetic means, standard deviations, and range of variation (extreme values) were calculated. All quantitative variables were tested with the Shapiro-Wilk test to determine their distributional type. The comparison of results between groups was performed using an independent-samples t-test. The comparison of results before and after the intervention within each group was performed using a dependent t-test. For all comparisons, the level $\alpha = 0.05$ was assumed, and the obtained values of "p" were rounded to 4 decimal places.

3. RESULTS

There was a statistically significant decrease in hemoglobin in patients using radon-sulfur water therapy in Przerzeczyn-Zdrój. Statistically significant increases in hemoglobin levels were observed among patients receiving radon water therapy in Świeradów-Zdrój (Table 1; Figure 1 and 2). The comparison between the groups' pre- and post-treatment results is presented in Table 2 and Figures 3 and 4.

Table 1. Intergroup results - HGB (g/dl) concentration.

	Przerzeczyn-Zdrój (n=122)				Świeradów-Zdrój (n=35)				p-value
	\bar{x}	Min	Max	SD	\bar{x}	Min	Max	SD	
HGB- before	14.3	9.9	17.4	1.28	13.65	10.2	16.1	1.06	0.0065*
HGB - after	14.1	9.8	17.4	1.32	13.68	10.1	16.2	1.17	0.0936*
n - number; \bar{x} - average; min - minimum value; max - maximum value; SD - standard deviation; * - t test for dependent samples									

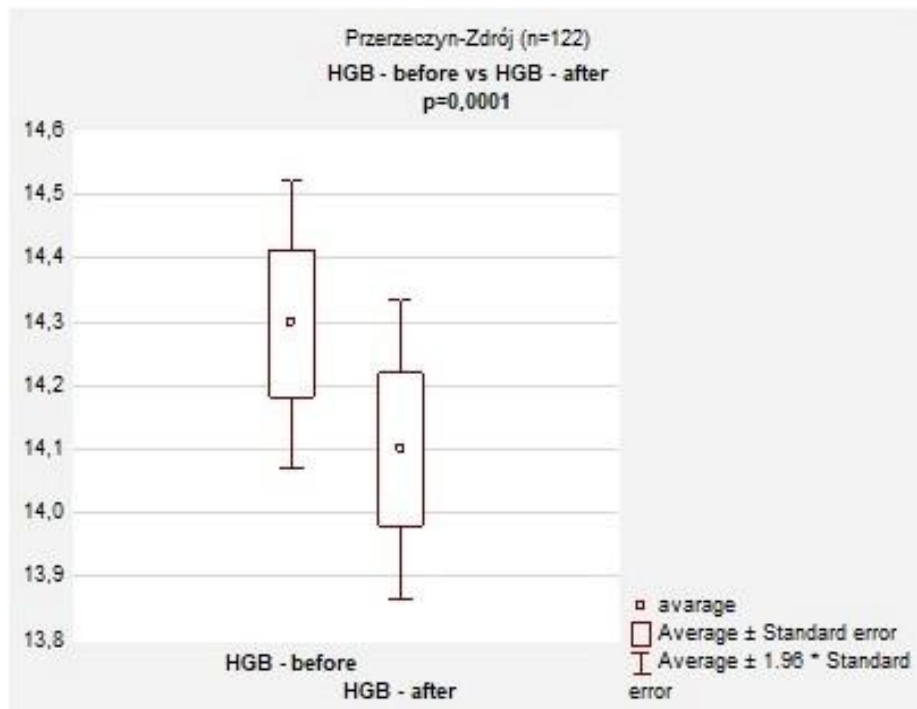


Figure 1. Change in HGB (g/dl) concentration radon-sulfur waters - Przerzeczyn Zdrój

