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Effect of Whole-Body Cryotherapy on Body Balance in Patients with Multiple Sclerosis

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Abstract

Purpose: Multiple sclerosis (MS) is characterised by multifocal and damage disseminated in time to the central nervous system. This causes various clinical symptoms, including spastically increased muscle tone and balance disorders, which already occur in the early stages of the disease, increasing the frequency of falls, which negatively affects the mobility and independence of patients. Whole-body cryotherapy (WBC) is used in the rehabilitation of MS patients, however, there are no reports on the effect of WBC without subsequent kinesiotherapy on body balance in patients with MS. The aim of the study was to assess the effect of a series of 10 and 20 WBC without kinesiotherapy on the degree of disability assessed by the Expanded Disability Status Scale (EDSS), muscle spasticity evaluated using the Modified Ashworth scale (MAS) and body balance in patients with multiple sclerosis. **Methods**: The study was completed by 51 patients, aged 23 to 65 years, with a disability grade of 3.5-6.5 on the EDSS scale and spasticity 0-3.0 assessed by the MAS. Patients were randomly assigned to the control group (n=18) or the experimental group participating in 20 WBC sessions (n=33). Balance assessment consisted of performing two, 30-second static tests on stabilometric platform, the first test with eyes open and the second one with eyes closed. During these tests, the centre of foot pressure displacement was monitored and analysed in real time. **Results:** A series of 20 daily WBC resulted in an improvement in the functional status of patients with multiple sclerosis in the form of a significant reduction in EDSS values and spasticity, both on the side with greater and less spasticity. Under the effect of whole-body cryotherapy treatments, there was slight improvement in the stability in patients with multiple sclerosis. **Conclusions:** Based on the obtained results, it can be concluded that WBC, without subsequent targeted kinesiotherapy, are not sufficient to obtain clear and measurable benefits in the rehabilitation of patients with multiple sclerosis.

Keywords: balance disorders; EDSS; spasticity; stabilometric platform; centre of pressure displacement

1. INTRODUCTION

Multiple sclerosis (MS) is an acquired, chronic and progressive autoimmune disease of the central nervous system (CNS), during which demyelination with axonal damage, limited remyelination, oligodendrocyte death, gliosis, neurodegeneration and variable symptoms occur [54]. Changes in the CNS are accompanied by clinical symptoms in the form of neurological deficits of varying severity, which ultimately destroy communication between the brain and the rest of the body [53]. It is estimated that approximately 2.8 million people suffer from MS worldwide [3].

MS is the most common non-traumatic cause of disability in young adults, and the disease constitutes a great medical and social problem. The disease is diagnosed mainly between the age of 20 and 40, over time, limiting patients mobility and intellectual abilities, which can cause an enormous financial burden and serious emotional problems for the patients themselves and their families [37, 54].

According to various sources, it is estimated that spasticity in the musculoskeletal system occurs in 40-90% of patients with multiple sclerosis [2, 19, 35]. Spasticity makes walking, daily self-care and hygiene activities difficult and contributes to the development of undesirable symptoms, such as pain and limited mobility in joints, leading to progressive disability [2, 13, 20]. A number of researchers link the phenomenon of spasticity with body posture control deficits in MS patients and balance disorders [11, 14], which translates into a decrease in their safety as well as an increased risk of falls, and their consequences [12, 41].

Balance disorders are a common symptom in patients with multiple sclerosis and already occur in the early stages of the disease, even in the absence of clinical symptoms of pyramidal dysfunction [9, 21]. The disorders intensify with age and disease progression, and the consequences of this are falls and injuries as well as an increasing fear of falls [5, 16, 38]. Balance disorders have a negative impact on everyday activity and, above all, on the safety of patients with MS; they are the most important factor increasing the risk of falls and their consequences [9, 12, 38]. It is estimated in clinical observations that over 50% of patients with MS have experienced at least one fall [3, 28].

The degree of balance disorder severity, their dynamics and course are a consequence of weakened body posture control mechanisms and vary individually. Balance impairment may also result from impaired cognitive functions, damage to the labyrinth, decreased muscle strength as well as sensory and coordination disorders [10]. The accumulation of deficits in individual parts of the body posture control system leads to its instability and, consequently, to an increased risk and frequency of falls, which negatively affects the mobility and independence of MS patients [10, 12, 22].

