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ORIGINAL ARTICLE

Impact of Whole Body Cryotherapy at −110 °C on Subjects with Arterial Hypertension

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Abstract Whole body cryotherapy (WBC) in a cryo-chamber as a medical treatment was first established in Japan in the 1980s, later in Central Europe, and is now becoming more popular also in the United States. The exposure to extreme, non-physiological environmental conditions in a cryo-chamber at −110 °C may exceed the normal adaption capacity. The aim of this study was to investigate the effects of WBC on blood pressure (BP) readings in adult subjects with rheumatic disorders and normal or moderately elevated BP. A sample of 23 subjects (8 female, 15 male) which were recruited according to their pathology between the age of 35 and 69 years undergoing 21 WBC applications was divided into three groups: a group of subjects with anti-hypertensive therapy, a group of subjects with mild arterial hypertension without medical treatment, and a normotensive control-group. A total of 483 BP readings were taken immediately before and after each WBC application. The systolic and diastolic BP were recorded, and the mean arterial pressure, and the amplitude of BP were calculated. A statistically significant rise of BP after WBC was found in the whole sample and in the normotensive group. Over the course of time, no significant change of BP behavior was observed, except for normotensive subjects, who showed a wider range in their systolic BP values. Generally accepted exclusion criteria were applied, and in our sample group WBC was safe with respect to unwanted BP alterations for adult subjects under 70 years—regardless of a pre-existing untreated mild or pharmacologically treated arterial hypertension. Greater changes of BP values might infrequently occur, so an individual monitoring of subjects is necessary.

Keywords Whole body cryotherapy · Cryo-chamber · Blood pressure · Blood pressure response · −110 °C · Arterial hypertension

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Objective

To assess the tolerability of the application of whole body cryotherapy (WBC) at a temperature of −110 °C in adult subjects with pharmacologically treated or mild untreated arterial hypertension suffering from rheumatoid disorders, we set out a study involving three groups of patients. To this end, BP readings were taken from normotensive subjects and subjects with pharmacologically treated or mild untreated arterial hypertension undergoing WBC treatment for rheumatoid disorders to detect potentially harmful changes of BP values. Depending on age and a pre-existing arterial hypertension, the ability of blood pressure regulation after the exposition to extreme cold might be limited and could lead to significant blood pressure (BP) alterations of this treatment in clinical practice. Our hypothesis was that subjects within these three groups would show different blood pressure behavior after exposure to extreme cold.

Introduction

There is a long tradition in cryotherapy. Ancient physicians like Hippocrates of Kos (about 460–370 BC) described the application of cold temperature to treat patients. For non-medical reasons, whole body cooling is nowadays also used as a spa treatment and as an adjunct in sports science to enhance sporting prowess and recovery after excessive physical effort (Bleakley et al. 2014).

Two forms of cryotherapy are common in modern medicine: the local application of cold, and a general cooling of the body. A general cooling of the body has become clinical routine to lower the central temperature and the basal metabolism of injured tissues (Shankaran et al. 2005; Storm et al. 2008). Different from this concept, Yamauchi (1986) developed WBC in the 1980s using a cryo-chamber to treat rheumatoid arthritis.

Exposure to cold temperatures has the potential to affect the superficial and the body core temperature (Westerlund et al. 2003), as well as neuro-muscular, cardiovascular, and humoral parameters (Smolander et al. 2009). In our opinion, all of these effects have a local and a systemic aspect, which influence each other. A well-known example is the "cold pressor test", in which changes of cardiovascular parameters occur after local cooling. This effect is mediated by neuronal and humoral factors (Buemi et al. 1997; Chen et al. 2008; Di Carli et al. 1997; Victor et al. 1987). Since different effects can be observed after cooling the face in the cold face test (Smolander et al. 2004), also the localization of cooling is evidently of importance (Westerlund et al. 2006).

