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Whole body cryotherapy as a novel adjuvant therapy for depression and anxiety

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Summary

Aim. The whole body cryotherapy (WBCT) is becoming a more popular adjuvant method in rehabilitation and renewal. The objective was to evaluate influence of WBCT on depressive and anxiety symptoms.
Materials and methods. The study group (n=26) was treated using a series of 15 daily visits to a cryogenic chamber (-110° to 160°C) which lasted 2-3 minutes each. A control (n=34) group was similar to the study group as concerning diagnoses (anxiety and depressive disorders), age and gender. Both groups received standard out-patient psychopharmacotherapy. The Hamilton Depression Rating Scale and Hamilton Anxiety Rating Scale were used to evaluate the severity of symptoms before and after WBCT (3 weeks observation). The self-rating life satisfaction scale was used as well. Two efficacy measures were established: a significantly greater reduction of the scales' scores and mean scores lower at the endpoint in the study group in comparison to the control group.
Results. Both efficacy criteria were fulfilled for the depression scale in 12 of the 16 HDRS items except gastrointestinal and genitourinary symptoms, hypochondria, body mass and criticism. Concerning the HARS scale, in 11 of 14 anxiety items (except gastrointestinal and genitourinary symptoms and behavior) the mean reduction was significantly bigger and the mean final status was better in the experimental group in comparison to the control one. As for the life satisfaction scale, efficacy was shown in 6 of the11 items: physical and mental health, everyday activity, vocational activity, hobbies and general life satisfaction - in the experimental group.
Conclusion. These findings suggest a possible role for WBCT as a short-term adjuvant therapy for depressive and anxious patients.

whole body cryotherapy / depression / anxiety / novel therapy

INTRODUCTION

At the end of the 1970's, Prof. Toshiro Yamauchi constructed the first cryogenic chamber and successfully used cryotherapy to treat rheumatism [1]. Nowadays, whole body cryotherapy (WBCT) is used to alleviate inflammation and pain in osteoarthritis [2, 3] or for pain relief in fibromyalgia [4, 5], in reduction of spasticity in neurological diseases [6] and as the method of physiotherapy in rheumatic diseases and sclerosis multiplex or giving a sedative effect in psoriasis and neurodermatitis [2].

The whole body cryotherapy results in analgetic, antiswelling, hormone, immune, circulatory system reactions[5, 7, 8]. The WBCT does not affect the heart rate, arterial blood pressure nor the value of the left ventricle fractional shortening index and its ejection, neither does it cause

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arrhythmias and ischaemic changes of the heart and is a safe treatment if the time of exposure is strictly controlled [5, 9]. However, WBCT should be applied with caution in susceptible individuals, such as asthmatics [10].

WBCT activates the body's system of temperature regulation [11] and a hormonal response (increase of body metabolism and the concentration of adrenaline, noradrenaline, adrenocorticotropic hormone (ACTH), cortisone, pro-opiomelanocortin (POMC) and beta-endorphins in blood plasma, as well as male testosterone levels) [8, 12, 13.]

POMC is the source of several important biologically active substances such as ACTH in the anterior pituitary gland and melanocyte-stimulating hormones (α-MSH) and β-endorphin in the intermediate lobe. α-MSH has a role in the regulation of appetite and sexual behavior. One of the neurobiological hypotheses of depression based largely on dysregulation of the hypothalamic-pituitary-adrenal axis. Brain opioid peptide systems are known to play an important role in motivation, emotion, attachment behaviour, the response to stress and pain, and the control of food intake [14]. The positive effects of WBCT in treating both external and internal pain are due to the activation of the endogenic opioid system and "pain control system" [13]. It is possible that such a multi-system reaction could play a role in the treatment of mental disorders [15]. The WBCT is successfully used in clinical work in several countries, however a very limited number of data is available.

The aim of the study was to assess the effect of whole-body cryotherapy (WBCT) on the symptoms observed in a group of patients suffering from affective and anxiety disorders and their own subjective assessment of life satisfaction.

MATERIAL AND METHODS

The study protocol was accepted by the Bioethics Commission. It is based on the evaluation of depressive and anxiety symptoms in a group of subjects exposed to WBCT with a control group and was carried out in the Department of Psychiatry of Wroclaw Medical University.