Since none of the pharmacological treatment methods used so far lead to a cure of the disease consequences, comprehensive rehabilitation should be implemented at each stage of the disease, starting from the moment of its diagnosis. Its aim is to prevent the negative effects of the disease, delay its development and maintain optimal physical and mental fitness of the patient for as long as possible, while also preventing unfavourable consequences of the disease. It has been proven that comprehensive and systematic rehabilitation has a positive effect on the quality of life among MS patients, extends lifespan, work efficiency and independence [32]. In addition to kinesiotherapy, the rehabilitation of MS patients employs various physical treatments to alleviate the symptoms accompanying the disease. These include individually selected physical therapy treatments, such as: electrotherapy, massages, hydrotherapy, cold therapy, magnetic therapy, magnetic stimulation, low-energy laser radiation, functional electrical stimulation (FES) or hyperbaric oxygen therapy [19, 30, 47, 48, 55]. Particular attention should be paid to the beneficial effects of whole-body cryotherapy treatments among patients with MS, both in their subjective assessment and in clinical trials [30, 32, 55].

Whole-body cryotherapy (WBC) has been used in the rehabilitation of MS patients since 1984, and the pioneer of using this form of cryotherapy in MS patients was the German rheumatologist Prof. Reinhard Fricke [1]. According to the latest position of an international group of experts, “WBC-related safety risks are within acceptable limits and can be proactively prevented by adhering to existing recommendations, contraindications, and common-sense guidelines” [25].

In previous studies, it has been shown that the use of whole-body cryotherapy combined with subsequent kinesiotherapy provides many benefits to patients with multiple sclerosis, such as reducing spasticity of the lower limb skeletal muscles [31, 50], decreasing of disability measured via the Expanded Disability Status Scale (EDSS) [29, 31], reducing the feeling of fatigue [29, 30, 43], antidepressant effect and well-being [45], improvement of cognitive functions [30, 45], increasing the strength of the upper limb muscles [28, 43] and the lower ones [29]. Improvement was found in antioxidant status among MS patients following WBC therapy [7, 31] as well as better locomotion [43].

However, the available literature does not contain any reports on the effect of whole-body cryotherapy alone, without subsequent kinesiotherapy, on biomechanical balance indicators among people suffering from multiple sclerosis. Moreover, only 10 WBC are usually prescribed at once and 20 per year in our country. Therefore, the aim of this study was to assess the effect of a series of 10 and 20 WBC, without subsequent kinesiotherapy, on balance in people with multiple sclerosis.

Research hypotheses:

1. Whole-body cryotherapy used in a series of 10 and 20 WBC may reduce disability assessed using the EDSS scale and lower limb spasticity in patients with MS.
2. Whole-body cryotherapy used in a series of 10 and 20 WBC may significantly improve static balance in MS patients.

2. METHODS

The study was conducted in accordance with the 1964 Declaration of Helsinki. The study protocol was approved by Bioethics Committee of the Regional Medical Chamber (OIL) in Krakow (No. 99/KBL/OIL/2019 of 2 April 2019). All participants read the written information regarding the purpose and course of the study, the possibility of resigning from participation without giving reason, and signed the "Subject Informed Consent" form to participate in the study.

2.1. Study group

At the beginning, the study involved 60 MS patients, aged 23 to 65. Diagnosis of MS (ICD G35.0) was made by a physician, specialist in neurology and in accordance with the diagnostic criteria proposed by McDonald and modified by Polman et al. [39]. The patients who participated in our study have a primary (22%) and secondary progressive (78%) form of MS without relapses. Forty percent of patients were taking MTX, 10% Dimethyl Fumarate, 10% Betaferon, 3% Fingolimod and 3% Natalizumab. As for Myorelaxants, 54% patients were taking Baclofen and 19% Sirdalud. Pharmacological treatment was not changed during this study, and the clinical condition of the patients was stable (no change over six months).

The Expanded Disability Status Scale (EDSS) is commonly used to evaluate the neurological status/disability of MS patients and to compare the applied therapy [24, 52].

The EDSS and MAS [6, 18] assessment was performed twice (at the beginning and end of the project) by the same neurologist.

The following inclusion criteria were used:

- diagnosis of MS (primary and secondary progressive form of the disease) based on McDonald's diagnostic criteria modified by Polman et al. [40, 52];
- disease lasting at least two years from diagnosis;
- age above 18 and below 65;
- disability level of 3-6.5 on the EDSS scale;
- spasticity of 0-3.0 on the Modified Ashworth Scale (MAS);
- ability to walk independently and cooperate during the study;
- no contraindications to cryochamber treatments [26];
- not using whole-body cryotherapy treatments within the past six months preceding the study.

Exclusion criteria were previously described by Lubkowska [26].

Thirty percent of our patients had hypertension, however, it was stable as result of typical treatment. One experienced compensated hyperthyroidism, two demonstrated compensated hypothyroidism, one had chronic heart disease and four suffered from diabetes type 2 without complications. The illnesses did not exclude the patients form our programme. The patients were randomly assigned to the control (CG, n=20) and experimental group participating in WBC therapy (EG, n=40). For various reasons, including pandemic lockdowns, nine people withdrew from the programme (two in the CG and seven people from the EG). It should be noted that in none of these , the reason for discontinuing participation in the study was poor tolerance of WBC. A total of 51 patients completed the study: 18 subjects in CG (female, n=14; male, n=4) and 33 subjects in EG (female, n=23; male, n=10) (Figure 1).

