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Influence of whole body cryotherapy on depressive symptoms – preliminary report

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Background: Cryotherapy has a long tradition in somatic medicine. Yet we know very little about its impact on psyche and mood disturbances in particular. Therefore there is a real need for scientific investigations into this problem.
Objective: The study reported here was an initial approach to whole-body cryotherapy (WBCT) as a potential treatment modality for depression and was expected to provide rough data helping to design a future project with extended methodology, larger sample groups and longer follow-up.
Methods: Twenty-three patients aged 37–70 years gave informed consent to participate in the study. Ten WBCT procedures (160 s, −150°C) were applied within 2 weeks. Participants were recruited from depressed day hospital patients. Antidepressive medication was not ceased. Symptoms were rated at the beginning and end of this intervention using the 21-item Hamilton Depression Rating Scale (HDRS). Changes in scores were analyzed in the group of patients for every item separately as well as for the sum of all items for each patient.
Results: Almost for each individual HDRS item, the overall score for all patients together was significantly lower after WBCT. This means that all symptoms, except for day–night mood fluctuations, were presumably positively influenced by cryotherapy. The HDRS sum-score for each patient after WBCT was lower than that of the baseline and reached statistical significance in a paired samples *t*-test. Every patient was therefore considerably relieved after WBCT.
Conclusions: It appears that WBCT helps in alleviating depression symptoms. Should this be confirmed in the extended study we are currently implementing, WBCT may become an auxiliary treatment in depression.

Key words: auxiliary treatment, depression, mood disturbances, whole body cryotherapy

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Introduction

Cryotherapy has a very long tradition as a treatment method. Egyptians were the first to realize that low temperatures had curing potentials and were beneficial for human body and made use of this knowledge almost 4500 years ago. Avicenna and Hippocrates were acquainted with this technique as well. Today cryomedicine divides into three main branches: cryoprotection, firmly associated with transplantology and pharmacology; cryodestruction, understood as a specific kind of surgery; and finally cryotherapy, which provides a variety of treatment modalities useful in many somatic complaints. For instance, in dermatology, locally applied, extremely low temperatures are a recognized and well documented method of treatment (1–3). In surgery they are successfully used in treatment of prostate cancer (4), liver original carcinomas and metastases (5–7), and neoplasms of other internal organs. Cryotherapy also has a well grounded place in ophthalmology (8). Despite the above, whole-body cryotherapy (WBCT) has been

introduced into medicine quite recently. In the late 1970s, Toshiro Yamauchi developed in Japan the world's first cryogenic chamber suitable for cooling down a patient's whole body and used it successfully in the treatment of people suffering from rheumatoid disorders (9). Research by Fricke in Germany in 1982 followed in his wake. The first Polish cryogenic chamber was built seven years later, in 1989 in Wroclaw. The second Polish cryogenic chamber, described below, was constructed in 1996 and is still used today (10).

At present WBCT is commonly utilized as an auxiliary procedure enhancing effects of primary treatment and rehabilitation of inherited disorders, inflammation, degeneration and various post-traumatic impairments of the musculoskeletal system (11–14). Its high effectiveness there has been empirically confirmed. It also proved to be very useful in the management of skin tissues and flesh damage, respiratory system dysfunction associated with syndromes such as asthma-bronchitis, bronchitis-emphysema, in rehabilitation of professional athletes (15) and in biological revitalization of healthy people.

The empirical evidence supporting the effectiveness of cryotherapy in somatic medicine is therefore plentiful and reliable, yet there is virtually no similar evidence proving its effectiveness in medicine understood in more spiritual terms. The attempt to find literature on the subject, i.e. dealing with whole body cryotherapy in mood disturbances, was unsuccessful. On-line databases such as Ovid – Medline – Biomedical Full Text Collections, Embase 1989+, EBSCOmed, PubMed, Neuroscion and PsychLit were searched and returned no references. However, clinical observations of people, both healthy and physically impaired, submitted to extremely low temperatures for a short period of time report the improvement of mood and feeling of deep relaxation and soothing shortly afterwards. It appears this effect persists in time for several hours and even longer (16). Furthermore, in patients suffering from fibromyalgia and exposed to cryogenic temperatures the alleviation of depression and sleep disturbance was observed (17). Unfortunately this does not constitute enough methodologically sound evidence to support or refute the idea of WBCT being useful in depression.