Exclusion criteria were as follows: circulatory and breathing insufficiency, clotting, embolism, inflammation in blood vessels, open wounds, ulcers, serious cognitive disturbances, fever, addictions, claustrophobia, and oversensitivity to cold.

After written informed consent, subjects (18-65 years old) from the control (n=34) and study group (n=26) received standard psychopharmacotherapy as prescribed in an outpatient psychiatric clinic. This treatment was not modified during the evaluation period.

Patients were diagnosed as having depressive and anxiety disorders (ICD-10 criteria) (Table 1).

Subjects in the study group were additionally exposed by a cycle of 15 visits (2-3 minutes) in a cryogenic chamber carried out 5 times per week according to Zagrobelny et al. guidance of the appropriate duration of exposure and temperature for adult patients, as well as a list of medical conditions [13]. The cryogenic chamber has the temperature between –1100C and –1600C. This temperature was systematically lowered over successive visits to permit the organism to adapt to low temperatures. Patients walked inside the chamber in swimming suits with their noses and mouths secured by a surgical mask lined from the inside with two layers of gauze, their ears covered by a woollen headband and feet in woollen socks and wooden clogs.

Observations were made before and after the WBCT (three weeks). Apart from standard medical documentation, the study used Hamilton's scales of depression and anxiety and the life satisfaction scale.

The 17-item Hamilton Depression Rating Scale (HDRS-17) is used to assess the severity of depressive symptoms and provides a valuable guide of a patient's progress over time [16]. Items are scored from 0 to 4 and, in general, the higher the total score the more severe the depression. The original 17-item HDRS reported to be the most sensitive scale for measuring response to treatment often used in clinical trials.

The Hamilton Anxiety Rating Scale (HARS) [16, 17] included 13 items, each item is rated on a five-point scale. The five scores are: none (0), mild (1), moderate (2), severe (3) and very severe (4). This is a widely used scale and an accepted outcome measure in clinical trials.

The life satisfaction scale[18] is the self rating scale composed of 11 items, which allows to

asses current satisfaction from different life domains. It's structure is based on a 7-point analogue scale.

The authors established two outcome measures for assessing the short term WBCT efficacy:

1. the reduction of the scales' scores have to be significantly greater in the study group than in the control one,
2. The mean of the scores in the study group have to be lower at the endpoint.

The authors used several statistical methods: the Fisher's exact test, the Wilcoxon rank test (changes within groups between both measure points) and the Mann-Whitney rank test (comparisons of these changes between groups).

RESULTS

There was no significant difference between two groups concerning sociodemographic features or clinical ones except the level of education (Tab. 1)

The results of items 16B and 17 from HDRS-17 scale were the same for all patients ("0") except one, so those items were not included to the analyses.

Before the experiment, the severity of anxiety symptoms were significantly higher in the study group in only few items (Tab.2) as well as concerning depressive symptoms (Tab.3) and life satisfaction scores (Tab.4).

After 3 weeks of the experiment more significant differences in each items of all tree scales were observed (Tab.2-4).

In the experimental group significant reduction of 13 from 14 HARS items were observed (10 items: $p<0.001$; Genitourinary symptoms: $p<0.05$). Only gastrointestinal symptoms did not improve significantly. Concerning the HDRS items, it was the reduction in most of the items at the level of 0.001 except guilt feelings, early waking, psychomotor retardation and hypochondrias on the level below 0.01. Only gastrointestinal symptoms and body mass did not change within 3 weeks.

The significant improvement concerning anxiety mood, tension and behaviour from HARS

Tab.1. Sociodemographic and clinical characteristics of the subjects.

	Experimental group (n=26)	Control group (n=34)	p-value
Women	22 (84.6%)	31 (91.2%)	NS
Age	47.04 (SD=13.05)	40.88 (SD=11.90)	NS
Civil state: single has partner Widowed/divorced	 5 (19.2%) 17 (65.4%) 4 (15.4%)	 6 (18.2%) 21 (61.8%) 7 (20.6%)	 NS
Having children	17	25	NS
Living alone	3 (11.5%)	3 (8.8%)	NS
education: primary technical secondary higher	 1 3 11 9	 1 17 15 1	 p=0.001
No. of working	7 (28%)	7 (20.6%)	NS
Diagnosis (ICD-10): F3 F4	 14 (53.8%) 12 (46.2%)	 20 (58.8%) 14 (41.2%)	 NS
Pharmacotherapy: Clasical thymoleptics New thymoleptics Benzodiazepines Neuroleptics	 13 7 14 5	 14 13 17 7	 NS

were observed in control group (p<0.05; p<0.01; p<0.05, respectively), without significant changes in HDRS items and life satisfaction items.