According to Janský et al. (2006), local cooling may have different effects on circulatory and humoral parameters compared to general cooling of the whole body. Taghawinejad et al. (1989) described an inconsistent influence of WBC at −110 °C on core body temperature. In most subjects a falling core temperature was measured, while in others no change or even a rise of the core body temperature was observed. Obviously, subjects can adapt to the exposure to cold temperatures, as proven by several Scandinavian studies about thermoregulation (Dugué and Leppänen 2000; Smolander et al. 2004). Interestingly, the duration of the exposure to extreme cold has different effects on circulatory parameters and on skin temperature (Fonda et al. 2014). Heart rate and blood pressure showed no significant difference, whether the exposure lasted 90, 120, 150, or 180 s, while the skin temperature changed significantly after a longer exposure. General temperature factors like seasonal variations, as described for arctic regions (Leppäluoto and Hassi 1991) or moderate climates (Alpérovitch et al. 2009; Brennan et al. 1982) can also influence BP behavior. Also local temperature stimuli may have systemic effects and can be dangerous for subjects suffering from a coronary heart disease. Wendt et al. (1983) provoked coronary spasms in coronary patients, in some cases even accompanied by ischemic changes of the ECG, both after the cold pressor test and after the inhalation of cold air. Importantly, this mechanism may differ in normotensive subjects compared to hypertensive subjects, as Antony et al. (1994) reported in their study. Subjects without hypertension showed a significant vasodilatation of epicardial coronary arteries, while a vasoconstriction was observed in the hypertonic group. These authors conclude that pre-existing arterial hypertension appears to impair the vasodilator response of coronary arteries to a cold pressor test. Also after a general cooling of subjects, the cardiovascular response was influenced by the presence of arterial hypertension (Zalewski et al. 2014), which was explained by a weaker autonomic response of hypertensive subjects to extreme stimuli.

WBC refers to the exposure of subjects to extreme cold air (−100 to −160 °C) for a short time to activate physiological regulatory mechanisms. One of these effects is the change of circulatory parameters after the exposure. A number of possible indications and contra-indications for WBC therapy have been suggested by members of the society for cryo-medicine (Papenfuß et al. 2006). Apparently, some of these criteria were introduced empirically rather than based on scientific studies. Members of this society recommend WBC, e.g., for patients with rheumatic diseases, chronic pain, elevated muscular tonus as a result of multiple sclerosis or infantile cerebral paresis, and diseases of the skin like psoriasis or neurodermatitis. They also recommend this therapy for patients suffering from any chronic inflammatory disease involving the gastrointestinal system, respiratory system, locomotor system, or any other tissue. In addition, WBC is recommended also after excessive sport or psychologically caused distress (Bleakley et al. 2014; Szczepańska-Gieracha et al. 2014). On the other hand, WBC is contraindicated for patients with severe cardiovascular diseases, severe untreated arterial hypertension, acute infectious diseases, malignant tumors, seizures, allergic reactions to cold, actual drug abuse, and some psychiatric disorders.

Regarding different effects of WBC on normotensive or hypertensive subjects, the aim of this study was to quantify these effects on different hypertension groups and to detect possible harmful changes of circulatory parameters during WBC.

Materials and Methods

Our study group was a sample of consecutive subjects (age 35–69) treated for rheumatic diseases in a rehabilitation center. Subjects with a BP value of more than 160 mmHg systolic or more than 95 mmHg diastolic before WBC were excluded, as well as subjects with one or more of the following risk factors: history of cold intolerance, acute infection, cardiac insufficiency NYHA II or higher, arrhythmia like atrial or ventricular fibrillation, atrioventricular or bundle branch heart block, anxiety disorders, history of seizures.

Subjects had to participate in at least 19 of the prescribed 21 applications to be included into the study. Criteria for exclusion of patients from further WBC treatment were aggravation of rheumatic symptoms, new onset of infections, or cardiovascular symptoms. Since only routine measurements of blood pressure before and after each application of WBC were taken, approval by the ethics committee was not required. All subjects gave written informed consent to participate in the study in accordance with local guidelines. The investigation confirms with the principles outlined in the Declaration of Helsinki. We used a cryo-chamber (Zimmer Medizin Systeme) divided into three sections with different temperatures, starting at a temperature of −15 °C, followed by a room with −60 °C, and finally a room with −110 °C. Subjects had to enter the chamber in swimwear. Shoes, gloves, a headband, and a facemask were mandatory to prevent the occurrence of frostbites. After passing through the first two rooms, subjects remained in the third section for approximately 3 min at a temperature of −110 °C while walking around and gently moving their limbs. After cryotherapy they had to rest for 30 min at ambient temperature. WBC treatments were performed daily over a period of 3–4 weeks.