As far as we are aware, attempts to investigate this issue closer have been undertaken recently in Japan but they have not yet been published. Therefore, this study aims to evaluate the correlation between WBCT and change in the mental condition of patients. It should be stressed that this is just an initial approach intended to provide rough information helpful in designing an extended, methodologically improved project with a longer follow-up period. Also this paper should be regarded as an announcement of potentially important findings derived from initial observations. Full study reports will follow as soon as the main project reaches its closure date.

Materials and methods

For the purpose of this study 23 patients, 18 women and five men aged between 37 and 70 years were examined. Subjects suitable for further investigations were sought among patients receiving either day hospital or outpatient treatment. There were no particular exclusion criteria for this study except for those resulting from bad general medical conditions such as cachexia, heart valve defects (mitral stenosis) with circulatory insufficiency, acute pectoral angina, profound cardiac arrhythmias, acute disorders of the airways, present or past thrombotic events, fever, Raynaud's disease, local blood flow disturbances, anaemia, cold intolerance or cold urticaria and hypothyroidism (16). Since all patients were day hospital attendees or outpatients, there was no need to design special psychiatric exclusion criteria such as 'severity of disorder' or 'suicidal ideation' because such patients, by definition, were not present in the outpatient or day hospital environment. Inclusion into the study was legitimated by diagnosed mood disturbance or depression, either unipolar or bipolar. The majority of patients were unipolar (recurrent depressive disorder, F33 according to ICD 10) with a few years' clinical history, previously treated several times in day hospital. During the recruitment phase, only 23 patients fulfilled the inclusion criteria. All of them exhibited symptoms of depression and on the Hamilton Depression Rating Scale scored between 29 and 46 points, mean 38.4 (Table 1).

Those eligible were invited to participate in the study. All participants gave written informed consent and continued their antidepressant medication simultaneously to cryotherapy as well as their day hospital attendance. This means the WBCT applied to each patient did not alter in any way medical interventions that were introduced earlier. Prior to the first cryogenic procedure, patients were acquainted with the construction of the cryogenic chamber and the safety measures undertaken. They also had a general medical check-up qualifying for the cryotherapy.

Table 1. Summary of Hamilton Depression Rating Scale (HDRS) sum-scores for each investigated patient before and after cryotherapy.

Patient no.	Sex	HDRS sum-score	
		Before WBCT	After WBCT
1	F	36	15
2	F	41	14
3	F	32	9
4	F	43	18
5	F	37	17
6	F	38	17
7	M	35	15
8	F	35	8
9	F	39	12
10	F	44	7
11	F	37	5
12	M	41	14
13	F	46	13
14	F	43	9
15	F	38	5
16	M	36	12
17	F	43	15
18	M	43	18
19	F	40	8
20	F	39	13
21	M	29	17
22	F	30	3
23	F	38	7

Patients had 10 cryogenic procedures between 14 May and 31 July 2001. The cycle took a fortnight for each patient and consisted of two series of five procedures performed daily on working days with a pause over weekend. Every procedure lasted approximately 160 s. During subsequent entries into the chamber, each patient was exposed to a temperature lower than the last time in order to allow a certain degree of adaptation of the organism. Temperature in the chamber was therefore successively lowered, starting with -110°C during the first entry and ending with -150°C during the last one. In the chamber, patients wore swimming trunks and their noses and mouths were secured with a surgical mask lined on the inside with two layers of gauze; their ears were covered with a woollen headband and on their feet they wore woollen socks and wooden clogs.

The cryogenic chamber has two rooms: a vestibule with temperature of -60°C and a main chamber were temperature is set in the range of -110°C to -160°C. External walls are shielded with multilayer insulation used for low temperatures and the outer surface maintains room temperature. Liquid nitrogen is used as a coolant. Functioning of the cryogenic chamber is entirely automated and the main working parameters are controlled by two electronic mechanisms.