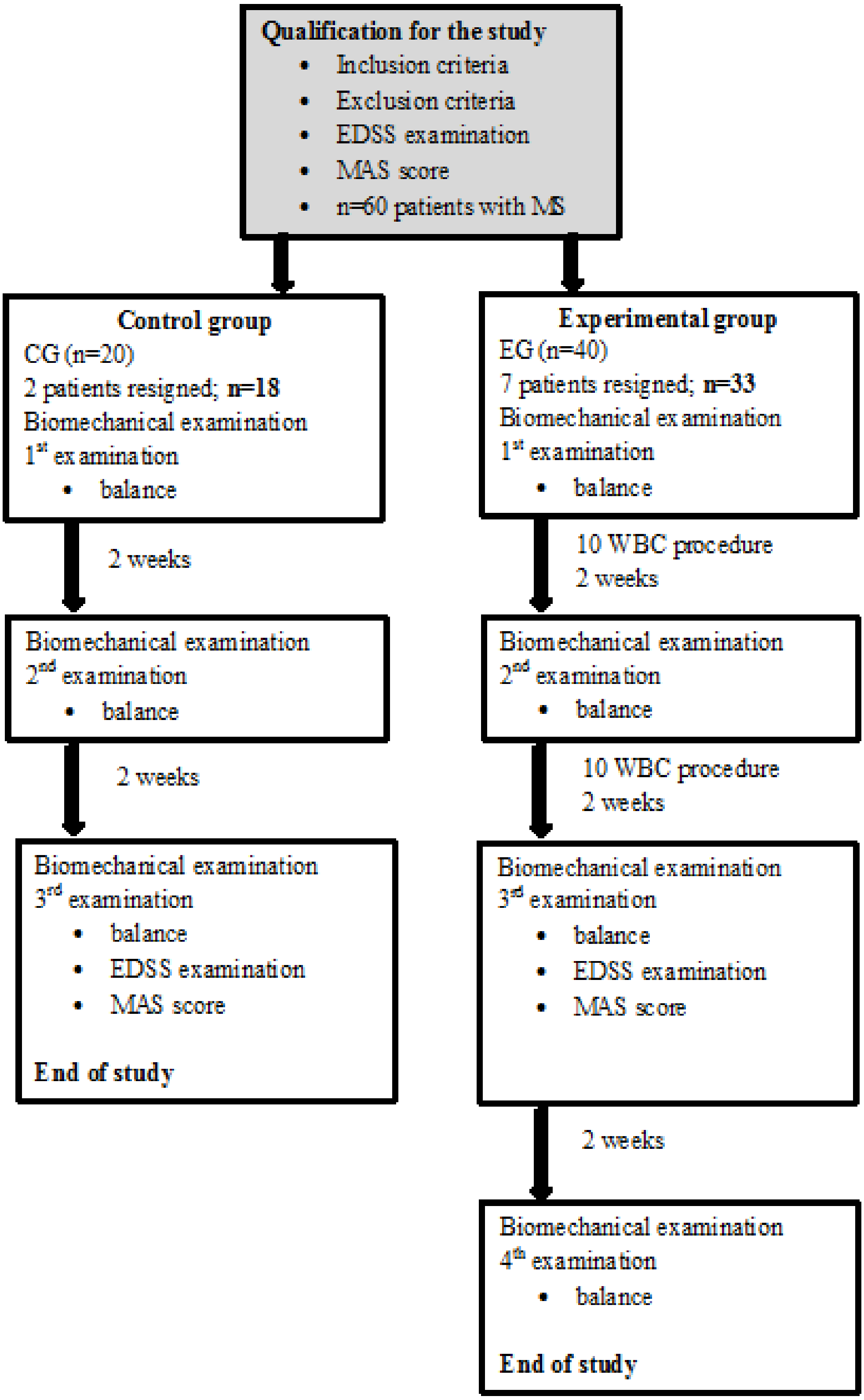

Figure 1. Block diagram of conducted study.

2.2. Course of study

Body balance tests in EG were performed before the start of WBC (1st measurement), after 10 WBC (2nd measurement) and 20 WBC (3rd measurement) and 2 weeks following the completion of therapy (Fig. 1). In CG, biomechanical tests were carried out three times – measurements 1, 2 and 3, which corresponded in time with the 1^{st}, 2^{nd} and 3^{rd} measurements in the EG group. The body balance tests consisted of two, 30-second static tests on the Zebris DM-S stabilometric platform, the first test with eyes open (EO) and the second one with eyes closed (EC). During these tests, the centre of foot pressure (COP) displacement was monitored and analysed in real time. The tests always took place in the morning, in similar thermal conditions – the temperature in the laboratory during the tests was 20-22°C.

