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Effects of whole body cryo-chamber therapy on pain in patients with chronic low back pain: a prospective double blind randomised controlled trial

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Background. **It is believed that treatment with low temperature can reduce pain perception in chronic pain patients, including chronic low back pain patients.**
Aim. **To evaluate the effects of a two-week repeated intervention of -67 °C cryo-chamber in patients with chronic low back pain.**
Design. **A prospective randomized double blind study design.**
Setting. **Hospital-based outpatients department**
Population. **Outpatients with chronic low back pain.**
Methods. **Comparing intervention group (-67 °C) with higher temperature (-5 °C) which was supposed as a control group in a cryo-chamber.**
Results. **Similar effectiveness in pain reduction in both intervention and control groups**
Conclusion. **Cryochamber therapy with -67 °C is not superior to (sham cryo chamber) with -5 °C.**
Clinical Rehabilitation Impact. **Cryo chambers therapy show positive effect by improving pain. For the treatment, -5 °C seems to be sufficient for these patients.**

KEY WORDS: Low back pain - Chronic disease - Cryotherapy.

In western countries low back pain is one of the most frequent musculoskeletal pain syndromes. Lifetime incidence is around 70% to 85%.[1] In most cases acute low back pain is self-limiting and there is a tendency that low back pain becomes a chronic pain syndrome.[1] Additionally, the treatment of chronic low back pain still is unsatisfactory.[2]

Multimodal rehabilitation programs are effective in terms of pain, reduction quality of life and return to work.[3, 4] Although many single physical modalities have been shown to reduce chronic low back pain, however, the long-term effects are not satisfactory (*e.g.* massages,[5] exercise and laser therapy [6]) This might be due to the fact that pathophysiology of low back pain is rather complex and may include many factors such as muscle weakness, muscle tension, joint dysfunction, immobility and psychosocial stress. However, single treatments for low back pain are still required, because intensive multimodal rehabilitation programs in many cases would be overdosed and its costs might be too high. Thus, research on the effects of single physical modalities are still of common interest.

Whole-body-cryotherapy is one type of physical therapies. This type of therapy was firstly used by Yamauchi in rheumatoid arthritis patients with -175 °C,[7] and could improve pain in this group of patients. Recently, the use of this type of physical therapies is quite broad from treatment of patients [8-11] to application for athletes as it can improve muscle damage recovery.[12, 13]

The pain mechanism in back pain patients is related

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to the increase of some proinflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6).[14] Interestingly, whole-body-cryo-therapy initially showed that the analgesic effects are caused by peripheral mechanism.[8] More recently this type of physical therapy can help reduce pain, and increase anti-inflammatory cytokines in rheumatoid arthritis patients [15] which may lead to the improvement of pain. Therefore this type of cryo-therapy might improve pain in other musculoskeletal disorder, including in chronic low back pain patients.

The aim of this paper was to evaluate the effectiveness of serial treatment of -67 °C in chronic low back pain patients. As a control/placebo group, we used similar intervention with temperatures of -5 °C. This study performed in a prospective randomised double blind study design in two weeks treatment duration.

Material and Method

The study was performed according to the Helsinki Declaration. It was approved by the Ethic Commission of the Medical Chamber Bremen. Patients participated according to the rules of an informed consent. Written and oral patient information was documented and signed both by the responsible physicians and the patients.

Patients

Patients were recruited based on broad-based recruitment strategy (advertisement in the public and in the regional newspaper).

Inclusion criteria of low back pain defined and measured using the Mainz Pain Staging System (MPSS) [16] of chronification. Myofascial pain was included. This was assessed by orthopaedic surgeon. The range of age was defined from 18 to 65 years.

As we recruited non-specific low back pain, per definition, we excluded diagnosis like symptomatic disc herniation, spinal stenosis, and spondylitis. Other exclusion criteria were defined as indication of back surgery, rheumatoid arthritis or tumors in spinal cord, acute cardiovascular diseases, especially cardiac insuffiency (>NYHA III), cardiac arrhythmia, pulmonary heart disease, arterial hypertension with