For the evaluation of severity of depression the 21-item Hamilton Depression Rating Scale (HDRS) was used. Ratings were collected only in two time points: T0, prior to the first WBCT procedure, and T1, after the last of 10 cryogenic procedures. In further analyses, patients that gave a negative response to a particular HDRS item during the first examination, which was rated null (i.e. no symptom present), were omitted. This was justified by the fact that those patients scored null as well during the T1 interview on the same items. This resulted in an unequal number of valid answers to HDRS items. Three of these had 22 valid answers (items P5, P6 and P19), one had 19 (P12) and one had 18 (P16_A). The remaining ones were complete, i.e. having 23 answers. Similarly, since only one patient gave a positive response to the position pertaining to present weight loss and only five reported having an insight into experienced depression symptoms, the corresponding HDRS items, 16-B and 17, were completely excluded from further analyses. Statistics used for the purpose of this study were rather elementary but sufficient to cast some light on the tendencies observed. For each of those HDRS items not excluded from analyses, the overall scores for the whole sample group of 18–23 patients were calculated. The accomplished figures in T0 and T1 were compared with each other. Any decrease in overall score for a given item in T1 was then expressed as a percentage reduction of the overall score for that particular item in T0 (Fig. 1). Descriptive statistics included calculation of mean value of HDRS sum-scores in T0 and T1, difference of means and standard deviations (SD). Testing of normality was performed using the Shapiro–Wilk method and testing of correlation was done using paired samples correlations and Student's *t*-test (Fig. 2). Finally the HDRS sum-scores in T0 and T1 for every patient were assigned to left-hand side closed class intervals of sum-scores building up a specific histogram (Fig. 3).

Results

For each separately analysed HDRS item, the overall score for the whole sample group in T1 was significantly lower than in T0. Results are presented graphically in Fig. 4. The level of reduction in intensity of given symptoms of depression, as expressed in the overall score for corresponding item, varied from 24% (item P21) to 100% (item P6). This means that patients experiencing a set of depression symptoms before the initiation of WBCT had those symptoms reduced by 24–100%

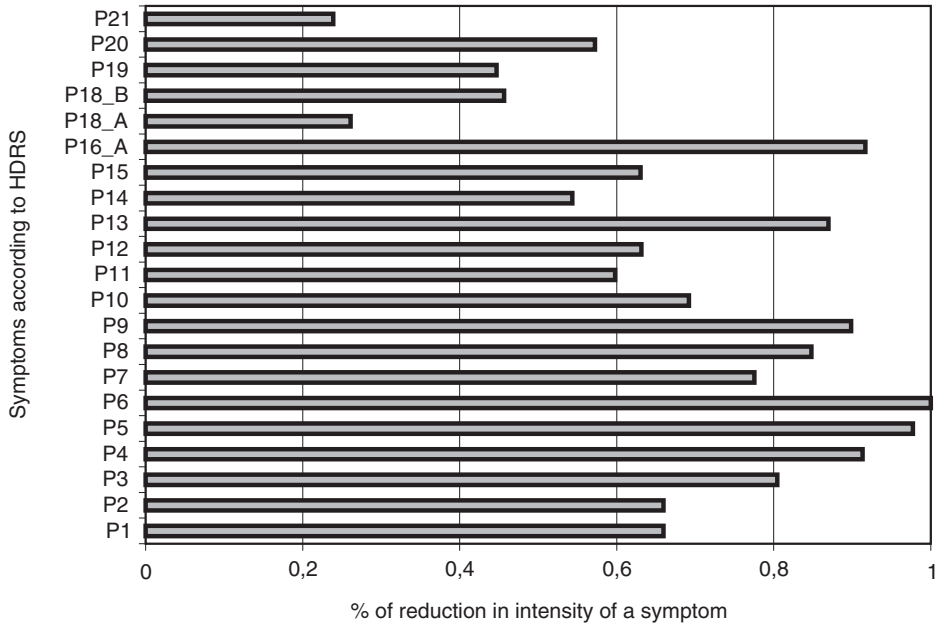

Fig. 1. Improvement of given depression symptom expressed as a percentage of decrease in the baseline (T0) score for each Hamilton Scale item calculated for the group of 18–23 patients.