During the tests conducted by the same neurologist, body sides were identified in terms of the spasticity grade regarding the lower limb muscles (the flexors and extensors of the hip and knee joints) assessed according to MAS. The side of the body with greater spasticity was referred to as MAS_{A1}, and the side with less spasticity was considered as MAS_{A0}, and these designations were used in the description of the study results.

The analysed variables characterising body balance, their abbreviations used in the text and the units in which they were expressed are summarised below:

·$CP_{AREA}EO$, $CP_{AREA}EC$ – area of the centre of pressure deflection envelope in a standing position with eyes open (EO) and eyes closed (EC), [mm^2].

·$CP_{L}EO$, $CP_{L}EC$ – path length of the centre of pressure in a standing position with eyes open (EO) and eyes closed (EC), [mm].

·$CP_{V}EO$, $CP_{V}EC$ – average velocity of the centre of pressure displacement in a standing position with eyes open (EO) and eyes closed (EC), [mm/s].

·%Q – percentage distribution of the subjects' body mass on the foot of the lower limb with greater and less spasticity (A1, A0).

2.3. Methodology of whole-body cryotherapy treatments

Patients from EG participated in 20 WBC in four, five-day series (from Monday to Friday) in the afternoon. The treatments took place at the Malopolska Cryotherapy Centre in Krakow, according to the procedures described in the study by Lubkowska [30]. Before entering the cryochamber, patients had to undress and dry their skin thoroughly. There was no ointment, cream or makeup on the skin. Glasses, jewellery, watches and other metal items had to be removed. The attire for the treatments was minimal – women wore light gymnastic or swimming suits, men wore shorts. Patients entered the cryochamber wearing clogs, and parts of the body sensitive to cold were protected with thick gaiters (lower legs and knees), gloves (hands), a mask (mouth and nose) and a hat or headband (ears). After preparation, patients were let into the vestibule of the cryochamber and stayed there at -60°C for half a minute, and then they were brought into the main part of the cryochamber where the temperature was -120°C. In the main part, the patients moved around slowly, one after the other, without deepening their breathing or talking. After 30 seconds, the direction of movement was changed. In the main part, patients stayed for 1.5 minutes for the first time, 2 minutes for the second time, and the time spent in the cryochamber in the remaining 18 treatments was 3 minutes each. Trained staff supervised the safe course of the procedure. The Bamet KN-1 cryochamber (Bamet, Poland) is cooled with liquid nitrogen. Thanks to two installed sensors (EurOx.O2 G/E, Krakow, Poland), a constant oxygen content was maintained at 21-22% in the cryochamber. The humidity level in the cryochamber was also regulated.

As mentioned above, there were no subsequent appropriately programmed kinesiotherapy sessions after the cryotherapy, however, the patients could undergo a short, 10-min aerobic exercise on a cycloergometer to support blood circulation.

2.4. Statistical processing of results

Statistical analysis was performed using the IBM SPSS Statistics statistical package and a Microsoft Excel spreadsheet.

The following descriptive statistics were used to describe the collected quantitative data:

·mean (M), standard deviation (SD), minimum (Min), maximum (Max), 25th, 50th (median) and 75th percentile values.

The following tests were used in the statistical analysis:

- the Shapiro-Wilk test examining the assumption of normal distribution of results. When the results of the Shapiro-Wilk test indicated that the distribution of the studied variables was close to normal distribution, two-way MANOVA analysis of variance was used to examine the interaction between the repeated measure factor (measurement 1 vs. measurement 2 vs. measurement 3) with the inter-group factor taken into account (control group vs. experimental group). In order to determine the force of the effect, partial eta squared (η^2_P) was calculated, the values of which being >0.01, 0.06 and 0.14 correspond to small, medium and large degrees of the effect force. If significant interactions were found, the probability for post-hoc tests was calculated using Bonferroni's post-hoc test.

- Friedman's test for dependent variables and the Dunn-Bonferroni post-hoc test when the assumptions for using multivariate analysis of variance for dependent variables were not met.
- Wilcoxon's test was applied when only two measurements were performed.
- In order to examine differences between the study groups depending on the distribution of variables, the Mann-Whitney U test and the Student's *t*-test were implemented.
- In order to examine the relationships between two variables, it was decided to use Sperman's rho correlation test.

In all analyses, the effects for which the probability value of p was lower than the assumed significance level totalling $\alpha=0.05$ ($p<0.05$), were considered statistically significant.

3. RESULTS

3.1. Study participants and their characteristics

Table 1 are presents data characterising the groups of examined patients in terms of age and duration of the disease, as well as the values of indicators describing body structure. There were no statistically significant differences between groups for any the variables described here ($p>0.05$).