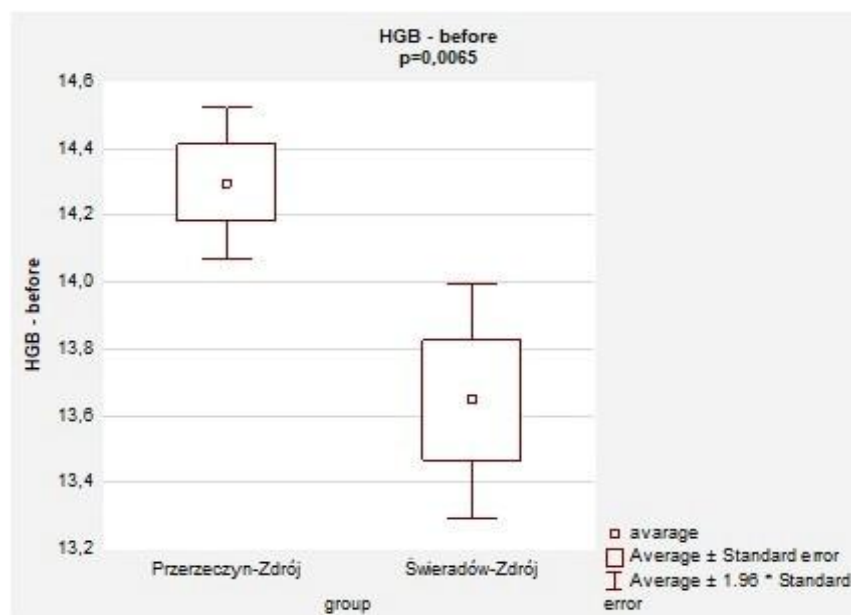
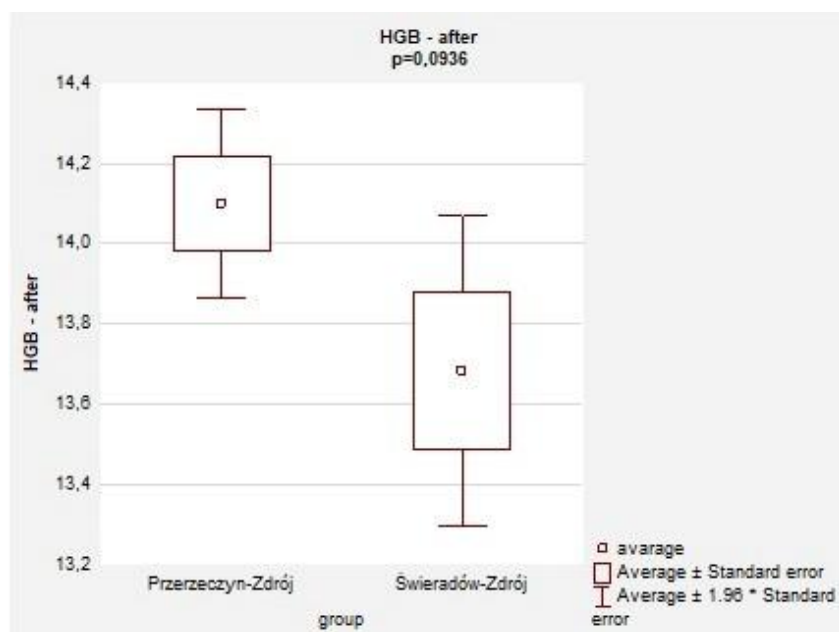


Figure 2. Change in HGB (g/dl) concentration in radon waters - Świeradów-Zdrój

Table 2. The comparison between the groups of the results before treatment and the results after treatment

	HGB – before				HGB – after				p-value
	\bar{x}	Min	Max	SD	\bar{x}	Min	Max	SD	
Przerzeczyn-Zdrój (n=122)	14.3	9.9	17.4	1.28	14.1	9.8	17.4	1.32	0.0001*
Świeradów-Zdrój (n=35)	13.65	10.2	16.1	1.06	13.68	10.1	16.2	1.17	0.7279*

n – number; \bar{x} - average; min – minimum value; max – maximum value; SD – standard deviation; * - t test for dependent samples;

**Figure 3.** Comparison of mean HGB (g/dl) in both groups before treatment**Figure 4.** Comparison of mean HGB (g/dl) in both groups after therapy

4. DISCUSSION

After searching the MEDLINE and Cochrane Library databases, studies assessing the impact of spa therapy on hemoglobin were found. The keywords used to search the databases: balneology, radon, and irradiated-sulfur therapeutic waters, comprehensive spa therapy, physical therapy, kinesitherapy, blood morphology, and hemoglobin. Attention was drawn to research published in the years 2000-2018. Observed different results, most often an increase in the value of hemoglobin. In the conducted studies, a statistically significant decrease in hemoglobin concentration after treatment in the resort of Przerzeczyn-Zdrój was found. However, the changes observed in the Świeradów-Zdrój health resort are not statistically significant, indicating no increase in hemoglobin concentration after therapy (Durda et al., 2011).