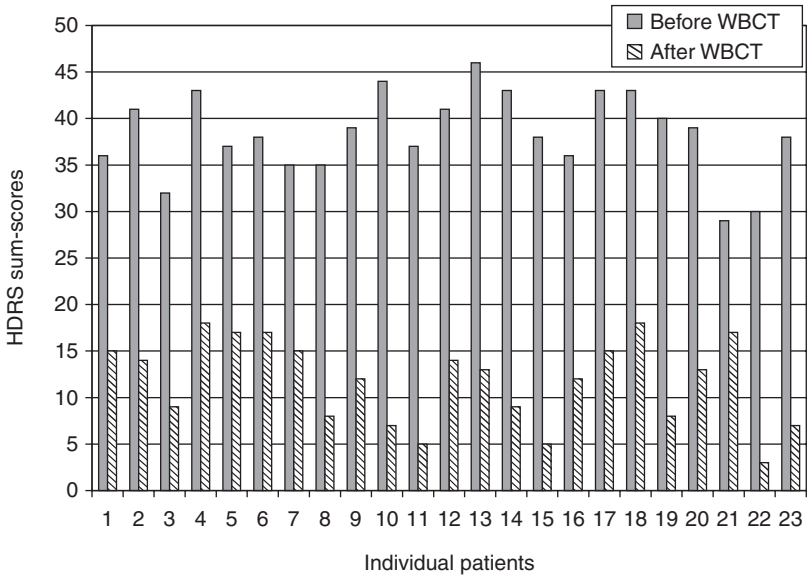

Fig. 2. HDRS sum-scores for each individual patient as assessed before the first WBCT procedure and shortly after the last one.

afterwards. Least prone to reduction were obsessions and compulsions (24%), day–night mood fluctuations (26%), depersonalization and derealization (45%), loss of libido and sexual drive (54%). Changes in scores for day–night mood fluctuations were coincidental and in statistical terms not associated with WBCT. The symptoms that improved most were anxiety and motor hyperactivity (90%), difficulties in falling asleep (91%), quality of sleep (98%) and early awakening (100%). It therefore appears cryotherapy had very positive influence on sleep disturbances.

For each patient the HDRS sum-score achieved after 2 weeks of cryotherapy was well below the original sum-score calculated on the day of WBCT initiation (Fig. 1). The distribution of HDRS sum-scores before and after the WBCT was normal (Shapiro–Wilk test), C-Pearson's correlation ratio was 0200 and $P = 0361$. Paired-samples Student's *t*-test showed that observed differences in T0 and

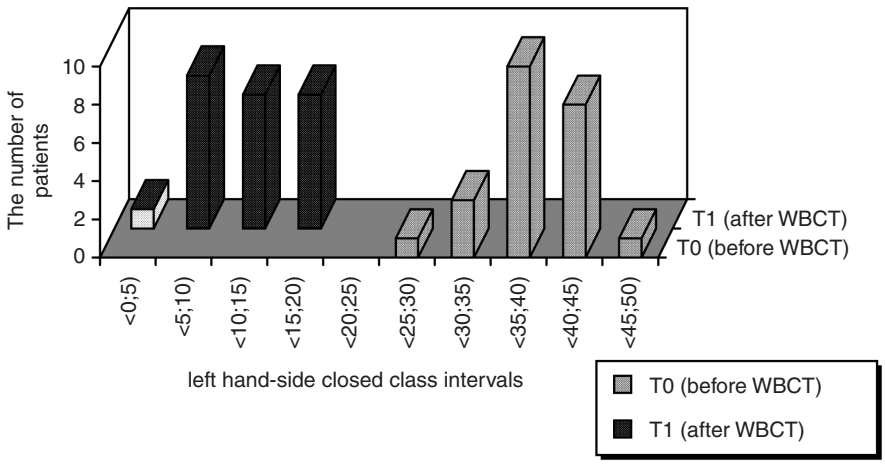

Fig. 3. The distribution of Hamilton Depression Rating Scale sum-scores before and after the Cryotherapy for all examined patients.