Table 1. Characteristics of the subjects

		Control group (CG)	Experimental group (EG)
Age [years]	M ± SD	54.5 ± 7.2	49.9 ± 10.0
	Min - Max	39.0 - 65.0	23.0 - 64.0
Disease duration [years]	M ± SD	12.3 ± 5.2	13.7 ± 7.0
	Min - Max	6.0 - 27.0	2.0 - 39.0
Body weight [kg]	M ± SD	67.81 ± 8.13	66.80 ± 9.14
	Min - Max	58.0 - 91.0	55.0 - 90.0
Body height [cm]	M ± SD	166.1 ± 7.9	168.6 ± 7.5
	Min - Max	154.0 - 182.0	154.0 - 182.0
BMI [kg/m^2]	M ± SD	24.6 ± 3.0	23.6 ± 3.9
	Min - Max	19.6 - 32.2	18.1 - 32.3

The duration of the disease was 12.3±5.2 years (from 6 to 27 years) in CG and 13.7±7.0 years (from 2 to 39 years) in the EG. The level of disability assessed according to the Expanded Disability Status Scale (EDSS) in both groups ranged, in accordance with the study assumptions, from 3.0 to 6.5 (4.75±1.1 in CG, 4.82±1.1 in EG).

In Table 2, the results are shown for medical assessment of the spasticity grade among the examined patients and the evaluation of their level of disability. Each person from the control and experimental groups was examined twice: at the beginning of the test cycle, during measurement 1 and during measurement 3.

Table 2. Level of disability (EDSS) and the spasticity grade (MAS_{A0}, MAS_{A1}) in both groups of patients

		Control group (CG)		Experimental group (EG)	
		Value before: measurement 1	Value after: measurement 3	Value before: measurement 1	Value after: measurement 3
EDSS	M ± SD	4.75 ± 1.1	4.78 ± 1.1	4.82 ± 1.1	4.48 ± 1.1*
	Min-Max	3.0-6.5	3.0-6.5	3.0-6.5	3.0-6.0
MAS_{A0}	M ± SD	1.11 ± 0.3	1.06 ± 0.2	1.23 ± 0.5	0.97 ± 0.3*
	Min-Max	1.0-2.0	1.0-1.0	0.0-3.00	0.0-2.00
MAS_{A1}	M ± SD	1.86 ± 0.8	1.78 ± 0.7	2.14 ± 0.7	1.55 ± 0.8*
	Min-Max	0.0-3.0	1.0-3.0	1.0-3.0	0.0-3.0

*$p < 0.05$

The baseline values of EDSS, MAS_{A0} and MAS_{A1} were not found to differ significantly among patients from the control and experimental groups (p>0.05). After 20 whole-body cryotherapy sessions in the experimental group (EG), there was a statistically significant reduction (Wilcoxon test) in the spasticity of both MAS_{A0} (Z=-2.994; p<0.001) and MAS_{A1} (Z=-3.650; p<0.001) values and the EDSS ones (Z=-3.642; p<0.001). In the control group, there were no statistically significant changes in the values of the above-mentioned variables during the six weeks of the experiment (p>0.05).

3.2. Assessment of static balance
3.2.1. Balance in test with eyes open (EO)

It was shown that the values of all indicators (total area of the centre of pressure deflection envelope, its absolute displacements and the velocity of these changes), at the corresponding measurement times, were always slightly higher in the experimental group (EG) (Table 3). At the same time, in this group, changes in $CP_{AREA}EO$, $CP_{L}EO$, $CP_{V}EO$ between the first and last measurements were smaller than in CG, although in both cases, the differences were not statistically significant. When analysing the data, it can also be noticed that in the group of patients undergoing WBC and in the control group, the tendency of changes in the values of the analysed indicators was similar. The lowest values were recorded in the first measurement, and the highest in the penultimate measurement.

Table 3. Descriptive statistics of indicators characterising the center of pressure displacements (CP) in the static balance test with eyes open (EO)

		Control group (CG)			Experimental group (EG)			
		Measurement 1	Measurement 2	Measurement 3	Measurement 1	Measurement 2	Measurement 3	Measurement 4
$CP_{AREA}EO$ [mm^2]	25 pct	127	215	172	159	264	309	224
	Median	219	278	454	268	421	445	440
	75 pct	573	562	738	608	710	895	744
$CP_{L}EO$ [mm]	25 pct	455	433	389	458	454	609	553
	Median	623	571	730	786	740	902	765
	75 pct	835	898	1015	1037	997	1113	1097
$CP_{V}EO$ [mm/s]	25 pct	16	15	14	16	16	21	19
	Median	22	20	26	28	26	32	27
	75 pct	29	31	36	36	35	39	38

In the experimental group, in the last measurement (two weeks after the end of the treatment session - measurement 4), the obtained values were higher by almost 10%.