Concerning life satisfaction scale significant improvement in mental health (p<0.001), physical health, hobbies and overall life satisfaction (p<0.01), vocational activity, everyday activities, and sexual life (p<0.05) was noticed. No significant improvement were observed in case of family, social and spiritual life as well as of material conditions.

Comparing changes of means within the treatment period between both groups, there were observed significantly higher changes of HARS scores in the experimental group than in the control group, except gastrointestinal and genitourinary symptoms (Tab. 5). Changes of HDRS scores during observation period were also significantly higher (p<0.0001) except gastrointestinal symptoms, which means that reduction of depressive symptoms was better in experimental group (Tab.6).

Higher increase in life satisfaction scale items was observed in the experimental group in comparison to the control group in several items: mental health, everyday activities and hobbies (p < 0.001), vocational activity and overall

Tab.2 Results of each item from Hamilton anxiety scale in both time points, comparison between groups (mean, SD)

Measures		I			II		
	Group	Study	Control	p-value	Study	Control	p-value
1.	Anxious mood	2.77 (0.95)	2.53 (0.83)	NS	1.92 (0.93)	2.32 (0.73)	NS
2.	Tension	3.27 (0.45)	3.06 (0.60)	NS	2.04 (0.92)	2.79 (0.48)	0.000
3.	Fears	1.58 (1.33)	1.35 (1.18)	NS	1.19 (1.27)	1.41 (1.10)	NS
4.	Insomnia	3.12 (0.59)	2.50 (1.21)	0.04	1.38 (1.13)	2.32 (1.21)	0.002
5.	Intellectual	2.38 (0.75)	2.15 (1.10)	NS	1.50 (0.91)	2.06 (1.07)	0.015
6.	Depressed Mood	2.73 (1.00)	2.18 (1.09)	NS	1.73 (1.12)	2.15 (0.99)	NS
7.	Somatic Complaints: Muscular	1.96 (0.77)	1.59 (1.05)	NS	1.15 (0.83)	1.41 (0.99)	NS
8.	Somatic Complaints: Sensory	1.50 (1.14)	1.76 (1.07)	NS	0.81 (0.98)	1.56 (1.05)	0.008
9.	Cardiovascular Symptoms	1.96 (0.96)	2.15 (0.89)	NS	1.19 (0.69)	1.97 (0.81)	0.000
10.	Respiratory Symptoms	2.00 (0.94)	1.91 (1.19)	NS	1.31 (0.74)	1.82 (0.99)	0.027
11.	Gastrointestinal symptoms	1.77 (0.95)	1.76 (1.30)	NS	1.54 (1.07)	1.79 (1.20)	NS
12.	Genitourinary symptoms	1.85 (1.05)	1.12 (1.17)	0.012	1.58 (0.90)	0.94 (0.95)	0.009
13.	Autonomic Symptoms	2.04 (0.82)	1.91 (0.93)	NS	1.35 (0.81)	1.76 (0.82)	0.032
14.	Behavior at Interview	2.35 (0.69)	1.76 (1.07)	0.031	1.69 (0.79)	1.62 (0.99)	NS

Tab.3. Results of each item from Hamilton depression scale in both time points, comparison between groups (mean, SD)