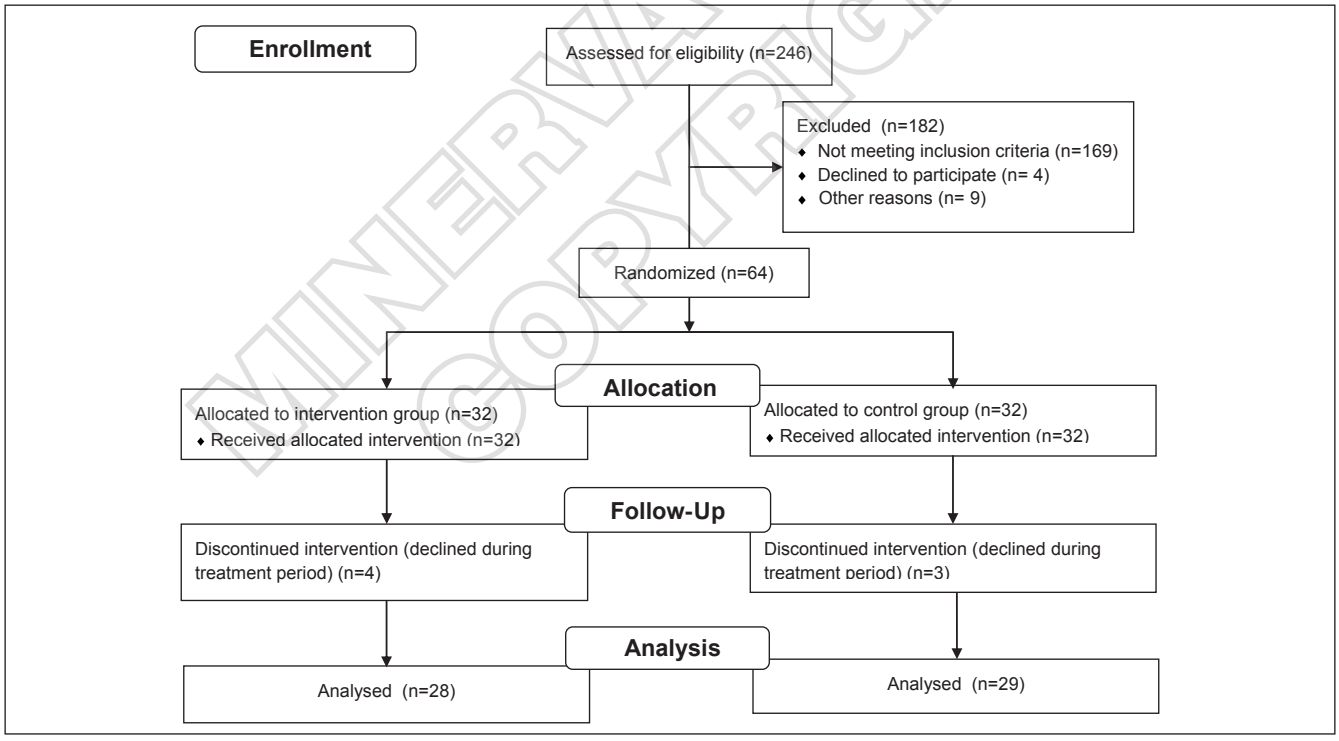

Figure 1.—Flowchart screening and allocation of the patients.

insufficient treatment and peripheral arterial occlusion higher than stage 3. Additionally, patients with morbus Raynaud, infections of the airways, cold sensitive bronchial asthma, pregnancy, claustrophobia, psychiatric diseases and previous treatment with cryo-chamber expositions were also excluded.

The randomization procedure was done at another institution. After inclusion of the patients into the study, a number was given to the patients and sent to the randomization team. There, the patients were grouped using a block random-number procedure. The result of randomization was sent back to the intervention institution via fax. Since this was double blind study design, the physician and the patients were not informed about the applied temperature.

Intervention

The interventions were done in a cryo-chamber (Crio-Med GmbH, Niefern-Öschelbronn). Cold air was produced with a cooling machine and inflated into the chamber until -67 °C.[8, 9] As control, the same chamber was used, however, the temperature was regulated only up to -5 °C.

Patients were exposed to cryo-chamber under supervision of therapist. In order to avoid tissue damage on the acra, patients had to wear shoes and gloves as well as an airway protection. Intervention duration was three minutes/day. Patients were treated in a total of 10 times (every weekday during two consecutive weeks).

Outcome measurements were done before the first treatment and before the last treatment.

Sample size calculation

Sample size was calculated in cooperation with Department of Biometry, Hannover Medical School. Pain intensity was used as a main outcome parameter. Level of significant was set at alpha 0.05. This resulted in a minimum number of patients of 29 (Greenhouse-Geisser-Approximation).

Statistical analysis

Statistical evaluation was performed using SPSS program version 14.0 (SPSS Inc., USA). The Kolmogorov-Smirnov test was used to test the distribution of the data. Student t-test was used to calculate significant treatment effect (before and after), and to compare intervention and control group. $P<0.05$ were defined as statistically significant.

Assessment tools

The following assessment tools were used:

1. MPSS: this tool classifies patients with chronic pain into three stages (I, II, III). Criteria are the duration of pain perception, localization of pain, drug treatment and the history of treatments and interventions.[16]

2. Pain intensity Visual Analogue Scale (VAS). A ten centimetre visual analogue scale was used with the endpoints "0= no pain" and "10= pain as bad as it could possibly be".