None of the described differences between patient groups turned out to be statistically significant. This concerned both the beginning of the study (measurement 1) and subsequent measurements (measurements 2 and 3), when the experimental group used whole-body cryotherapy treatments (p>0.05).

Analysing the percentage distribution of the subjects' body mass (%Q) on the foot of the lower limb with greater and less spasticity (A_1, A_0), it was noted that in static balance tests performed with eyes open in both groups of patients, the limb with less spasticity took over the greater part of the body mass (53% vs. 47%) and no statistically significant changes were noticed under the effect of whole-body treatments in the cryochamber.

3.2.2. Balance in test with eyes closed (EC)

In Table 4, descriptive statistics are presented with regard to changes in the position of the centre of foot pressure (CP) in the static balance test performed with eyes closed. In the case of the first measurement, subjects from the EG were characterised by statistically significantly higher values: area of deflection envelope CP_{AREA} (Z=2.060; *p*=0.039), path length CP_L (Z=2.839; *p*=0.005) and average velocity of displacement CP_V (Z=2.839; *p*=0.005) in relation to the CG. In the second and third measurements, there were no statistically significant differences between the study groups (*p*>0.05). In the control group (CG), the total area of the centre of pressure deflection envelope ($CP_{AREA}EC$), its absolute displacements (CP_LEC) and the velocity of these changes (CP_VEC) increased in subsequent measurements, although these changes were not statistically significant. In the case of the experimental group (EG), this tendency was opposite – the values of the discussed variables decreased.

Table 4. Descriptive statistics of indicators characterising the centre of pressure displacement (CP) in the static balance test with eyes closed (EC)

		Control group (CG)			Experimental group (EG)			
		Measurement 1	Measurement 2	Measurement 3	Measurement 1	Measurement 2	Measurement 3	Measurement 4
$CP_{AREA}EC$ [mm^2]	25 pct	378	450	493	631	572	800	587
	Median	671*	811	946	1083*	939	1075	860
	75 pct	819	1346	1489	1875	1585	1861	2072
CP_LEC [mm]	25 pct	627	807	776	1021	752	914	827
	Median	985*	914	1105	1393*	1168	1089	1147
	75 pct	1148	1354	1400	1549	1434	1585	1444
CP_VEC [mm/s]	25 pct	22	28	27	36	26	32	29
	Median	35*	32	39	49*	41	38	40
	75 pct	40	47	49	54	50	55	51

* CG vs EG; $p < 0.05$

In the test with eyes closed, similarly to the that performed with eyes open, the relative load on the limb on the side with greater spasticity was lower (47%) than on the side with less spasticity (53%) (in both groups of patients, the limb with less spasticity assumed most of the body mass). There was also no statistically significant group × time interaction (*p*>0.05), which indicates no significant effect of whole-body cryotherapy treatments on the changes in limb load.

No correlations were demonstrated between indices characterising balance or EDSS. At the same time, significant correlations were found between MAS_{A0} and path length of the centre of pressure (CP_L) as well as velocity of the centre of pressure displacement (CP_V) in balance assessment conducted with closed eyes (EC) carried out after 20 WBC. The calculated values of correlation coefficients were as follows: rs=0.39 (p=0.04) and rs=0.40 (p=0.03), respectively.

4. DISCUSSION

The aim of this study was to assess the effect of a series of 10 and 20 WBC treatments on spasticity grade, functional status and balance among multiple sclerosis patients. In the most previous studies on the use of whole-body cryotherapy among patients with multiple sclerosis, WBC were combined with kinesiotherapy treatments performed after leaving the cryochamber [27, 36, 43, 50]. In the case of a patient's functional improvement, it is not obvious which of the factors had a decisive effect on the obtained results. Patients with MS are usually referred to a series of 10 treatments in a cryochamber. Sometimes, but this is not a rule, active free exercises are ordered after the treatment and not those indicated according to a deliberate kinesiotherapy programme. As stated by Gregorowicz and Zagrobelny [17], the use of cryotherapy alone does not improve the fitness of patients.

4.1. Effect of WBC on EDSS values and spasticity grade in patients with MS

Analysis of the results of this study showed a beneficial effect of 20 whole-body cryotherapy treatments on reducing spasticity (MAS) and improving functional status assessed using the EDSS disability scale among patients with MS. It turned out that in the experimental group (EG) participating in WBC, there was a significant reduction in spasticity on both sides of the body, both in the limbs with less (decrease by 0.26) and greater spasticity (decrease by 0.59), as well as a decrease in the average EDSS numerical value by 0.34. Such changes were not observed in the control group (CG) not participating in WBC, but examined at the same time intervals as the experimental group.