The average age of all subjects was 53.0 (±10.1) years, with a trend of females being older [58.6 (±8.4) years] compared to males [50.1 (±9.8) years; $p = 0.05$]. Five subjects were on antihypertensive medication at study entry. They received either calcium channel or beta-receptor blockers or angiotensin-converting enzyme inhibitors and were referred as "pharmacologically treated hypertension". The average age in this group was 61.2 years (±7.6). All other hypertensive subjects (BP values were higher than 140 mmHg systolic and/or 90 mmHg diastolic in at least more than 25 % of measured values) were included in the group with "untreated hypertension", with an average age of 56.4 years (±9.1). The normotensive reference group consisted of 13 subjects without arterial hypertension (average age 48.6 years ± 9.2). A total of 483 BP readings were taken in 23 subjects immediately before and after each WBC application with the method of Riva-Rocci, and the following values were ascertained: systolic and diastolic BP, pressure amplitude (systolic–diastolic BP), and mean arterial pressure (MAP).

Statistical Evaluation

Normal distribution of analyzed continuous variables was assessed using the Kolmogorov–Smirnov test. Values are given as mean ± SD. BP values for each subject as well as BP readings within the three hypertension groups before and after WBC were assessed with Student's paired *t* test. In addition, mean values of systolic and diastolic blood pressure before and after WBC in the three hypertension groups were analyzed using two-way analysis of variance (ANOVA) with group (3 levels) as a between-subject factor and time (2 levels) as a within subject factor. Two-tailed *p* values <0.05 were considered significant. Missing values were completed applying the LOCF (last observation carried forward) procedure. The analyzed sample size allowed to detect effect sizes of approximately 0.8 standard deviations for the normotensive group ($n = 13$) and 0.5 standard deviations for the two other study groups ($n = 5$).

Results

BP Changes in All Subjects

In the total sample of all subjects, we observed an average rise of systolic values of 4.84 mmHg [from 120.43 (±13.32) to 125.28 mmHg (±13.68), $p < 0.001$] and an average rise of diastolic values of 1.71 mmHg [from 76.06 (±9.03) to 77.76 mmHg (±8.21), $p = 0.001$] after WBC compared to BP values before WBC (Student's paired *t* test, see Table 1; Fig. 1). After 483 applications of WBC, in 59.8 % of the applications a rise of systolic BP values could be found, and in 20.5 % the systolic pressure was unchanged, and, finally, in 19.7 % the systolic pressure was falling. In contrast, the diastolic BP measurements were rising in 42.4 % after WBC, equal in 38.7 %, and falling in 18.8 %.

In addition, MAP (2.75 mmHg ± 7.13, from 90.85 (±9.31) to 93.60 mmHg (±8.91), $p < 0.001$) and BP amplitude (3.14 mmHg ± 11.25, from 44.38 (±10.98) to 47.52 mmHg (±11.20), $p = 0.002$) values showed a significant rise immediately after WBC compared to values before WBC.

BP Changes in Relation to Arterial Hypertension

Regarding systolic blood pressure, analysis with a two-way ANOVA indicated a statistically significant difference between the patient groups ($p < 0.001$) and within pre- and post-measurement ($p < 0.001$). There was no significant interaction between group and time ($p = 0.745$). Regarding diastolic blood pressure, analysis with a two-way

Table 1 Summary of mean systolic and diastolic values for each subject immediately before and after all applications of WBC, systolic and diastolic differences, and significance of differences