T1 sum-scores were statistically significant for all investigated patients (Table 2). Every one of them responded positively to the cryotherapy and all examined subjects reported significant improvement in their global mental condition shortly after all 10 cryogenic procedures. In order to visualize the above more clearly, we grouped together all individual HDRS sum-scores, both in T0 and T1, and assigned them to several five-point step left-hand side closed class intervals. This resulted in a specific histogram comprising two disconnected parts, one representing HDRS sum-scores prior to WBCT and the other representing sum-scores after 2 weeks of WBCT (Fig. 2). Since those parts do not overlap at any point, it is clear that all interviewed patients moved from 'being depressed' to 'feeling much, much better' probably due to this specific intervention of WBCT.

Of course, other reasons for improvement of mental condition have to be considered here. Unfortunately this is not possible within this study. Furthermore, the persistence of observed antidepressive effects of WBCT in time is not currently known since there were no follow-up examinations. Due to the gender bias in the sample, it was also not possible to investigate the relationship between gender and efficacy of cryotherapy in alleviating symptoms of depression. These questions have to wait a little longer and will be dealt with in a future project addressing WBCT and its association with depressed mood and sleep disturbance.

Table 2. Mean sum-scores before and after whole-body cryotherapy (WBCT), difference of means for the whole sample group and paired samples tests

HDRS sum-score	Mean	SD	The difference of means	Paired samples Student's t- test (d.f.)	Significance (two-tailed)
Before WBCT (T0)	38.4	4.4			
After WBCT (T1)	11.8	4.6	26.6	22.41 (22)	0.000

Discussion

The nature of observed psychological effects of cryogenic temperatures applied to depressed patients is only hypothetical. In order to understand the process, one should realize what are physiological mechanisms and reactions of living organisms to extremely low temperatures.

Cryogenic temperatures are responsible for activation of thermoregulative mechanisms aimed at maintaining constant body temperature, especially the temperature of vital organs such as brain, heart, kidneys mainly by sacrificing less important parts of the body such as extremities. There are two ways of maintaining constant temperature whilst being exposed to extremely low environmental temperature. On the one hand, heat is being preserved in the body and on the other it is being actively generated. The above-mentioned mechanisms are coordinated by two highly specialized parts of the posterior hypothalamus which has links to other specific centers in the mesencephalon such as the center responsible for muscle tonus, the center controlling hypothalamus–pituitary–peripheral endocrine glands (thyroid and suprarenal) axis, the autonomic system center, and the vasomotor center (17, 18). Low environmental temperature stimulates skin thermosensitive receptors, nociceptors and thermosensitive mechanoreceptors. Conveyance of these stimuli into CNS triggers, among others, specific neurohumoral chain reactions with servomechanisms

known as the hypothalamus–pituitary–peripheral glands axis. This results in excretion of corticotropin-releasing hormone (CRH) and thyrotropin-releasing hormone (TRH) in the hypothalamus. CRH not only increases the pituitary secretion of adrenocorticotropine hormone (ACTH) but also the secretion of proopiomelanocortine (POMC), which is regarded as a β-endorphin and ACTH precursor. The secretion of β-endorphin itself is then increased as well (19). On the other hand, increased secretion of TRH results in the release of thyroid-stimulating hormone (TSH) and thyroid hormones such as thyroxine and this all leads finally to switching basic metabolic rate onto the higher level, which is responsible for intensified heat production (17).