Comparing the authors' results to the data obtained by other authors is difficult because in only one study, for which a decrease in the EDSS value of 0.2-0.3 was observed, kinesiotherapy probably not used after the WBC procedures. In this study, in 48 patients with progressive MS and fatigue syndrome, a statistically significant reduction in the EDSS value and improvement in the functional status, assessed using the RMA (Rivermead Motor Assessment) and the MSIS-29 (Multiple Sclerosis Impact Scale), was observed after 10 sessions in a cryochamber. Unfortunately, spasticity was not examined in the patients observed in this trial [29].

Improvement in the functional status of patients with secondary progressive MS assessed via the EDSS scale was noted after 5 and 10 WBC sessions combined with kinesiotherapy [32, 50].

A significant reduction in the EDSS value (the authors do not specify by how much) and an increase in the strength of the lower limb muscles (quadriceps femoris and iliopsoas muscles) were observed after 10 WBC combined with kinesiotherapy in studies conducted on 60 randomly selected MS patients [29]. Similarly, beneficial effects in the form of EDSS value reduction (without providing values) were observed in 22 patients with secondary progressive multiple sclerosis (SPMS) after 10 WBC , and the beneficial changes persisted for a period of three months following completion of the therapy [33].

A 0.5-degree reduction in the EDSS value was observed in a study involving 28 patients (women and men) with multiple sclerosis in remission, even after five daily WBC (-110 to -120°C), and still exercising for an hour immediately after the treatments according to a scheme based on Frenkel's exercises. In 13 of the subjects, the spasticity of the lower limb muscles decreased, however, in three patients, the disease worsened after three months [50].

In another study [34], muscle tone of the lower limbs was assessed using the 6-point Modified Ashwort scale in 26 patients who underwent 20 WBC (temperature from -110 to -150°C, treatment time of 2-3 min). Also in this case, specialised individual or group kinesiotherapy was used after the treatments, during which patients performed balance and coordination exercises with elements of the Frenkel method, active weight-bearing as well as active-passive and passive exercises, supplemented with some performed on a cycle ergometer. In the majority of patients, excessive muscle tension was reduced (a decrease by 1 degree on the Ashworth scale) in the right or left lower limb, without taking into account which limb was more or less spastic. It should be noted, however, that this study included patients with spasticity grades from 1 to 4 on the Ashworth scale, and the best results were obtained in patients with the least spasticity (1 and 1+) before starting the treatments.

Relaxation of pathologically tense muscles after cryotherapy treatments is possible because under the influence of cold, there is a decrease in nerve conduction, as well as a decrease in the reactivity of sensory endings in the muscles, a reduction in pain symptoms and an increase in pain tolerance [15, 50]. Reducing muscle tension allows for an increase in the range of motion in the joints, improved mobility and more effective rehabilitation [17].

According to Westerlund et al. [53], positive adaptive changes in muscle tension appear only after 15 WBC sessions. It should be emphasised, however, that the study conducted by these authors involved healthy and relatively young people (average age of 33 years).

Based on the results of the authors' research and that of other researchers, it can be concluded that WBC treatments, without subsequent kinesiotherapy, improve the functional status of MS patients assessed using the EDSS scale and reduce muscle spasticity measured with the Modified Ashwort Scale.

4.2. Effect of WBC therapy on balance of MS patients

In light of the above information, similar beneficial changes could be expected in relation to postural control or the broader approach to the phenomenon of postural stability, usually identified with human balance. As already mentioned in the 'Introduction' section, balance disorders are a commonly appearing symptom in MS patients [9, 21].

Although many authors have studied balance disorders among patients with multiple sclerosis [4, 9, 11, 12, 21, 23], this study was the first to attempt to assess changes in balance under the effect of whole-body cryotherapy treatments alone, assuming that these treatments would improve postural stability in MS patients. Unfortunately, the results of the study did not provide a uniform image.

Indicators characterising balance in a standing position with eyes open in both groups (EG and CG) did not differ significantly in the baseline tests (measurement 1), although all balance indicators (total area of the centre of pressure deflection envelope, its absolute displacements and the velocity of these changes) were slightly higher in the experimental group. After 10 (measurement 2) and 20 sessions (measurement 3) in the cryochamber, no statistically significant changes in these indicators were found, which proves the lack of effect of whole-body cryotherapy used in the experimental group on the patient's postural stability in the test with eyes open using 10 and 20 WBC. No significant changes were observed either in the control group during three measurements carried out at the same time intervals as in the experimental group. There were also no differences between groups at the three measurement points.