Measures		I			II		
Group		Study	Control	p-value	Study	Control	p-value
1.	Depressed mood	1.96 (1.43)	1.53 (1.19)	NS	1.15 (1.12)	1.47 (1.05)	0.00
2.	Guilt feelings	1.65 (0.63)	1.56 (0.61)	NS	1.15 (0.37)	1.56 (0.61)	0.00
3.	Suicide	0.69 (0.68)	0.76 (0.78)	NS	7.7e-02 (0.27)	0.65 (0.54)	0.00
4.	Insomnia-early	1.77 (0.43)	1.56 (0.61)	NS	0.62 (0.57)	1.56 (0.61)	0.00
5.	Insomnia-middle	1.54 (0.51)	0.94 (0.74)	0.002	0.46 (0.71)	0.85 (0.70)	0.00
6.	Insomnia-late	1.35 (0.63)	1.29 (0.68)	NS	0.69 (0.74)	1.21 (0.64)	0.00
7.	Work and activities	2.12 (0.77)	1.79 (0.77)	NS	0.62 (0.85)	1.79 (0.69)	0.00
8.	Retardation-psychomotor	0.69 (0.68)	0.65 (0.65)	NS	0.38 (0.64)	0.65 (0.65)	0.00
9.	Agitation	1.19 (0.75)	0.94 (0.81)	NS	0.65 (0.69)	0.94 (0.81)	0.00
10.	Anxiety-psychological	2.19 (0.91)	1.91 (0.57)	NS	1.46 (1.07)	1.88 (0.54)	0.00
11.	Anxiety-somatic	1.92 (0.81)	1.65 (0.85)	NS	0.88 (0.86)	1.62 (0.78)	0.00
12.	Gastrointestinal symptoms	0.42 (0.58)	0.56 (0.66)	NS	0.35 (0.56)	0.59 (0.66)	NS
13.	General somatic symptoms	1.38 (0.57)	1.38 (0.65)	NS	0.42 (0.50)	1.44 (0.61)	0.00
14.	Sexual dysfunction/menstrual disturbance	1.69 (0.55)	1.12 (0.81)	0.004	1.19 (0.63)	1.12 (0.81)	0.00
15.	Hypochondrias	1.19 (1.13)	0.74 (0.93)	NS	0.88 (0.95)	0.76 (0.92)	0.00
16.	Weight loss	0.42 (0.70)	0.24 (0.51)	NS	0.31 (0.62)	0.24 (0.51)	NS

Tab.4 Results of each item from life satisfaction scale in both time points, comparison between groups (mean, SD)

Measures		I			II		
	Group	Study	Control	p-value	Study	Control	p-value
1.	Physical health	-0.73 (1.61)	-1.48 (1.12)	NS	0.35 (1.64)	-1.44 (1.11)	0.00
2.	Mental health	-1.15 (1.67)	-2.03 (0.85)	NS	-0.22 (1.64)	-2.00 (0.88)	0.00
3.	Family life	1.12 (1.48)	0.18 (1.69)	0.05	1.13 (1.55)	6.3E-02 (1.61)	0.01
4	Social relationship	0.54 (1.42)	-0.30 (1.61)	NS	0.87 (1.25)	-0.25 (1.48)	0.006

5.	Everyday activities	-0.50 (1.77)	-0.15 (1.66)	NS	0.30 (1.77)	-0.25 (1.70)	NS
6.	Vocational activity	-1.19 (1.74)	-1.41 (1.64)	NS	-0.61 (1.88)	-1.38 (1.64)	NS
7.	Hobbies	-0.69 (1.69)	-0.91 (1.84)	NS	8.7E-02 (1.68)	-1.03 (1.47)	0.015
8.	Sexual life	-1.35 (1.70)	-0.91 (1.84)	NS	-0.96 (1.85)	-0.94 (1.79)	NS
9.	Material conditions	-8.E-02 (1.87)	-0.24 (1.64)	NS	0.22 (1.73)	-0.34 (1.56)	NS
10.	Spiritual life	0.96 (1.42)	0.91 (1.21)	NS	1.17 (1.30)	0.84 (1.22)	NS
11.	Overall life satisfaction	-0.65 (1.67)	-0.87 (1.19)	NS	0.13 (1.66)	-0.97 (1.78)	0.008

Tab. 5. Comparison of mean changes in Hamilton anxiety scale between experimental and control group

Items	Group	Mean II-I	p-value
1. Anxious mood	Experimental	0.85	0.001
	Control	0.21	
2. Tension	Experimental	1.23	0.000
	Control	0.26	
3. Fears	Experimental	0.38	0.032
	Control	-6.E-02	
4. Insomnia	Experimental	1.73	0.000
	Control	0.18	
5. Intellectual	Experimental	0.88	0.000
	Control	8.8E-02	
6. epressed mood	Experimental	1.0	0.000
	Control	2.9E-02	
7. Somatic complaints: muscular	Experimental	0.8	0.001
	Control	0.18	
8. Sensory	Experimental	0.69	0.007
	Control	0.21	
9. Cardiovascular	Experimental	0.77	0.001
	Control	0.18	
10.Respiratory	Experimental	0.69	0.001
	Control	8.8E-02	
11. Gastrointestinal	Experimental	0.23	NS
	Control	-3.E02	
12. Genitourinary	Experimental	0.27	NS
	Control	0.18	
13. Autonomic	Experimental	0.69	0.005
	Control	0.15	
14. Behavior in interview	Experimental	0.65	0.002
	Control	0.15	