The reaction to cryotherapy is very varied and depends on the time of exposure to cold and the temperature applied. Not all mechanisms are active after cryotherapy. In the case of cryogenic procedures at −110°C, lasting 2 min, the following changes were observed in healthy subjects: (i) plasma levels (measured 10 min after cryotherapy) of ACTH, norepinephrine, epinephrine and α-endorphin were significantly higher in men and women; (ii) testosterone plasma level was significantly higher only in men. The following parameters did not change after cryotherapy: (i) heart rate, diastolic and systolic blood pressure and other heamodynamic parameters; (ii) electrocardiograph diagrams; (iii) cortisol, thyroid hormones and growth hormone plasma levels (19). The inner body temperature as measured inside the mouth was preserved during the cryotherapy procedure, meaning that no hypothermia was observed. Only surface skin temperature was lowered for about 15 min after the procedure. It was 0.5–3.2°C below normal temperature on the trunk and 9.5–11.5°C on lower extremities (16). Based on the above it could be suggested WBCT acts through stress chain reactions which results in temporal improvement of mental condition and in that respect it resembles other stressors used in treatment of depression such as sleep deprivation.

Disturbances of biological cycles, especially sleep disturbances, were those symptoms patients in this study reported as virtually completely retreated. Since these disturbances are commonly attributed to dysfunctions of regulative mechanisms of the hypothalamus and reticular formation, and in the light of evidence that cryotherapy influences the hypothalamus triggering thermoregulative reactions, the conclusion could be formed that cryotherapy plays an important role in regulating disrupted functions of both hypothalamus and reticular formation, thus improving all biological cycles in general. Another piece of evidence supporting the above is the fact that the menstrual cycle improved after 10 entries into the cryogenic chamber.

These rough observations lead to the formulation of the presumption that extremely low temperatures cause multiple modifications in neurotransmission in the central nervous system (CNS). However, the nature of the changes is not fully understood. For sure, cryotherapy influences somehow disrupted noradrenergic and serotoninergic neurotransmission systems but the direction of these changes is not obvious. A rise in norepinephrine plasma levels after cryotherapy may or may not be associated with its positive effects on depressed mood since studies by Kelly and Cooper (20) showed that improvement of depressed patients was associated with decrease in norepinephrine plasma levels. On the basis of research investigating the correlation between catecholamine levels and extremely low temperatures, and also serotoninergic meditative theory, another presumption could be made that low temperatures cause changes of serotonin–dependent transmission as well. Clinical observations demonstrate that inhibition of serotonin reuptake and increment of its availability correlates positively not only with antidepressive effect but also with sedation and anxiety reduction (21). The positive effects of α-endorphins and endogenous opioids in general in depressed patients in this study were probably marginal but should not be underestimated automatically. It is possible that alleviation of somatic complaints, various kinds of aches and pains through α-endorphins, pain gating mechanisms by Melzack and Wall on the spinal cord and thalamic level as well as decreased conveyance speed of afferent stimuli in pain conveying neurons (10, 16, 22) resulted in specific analgesia subjectively perceived by patients as an improvement in mental condition. Other factors related to discontent could also influence observed outcomes of this study and should be considered here, but main mechanisms responsible for the positive effects of cryotherapy were probably associated with the hypothalamus–pituitary–peripheral endocrine glands axis.

We are aware that the design of the study described here was highly imperfect and did not give a strict and reliable answer to the question of whether WBCT could serve as an easy, cheap and safe treatment modality in mood disturbance, enhancing primary approaches such as psychotherapy or pharmacotherapy. The number of recruited patients was low, there was no control group, inclusion and exclusion criteria were not

laid down clearly, overly non-standardized instruments were used and finally there was no follow-up period. It has to be underlined here that it was not the main goal of the study to provide exhaustive and definite answers to the unknown but merely to give a 'scent' of possibilities, to determine whether further investigations are really worth doing and, if they are, to aid authors in designing a reliable project that would comply with statistical standards. Since first conclusions drawn from raw results were encouraging, another study was designed, prepared and then 'brought to life'. At the moment it is still running, but final and statistically sound results will be available in the very near future.