In both study groups, as was to be expected, a greater stability disturbance was noted when trying to maintain a standing position with eyes closed. However, the results recorded in patients from the experimental group are surprising. The $CP_{AREA}EC$, $CP_{L}EC$ and $CP_{V}EC$ values recorded in this group were higher in all three measurements than in the control group, which indicates greater stability deficits in patients from the experimental group, although only in the first measurement the intergroup differences were statistically significant.

However, it is worth noting the fact that under the effect of cryochamber treatments, stability improved in patients from the experimental group, and in subsequent measurements, the intergroup differences were no longer as large and statistically significant as in measurement 1. In patients from EG, in the first test (measurement 1), higher mean values obtained on the EDSS scale and greater muscle spasticity were also noted compared to the control group. It should be highlighted, however, that the intergroup differences were not statistically significant. The reason for the worse stability in patients from EG could be the longer duration of the disease, on average, by 1.5 years, compared to patients from CG.

The values of the main indicators (the total area of the centre of pressure deflection envelope, its absolute displacements and the velocity of these changes) were higher in the stability test performed with eyes closed than when the eyes remained open, and the obtained results are similar to those described by other authors [21, 22, 42]. Inojosa et al. [21] emphasise that balance indicators measured in a patient standing with eyes closed are sensitive parameters for assessing balance impairment. The differences in the values of variables recorded in the posture with eyes open and closed are caused by the fact that maintaining balance without visual control was much more difficult, because the posture regulating system is deprived of important information in such a situation. The determinants of this process are based on the system-theoretical model of human motor behaviour [39].

Postural stability in patients with MS is significantly worse than in healthy people, and it is affected by many factors [14, 22, 44]. The disease results in multifocal damage to the central nervous system. Balance impairment may result from impaired cognitive functions, visual disturbances, damage to the labyrinth, decreased muscle strength, sensory and coordination disorders. Each patient has a different degree of damage to the above-mentioned mechanisms and their effect on balance disorders varies individually [41, 42]. Until recently, it was believed that damage to the cerebellum was responsible for the occurrence of balance disorders. This was due to the fact that the gait of MS patients suggests ataxia, and ataxia and balance disorders are symptoms of multiple sclerosis. A different approach to the cause of balance disorders was presented by Cameron et al. [8]. They believe that balance disorders in MS patients are the result of damage to afferent pathways and are more similar to those that appear in peripheral polyneuropathy, e.g. in diabetic polyneuropathy. They differ from the latter in greater damage to afferent pathways with relatively preserved efferent pathways. MS patients with balance disorders have significantly delayed conduction of somatosensory evoked potentials (SSEP) in the spinal cord. The severity of demyelinating and neurodegenerative changes located in the posterior columns of the spinal cord correlates with the degree of SSPE relief and balance disorders [8]. It is increasingly underscored that balance disorders are related to cognitive disorders occurring in patients with multiple sclerosis [31, 44]. According to Schwarz and Schitz [46], inflammatory processes in the grey matter of the brain in the course of multiple sclerosis cause dysfunctions of brain synapses. These dysfunctions appear very early, regardless of demyelinating processes in the white matter, and correlate with mental as well as cognitive disorders in MS patients.

Redlicka et al. [44], in their study involving 76 patients with MS (EDSS 3.5-6), showed that even moderate perception disorders in patients with MS cause balance disorders. This study also allowed to note that worse results on the stabilometric platform were achieved by men compared to women and that obesity predisposed to poorer stability control.

Soyuer et al. [51] compared 124 patients with three forms of MS (PPMS, SPMS, RRMS) and 31 healthy volunteers matched for age, sex, weight and height. They found that stability control was impaired in balance tests among all patients with MS. This especially concerned those with progressive forms of the disease.

Based on the results of research and clinical data obtained by other authors, whole-body cryotherapy can be considered a safe and effective method of therapy for MS patients, especially since MS patients tolerate cryochamber treatments very well [29, 31, 55].

STUDY LIMITATIONS

It is possible that the more beneficial effects of whole-body cryotherapy in MS patients than those observed in the present study would be revealed after a longer series of WBC than 20 sessions performed less frequently (e.g. three times a week) but for a longer period of time. It would also be important to select a homogeneous group of patients, which is extremely difficult in the case of MS patients with an EDSS above 4 due to damage to various CNS structures. Since the EDSS scale is not very precise for measuring the effectiveness of short-term therapies, it would be better to use other functional test (e.g. TUG, Rivermead Motor Assessment or the Multiple Sclerosis Impact Scale) to estimate functional improvement among patients with MS.

5. CONCLUSION

A series of 20 daily WBC resulted in improved functional status of patients with multiple sclerosis in the form of a significant reduction in spasticity and the values obtained on the EDSS scale. However, following a series of 10 and 20 WBC, without subsequent targeted kinesiotherapy, only slight improvement was noted in the stability in patients with multiple sclerosis.

Disclosure of interest

The authors declare that they have no competing interests.

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