Subject (P) hypertension groups[a,b,c]	Systolic before (mmHg)	Systolic after (mmHg)	Difference (mmHg)	Level of significance (*p*)	Diastolic before (mmHg)	Diastolic after (mmHg)	Difference (mmHg)	Level of significance (*p*)
P01[b]	131.19	141.19	**10.00**	**0.001**	87.14	90.48	3.33	0.045
P02[c]	118.81	130.24	**11.43**	**0.001**	83.81	87.38	3.57	0.048
P03[b]	117.14	118.10	0.95	0.644	76.19	78.10	1.90	0.258
P04[a]	114.29	113.33	−0.95	0.680	73.33	75.00	1.67	0.329
P05[a]	117.38	122.62	5.24	0.256	74.29	78.10	3.81	0.152
P06[c]	139.05	139.76	0.71	0.874	78.33	77.62	−0.71	0.809
P07[a]	114.76	118.33	3.57	0.182	73.10	74.29	1.19	0.424
P08[c]	126.43	130.24	3.81	0.069	81.90	80.95	−0.95	0.741
P09[a]	119.05	122.86	3.81	0.076	79.05	76.67	−2.38	0.153
P10[a]	108.33	113.10	4.76	0.007	67.86	70.71	2.86	0.010
P11[c]	129.52	132.38	2.86	0.346	80.24	79.29	−0.95	0.479
P12[a]	120.71	125.24	4.52	0.056	80.00	80.24	0.24	0.833
P13[b]	148.10	151.90	3.81	0.141	88.33	88.10	−0.24	0.909
P14[a]	115.48	115.48	0.00	1.000	72.86	73.81	0.95	0.384
P15[a]	116.43	119.52	3.10	0.142	74.52	76.90	2.38	0.056
P16[b]	121.67	130.71	**9.05**	**<0.001**	77.14	79.29	2.14	0.016
P17[b]	118.57	124.52	5.95	0.003	73.57	77.14	**3.57**	**0.001**
P18[a]	108.10	119.05	**10.95**	**<0.001**	62.62	70.71	**8.10**	**<0.001**
P19[c]	134.76	137.38	2.62	0.094	78.57	79.29	0.71	0.267
P20[a]	108.57	120.24	**11.67**	**<0.001**	72.62	75.48	2.86	0.049
P21[a]	116.90	120.24	3.33	0.016	75.48	76.67	1.19	0.309
P22[a]	108.33	112.38	4.05	0.015	68.81	70.24	1.43	0.137
P23[a]	116.43	122.62	**6.19**	**<0.001**	69.52	72.14	2.62	0.024
All subjects	120.43	125.28	**4.84**	**<0.001**	76.06	77.76	**1.71**	**0.001**

Differences of statistical significance are shown in bold

Hypertension groups: [a] normotensive, [b] treated hypertension, [c] untreated hypertension

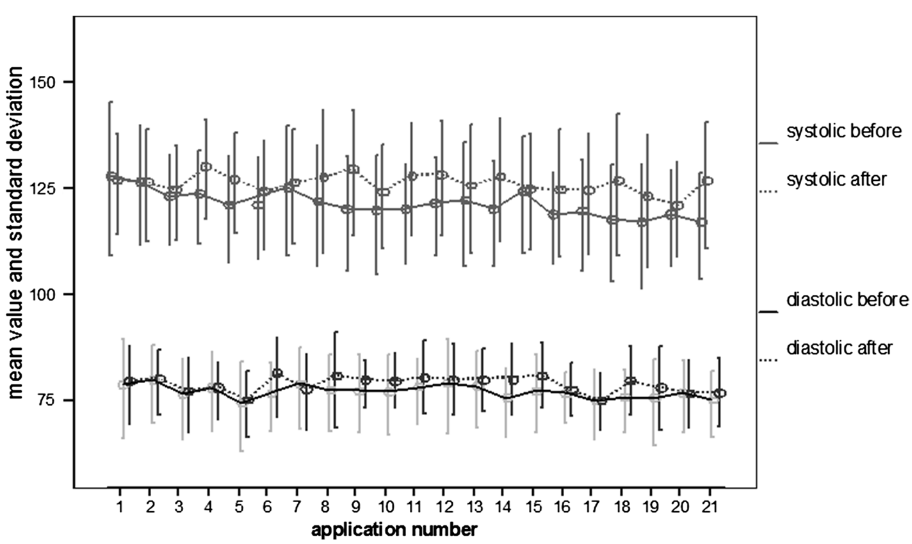

Fig. 1 Mean values and standard deviation of systolic and diastolic measurements of all subjects before and after each application of WBC (in mmHg)

ANOVA indicated a statistically significant difference between the patient groups ($p = 0.002$) and within pre- and post-measurement ($p = 0.006$). There was no significant interaction between group and time ($p = 0.29$) (Table 2; Fig. 2a, b).