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References

1. Nouri K, Chartier TK, Eaglstein Wh, Taylor JR. Cryotherapy for psoriasis. Arch Dermatol 1997; **133**:1608–1609.
2. Bourke JF, Berth-Jones J, Hutchinson PE. Cryotherapy of common viral warts at intervals of 1, 2 and 3 weeks. Br J Dermatol 1995;**132**:433–436.
3. Cook DK, Georgouras K. Complications of cutaneous cryotherapy. Med J Australia 1994;**161**:210–213.
4. Bahn DK, Lee F. Cryosurgical ablation therapy for prostate cancer. Arch Italiano Urologia Androl 2000;**72**:302–304.
5. Chung Mh, Ye W, Ramming KP, Bilchik AJ. Repeat hepatic cryotherapy for metastatic colorectal cancer. J Gastrointest Surg 2001;**5**:287–293.
6. Silverman SG, Tuncali K, Adams DF, vansonnenberg E, Zou Kh, Kacher DF, Morrison PR, Jolesz FA. MR imaging-guided percutaneous cryotherapy of liver tumors: initial experience. Radiology 2000;**217**:657–664.
7. Seifert JK, Junginger T, Morris DL. A collective review of the world literature on hepatic cryotherapy. J Roy Coll Surg Edin 1998;**43**:141–154.
8. Quinn GE, Dobson V, Siatkowski R, Hardy RJ, Kivlin J, Palmer EA, Phelps DL, Repka MX, Summers CG, Tung B, Chan W. Cryotherapy for retinopathy of prematurity cooperative group. Does cryotherapy affect refractive error? Results from treated versus control eyes in the cryotherapy for retinopathy of prematurity trial. Ophthalmology 2001;**108**:343–347.
9. Yamauchi T. Whole body cryotherapy is method of extreme cold −175°C treatment, initially used for reumathoid artritis. Z Phys Medical Baln Klim 1986;**19**:311.
10. Bialy D, Zimmer K, Zabrobelny Z. Cryogenic chamber – advantages, application in physiotherapy – own experience. Acta Bio-Optica Informatica Med 1998;**4**:169–171.
11. MacAuley DC. Ice therapy: how good is the evidence? Int J Sports Med 2001;**22**:379–384.
12. Metzger D, Zwingmann C, Protz W, Jackel WH. Whole-body cryotherapy in rehabilitation of patients with rheumatoid diseases – pilot study. Rehabilitation 2000;**39**:93–100.
13. Swenson C, Sward L, Karlsson J. Cryotherapy in sports medicine. Scand J Med Sci Spor 1996;**6**: 193–200.
14. McDowell Jh, McFarland EG, Nalli BJ. Use of cryotherapy for orthopaedic patients. Orthopaedic Nursing 1994;**13**:21–30.
15. Bell GW. Aquatic sports massage therapy. Clin Sports Med 1999;**18**:427–435.
16. Gregorowicz H, Zagrobelny Z. Whole body cryotherapy – indications and contraindications, the procedure and its clinical and physiological effects. Acta Bio-Optica Informatica Med 1998;**4**:119–131.
17. Zagrobelny Z, Zimmer K. Cryogenic temperatures application in sports medicine and physiotherapy. Sports Med 1999;**94**:8–13.
18. Bauer J, Skrzek A. Physiological basis of cryotherapy. Sports Med 1999;**94**:3–6.
19. Zagrobelny Z, Halawa B, Jezierski Cz Wawrowska A. Effect of a single cooling of the entire body in the cryogenic chamber on selected hemodynamic parameters and blood serum hormone levels in healty subjects. Pol Tyg Lek 1993;**14–15**:303–305.
20. Kelly CB, Cooper SJ. Differences and variability in plasma noradrenaline between depressive and anxiety disorders. J Psychopharmacol 1998;**12**:161–167.
21. Rymaszewska J, Bialy D, Zagrobelny Z, Kiejna A. The influence of wholebody cryotherapy on mental health. Psychiatr Pol 2000;**4**:649–653.
22. Schroder D, Anderson M. Kryo- und Thermotherapie. Grundlagen und praktische Anwendung. Stuttgart: Gustav Fischer Verlag 1995.