Tab.6.Comparison of mean changes in Hamilton depression scale between experimental and control group

Items	Group	Mean II-I	p-value
1. Depressed mood	Experimental	0.8	0.000
	Control	5.9E-02	
2. Guilt feelings	Experimental	0.5	0.000
	Control	0.0	
3. Suicide	Experimental	0.62	0.000
	Control	0.12	
4. Insomnia-early	Experimental	1.15	0.000
	Control	0.0	
5. Insomnia-middle	Experimental	1.08	0.000
	Control	8.8E-02	
6. Insomnia-late	Experimental	0.65	0.000
	Control	8.8E-02	
7. Work and activities	Experimental	1.5	0.000
	Control	0.0	
8. Retardation-psychomotor	Experimental	0.31	0.001
	Control	0.0	
9.Agitation	Experimental	0.54	0.000
	Control	0.0	
10. Anxiety-psychological	Experimental	0.73	0.000
	Control	2.9E-02	
11. Anxiety-somatic	Experimental	1.04	0.000
	Control	2.9E-02	
12. Gastrointestinal symptoms	Experimental	7.7E-02	NS
	Control	-3.E-02	
13. General somatic symptoms	Experimental	0.96	0.000
	Control	-6.E-02	
14. Sexual dysfunction 15. / menstrual disturbances	Experimental	0.5	0.000
	Control	0.0	
16. Hypochondrias	Experimental	0.31	0.000
	Control	-3.E-02	
17. Weight loss	Experimental	0.12	0.000
	Control	0.0	

life satisfaction ($p < 0.01$) and physical health ($p < 0.05$).

Summing up, both efficacy criteria were fulfilled for the depression scale in 12 of the 16 items of HDRS except gastrointestinal and genitourinary symptoms, hypochndriasis, body mass and criticism. Concerning the HARS scale, the mean reduction was significantly bigger and the mean final status was better in the experimental group in comparison to the control group in 11 of the 14 anxiety items (except gastrointestinal and genitourinary symptoms and behavior). As for the life satisfaction scale, efficacy was proved in the experimental group in 6 of the 11 items: physical and mental health, everyday activity, vocational activity, hobbies and general life satisfaction.

DISCUSSION

There is a lack of evidence based findings on whole body cryotherapy as a method for treating mental disorders except one paper of Rymaszewska and al. [15]. Only few studies proved the positive role of WBCT in fibryomyalgia [19] and other diseases of the motor system [1, 2, 5].

Concerning mental disorders, several new biological treatment methods are being developed.

Methods involving neurostimulation include repetitive transcranial magnetic stimulation, magnetic seizure therapy, vagus nerve stimulation, deep brain stimulation and transcranial direct current stimulation. These methods may be effective in treating depression and have minimal side effects [20, 21, 24].

The presented findings indicate that cryotherapy may play a positive role in the process of treating patients with affective and anxiety disorders, since the decrease of anxiety and depressive symptoms were significantly higher in the group of patients who were exposed onto extremely low temperature sessions.

Comparing to controls. Analysis of the long term observations will indicate whether this effect is long lasting. Even if the follow-up results indicate that the long term effects of treatment are the same in both groups, the rapid initial improvement achieved using cryotherapy means that such adjunctive treatment may be of value.

It may be assumed, that the physiological mechanisms of WBCT such as those associated with HPA axis and endogenous opioids can explain the positive influence of WBCT on mood and other symptoms. However, it is highly possible that also other, not yet recognized mechanisms can be associated with WBCT effect.

Those hypotheses need to be confirmed in further research. Limitations of the current study (small sample size and the lack of a procedure randomly assigning patients to a group) forced the authors to emphasize the need of caution in interpreting and generalizing the presented findings. The continuation of the study is planned involving several biological diagnostic methods as neuroimaging and biochemical measures with the aim of clarifying the effect of WBCT on mental health.

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