Studies using sulfur- and hydrogen sulfide-rich waters reported increased hemoglobin levels. The authors believe that oxydoreductive oxidation processes strengthen after baths, as evidenced by increased hemoglobin and erythrocyte counts. The action in this case concerns the effects of sulfur on the metabolism of cells and tissues. Sulfur, as a very active element, can stimulate a number of metabolic pathways, initiate free radical reactions (an important component of glutathione and antioxidant system enzymes) (Durda et al., 2011; Bilska et al., 2007). Misztela et al., (2001) also observed an increase in hemoglobin in patients with rheumatoid arthritis treated with artificial sulfide and hydrogen sulfide baths.

A study by Frih et al. (2017) showed that hemoglobin levels were not observed in patients undergoing dialysis with kinesitherapy. The next study of Huang et al., (2018) a study conducted in a group of patients with peripheral circulation disorders in the course of diabetic foot and atherosclerotic atherosclerosis, showed that after 3 months of kinesitherapy, hemoglobin levels increased. Draghici et al., (2018) conducted a study using an infrared spectroscope to measure blood flow in the lower limbs and hemoglobin levels after kinesitherapy in patients after spinal cord injury and in healthy people. The results showed that in healthy people, blood flow to the lower limbs increased, and hemoglobin levels increased. However, no changes were observed in patients with spinal cord injury.

Xu et al., (2017) studies showed that balneotherapy increased red blood cell counts, hemoglobin, and hematocrit. In studies of patients after myocardial infarction participating in the rehabilitation program, changes in blood counts and blood rheological properties have been observed. There was, inter alia, a slight increase in hemoglobin (not statistically significant) following kinesiotherapy (Pabisiak et al., 2016). Increased hemoglobin was also observed during exercise with a submaximal initial load and during bathing with different forms (Okushima et al., 2016; Rifkind et al., 2004).

The observations indicate different results, which depend mainly on the type of treatments used. In the case of medicinal waters, the composition and pharmacodynamic properties of the waters used in therapy depend. Clear changes (increase in hemoglobin) occurred under the influence of kinesitherapy and curative waters with sulfur content, showing a specific metabolic activity. So, how do you explain the reduction in HGB levels in the group from Przerzeczyn? KochOne can only assume that radon and sulfur ions are strong balneological stimuli that activate free radical reactions in the body. Low doses of absorbed alpha radiation are considered the main factor activating the transformation. The main mechanism of activation can be a radiation hormone. The study's results may indicate only the activation of free radical reactions. Hemoglobin, its iron ions, and protein chains are primarily responsible for oxygen transport, catalyze free radical reactions, and prevent the formation of ROS (Rifkind et al., 2004; Chobot and Hadacek, 2010).

Undoubtedly, there are no randomized studies. This is the consequence of the inability to make blind attempts during spa therapy. Due to discrepancies, further assessment of the discussed parameter requires multidisciplinary testing, including blood morphology, changes in haem-degradation products, and iron economy. Because it is impossible to clearly identify the factors that determine such different results, it is advisable to design randomized trials involving large groups of patients using isolated forms of therapy. It seems quite significant, especially given the need to objectively assess the value and effectiveness of comprehensive spa therapy.

5. CONCLUSION

Spa therapy using radon-sulfur waters reduced hemoglobin levels in patients with degenerative musculoskeletal disease ($p < 0.001$). Spa therapy using radon water did not significantly influence the increase in hemoglobin levels in patients with degenerative disease of the musculoskeletal system ($p > 0.05$). In the conducted observation, it is not possible to unequivocally assess which procedures cause the greatest changes; only an indirect end result, a decrease in hemoglobin levels, is visible following comprehensive therapy. Both in vivo and in vitro studies could pave the way for scientific progress in balneology.

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Authors' Contributions

This manuscript has been read and approved by all the authors. Each of the authors believes that this manuscript represents honest work done by us.

Informed consent

Written & Oral informed consent was obtained from individual participants included in the study.

Ethical approval

The study was done in conformity with ethical guidelines. Participation was entirely voluntary, and all respondents provided informed consent. The participants' anonymity and confidentiality were ensured, and the data obtained were utilized purely for the study. The ethical guidelines for Human Subjects are followed in the study.

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Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data are contained and described within the manuscript. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. Trial registration: The numbers of clinical trials are NCT03274128 and NCT03405350. All information about this study is available under this number. No reprints are available for this manuscript.

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