3. Pain perception scale (PPS). Pain perception scale is a questionnaire of 24 items. It can be evaluated in two scales (effective pain sensation and sensory pain sensation). An overall score can be calculated. The total range is 1-96.[17]

4. Pain Disability Index (PDI). This instrument uses 11 steps rating scale from 0 ("no disability") to 10 ("complete disability"). This includes life areas such as family and house work, recreation, social activities, remunerative employment, sexual life, self-care and other activities of daily living.[18-21]

5. Additional to these standardised instruments a self-designed patient questionnaire was used. It contained questions about the subjective pain perception and the general comfort. Both dimensions a ten-interval numeric rating scale was used. The endpoints of the general comfort rating scale are 1= extremely uncomfortable and 10= very comfortable. The endpoints of the perception of temperature are 1: very cold and 10: very hot.[9]

Results

Two hundred forty-six patients have been investigated in the recruitment process. Sixty-four patients fulfilled the inclusion criteria and were without any exclusion criteria. They were randomized into two groups (intervention group [IG] and in the control group [CG]). At the end of study, 28 patients of IG and 29 patients from CG were included in analysis.

Mean of age of IG was 54.7 and CG was 55.1 years (Table I). These differences were not significant (P=0.683). In IG 13 patients were male (46%) and 15 female (54%), in CG the number of males was 11

TABLE 1.—*Characteristics of patients.*

Parameter	Group	Value	P
Gender (male/female)	IG	13/15	0.516§
	CG	11/18	
Age (years)	IG (N.=28)	54.71±9.47 (39-65)	0.683§§
	CG (N.=29)	55.14±7.19 (28-65)	

Data for age is shown in mean±SD; (min-max). IG: intervention group; CG: control group.
§Chi-square test; §§t-test.

TABLE II.—*Comparison of main outcome parameters before and after treatment.*

Parameter	Group	Before treatment		After treatment		Difference (before *vs.* after treatment)	
		Mean±SD (min-max)	p (inter-group)	Mean±SD (min-max)	P (inter-group)	P (intra-group)	Effect size (Cohen's d)
Pain (VAS)	IG	3.97±2.40 (0.0-10.0)	0.381	2.87±2.26 (0.0-9.2)	0.386	<0.001	0.4179
	CG	4.48±1.98 (0.0-8.6)		3.36±1.98 (0.0-7.9)		<0.001	0.5626
PPS	IG	53.6±10.8 (42-74)	0.489	48.2±8.28 (37-65)	0.549	<0.001	0.5612
	CG	52.3±10.3 (38-75)		49.7±10.0 (37-74)		0.104	0.2561
PDI	IG	31.6±12.3 (12-60)	0.847	23.7±12.5 (4-51)	0.546	0.007	0.6371
	CG	32.1±11.5 (11-55)		24.9±11.9 (4-53)		<0.001	0.6153

Data is shown in mean±SD, (min-max). VA: Visual Analog Scale; PPS: Pain Perception Scale; PDI: Pain Disability Index.

(38%) and females 18 (62%). Using Chi-square test, the distribution of gender between the group was not statistically significant (P=0.516).

The results of the main outcome parameters are summarized in Table II. The statistics comparison of mean values at the beginning of treatment shows no differences in the pain intensity which was measured by VAS (P=0.381), PPS (P=0.489) or PDI (P=0.487). In the intervention group, mean values of pain intensity (VAS), PPS and PDI were significantly lower at the end of the treatment as compared to before treatment. Pain (VAS and PDI) showed moderate effect size both in IG and CG. However, in the PPS, the effect size of IG was moderate, meanwhile in CG was low. In the CG, statistically significant reductions in pain (VAS) and PDI were also demonstrated, but not in PPS (P=0.104). Testing differences between groups at the end of the treatment in all three parameters, no statistical differences could be detected (VAS, P=0.386; PPS, P=0.549; PDI, P=0.546). Thus, it can be concluded that difference of temperature between IG and CG showed similar effect in improving pain after two weeks of serial treatment.

In order to control the blindness of the patients, the thermal perception scales were evaluated and shown in Table III. It demonstrated that the pain perception in the IG was significantly lower as compared to the CG. This shows that the tempera-

TABLE III.—*Perception of cold temperature in cold chamber.*

Parameter	Group		Significance (between group)
	IG	CG	
Thermal Comfort	7.32±2.23	8.46±1.37	P=0.056
Perception of temperature	3.89±1.83	5.57±1.77	P=0.001

Data (mean±SD).
IG: intervention group (N.=28); CG: control group (N.=29). Thermal comfort scale endpoints: 1= extremely uncomfortable, 10= very uncomfortable; Perception of temperature scale endpoints: 1= very cold, 10= very hot.

ture difference could be perceived by the patients (P=0.001). Thermal comfort difference qualitatively seems to be similar, as the difference between the group values was not statistically significant (P=0.056).

Discussion

The purpose of this study was to evaluate the effectiveness of -67 °C whole body cryotherapy in treating chronic low back pain patients and compared with -5 °C as control. Our results showed that intervention with both temperatures could improve pain. Interestingly, this serial intervention of chronic low back pain patients with -67 °C was not superior to -5 °C or in other words the results show similar effectiveness in pain reduction in both intervention and control groups. This confirms that this approach is feasible. Obviously, there is no need to treat patients with low back pain with very low temperatures (below -60 °C). If this result will be confirmed by further studies, cryo-chamber treatment could be driven with less cold temperatures which will save significant amount of energy.

The use of -5 °C in this study was to define the control/sham group for the blinding purpose. As -5 °C could still be felt quite cold for the patients, these results showed that blinding of the patients was not completely diminished, because patients can still feel the temperature perception. However, the significant differences in the effect of both treatments are even more relevant for this study. Although in the end the general comfort of the temperature was significantly different in both groups. And this comparison leads to the new finding that -5 °C could show similar effect as lower temperature, in this case -67 °C.

Whole body cryotherapies have been used in different type of musculoskeletal diseases and show effectiveness. For example, it improved pain in rheumatic diseases,[15] fibromyalgia syndrome,[8, 9] and could also improve health-related quality of life in fibromyalgia syndrome patients.[11]

Regarding the mechanism it is not likely that the analgesic effect of cold application has caused the changes in pain perception. For such a long-lasting analgesic effect, the intervention was too short (three minutes/intervention). In physical medicine, analgesic effect of cold longer treatment is mainly recommended for a local treatment.[22] For such treatment, analgesic effect is well known. Possible explanation could be analgesic effect of repeated intermittent cold-chamber therapy is an adaptation in autonomic regulation effecting pain sensitivity as well.[23] For other physical treatments, it has been shown in many studies that they act as adaptive stimuli causing functional adaptation.[24] It has been shown that functional adaptation with changes in the activity of the HPA axis may moderate pain syndromes. Although it cannot be excluded that the natural cause of the disease was causal for the effect. This is not very likely as the selected patients had a very high grade of chronicity and in these cases, within two weeks not much change of pain could be expected.

The effectiveness of this physical therapy for musculoskeletal diseases as aforementioned could be related to the alteration of pathomechanism after treating with whole-body cryotherapy. The level of proinflammatory cytokines, such as IL-6 and TNF-α in back pain patient, increased.[25] Meanwhile, intervention of whole body-cry therapy could decrease pro-inflammatory cytokines, such as IL-1α,[26] on the other hand it could increase anti-inflammatory cytokines, including IL-10.[26] Further studies related to whole body cryotherapy in rheumatic diseases targeted vascular endothelial growth factor, cartilage-degrading enzymes, and pro-inflammatory cytokines.[15] Other mechanism of the effects of whole body cryotherapy includes an increase of serum dopamine concentration and a decrease of beta-endorphin, serotonin and inhibition of the C-fiber system and muscle relaxation.[9] These alterations could lead to the effect of whole body cryotherapy as an analgesic.

Multimodal rehabilitation programs are effective in terms of pain, reduction quality of life and return to work.[3, 4] Although many single physical modalities have been shown to reduce chronic low back pain, however, the long term effects are not satisfactory (*e.g.* massages: 5; exercise and laser therapy: 6) This might be due to the fact that pathophysiology of low back pain is rather complex and may include many factors such as muscle weakness, muscle tension, joint dysfunction, immobility and psychosocial stress. However, single treatments for low back pain are still required, because intensive multimodal rehabilitation programs in many cases would be overdosed and its costs might be too high. Thus, research on the effects of single physical mo-

dalities are still of common interest. And this study could show the effectiveness of single treatment for chronic low back pain, although further studies are needed to confirm the effect and to evaluate the changes of pathomechanism.

Conclusions

In conclusion, our studies showed that there is no difference between the effects of moderate and high intensity intermittent cryo-chamber therapy in chronic low back pain, and the results suggest that both treatments may be helpful for this syndrome. In other words, it can be concluded that temperatures below -5 °C do not lead to stronger treatment effect, at least for patients with chronic non-specific low back pain. Further studies should clarify if this is an effective treatment, even if other controls are used. It would be more interesting if pathomechanism of this type of treatment will be evaluated.

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