In the first group of normotensive subjects, the systolic rise after WBC was from 114.21 (±9.22) to 118.85 (±9.49) mmHg, i.e., plus 4.63 (±10.55) mmHg. The diastolic rise was from 72.62 (±8.01) to 74.69 (±6.40) mmHg, which is plus 2.07 (±6.73) mmHg. The difference in normotensive subjects was statistically significant ($p = 0.001$ for systolic and $p = 0.008$ for diastolic BP changes, Student's paired *t* test, see Table 3; Fig. 3). After WBC applications, we observed a rise of systolic BP measurements in the group of subjects with pharmacologically treated arterial hypertension from 127.33 (±14.55) to 133.28 (±15.36) mmHg, which is plus 5.95 (±10.15) mmHg. The diastolic rise in this group was from 80.47 (±8.81) to 82.62 (±8.89) mmHg, which is plus 2.15 (±6.75) mmHg, both of borderline significance ($p = 0.023$ and $p = 0.034$, respectively). The third group consisted of subjects with mild arterial hypertension, but no medical treatment. In these subjects we observed a systolic rise from 129.71 (±12.34) to 134.00 (±12.06) mmHg, i.e., plus 4.29 (±13.79) mmHg after WBC, the diastolic rise in this sample was from 80.57 (±7.79) to 80.91 (±8.23) mmHg, i.e., 0.34 (±9.49) mmHg, both not significant.

Extreme BP Values

Although most measurements showed only modest BP elevations after WBC applications, we observed rises of systolic values of 20 mmHg and above in 58 cases (12.0 %), as well as diastolic rises of 10 mmHg and above in 95 cases (19.7 %). Pronounced BP elevations were mainly not related to the number of WBC applications or to a pre-existing arterial hypertension, but to the age of subjects. Extreme systolic rises were found more often in subjects with an age over 60 years. One subject showed a decrease of systolic and diastolic measurements after WBC for several times, another one a rise of systolic, but a decrease of diastolic values. In one case a systolic rise of 55 mmHg after WBC (105–160 mmHg) could be measured, in three cases a systolic rise of 35 mmHg, in 11 cases plus 30 mmHg, and, finally, in thirteen cases a systolic rise of 25 mmHg. In all of these subjects the treatment with WBC was well tolerated, and no adverse symptoms or clinical complications were observed.

Discussion

We analyzed blood pressure values of 23 subjects in series of 21 applications of WBC in a retrospective, observational study. A gentle rise of systolic and diastolic BP values could be observed. Over the course of time, no significant changes of the BP performance based on age, gender or a pre-existing arterial hypertension could be observed, although elderly subjects showed a trend towards higher values. Possible shortcomings of this study may result from the small sample of subjects, the dissimilar gender distribution and the lack of other circulatory values (Missmann et al. 2007). We did not use psychological tools to test stress and anxiety levels, which might have taken influence on BP measurements.

We observed a small, but significant rise of systolic and diastolic BP after WBC applications in our study (all subjects). Different from our observations, previous reports described significantly larger BP alterations after WBC therapy. In the study by Taghawinejad et al. (1989) a systolic rise of 10 mmHg and a diastolic rise of 5 mmHg were reported. Yamauchi (1986) found systolic rises of 20–25 mmHg after WBC in subjects with rheumatoid arthritis. In general, the rise of blood pressure readings in our study was smaller than described in other studies.

In a previous study a significant rise of systolic blood pressure was observed in both hypertensive and normotensive subjects after ten applications of WBC (Koczorowska et al. 2008). They concluded that after ten applications of WBC an overload of the circulatory system in subjects with hypertension might occur. Different to this

Table 2 Mean values of systolic and diastolic blood pressure before and after WBC in the three hypertension groups

	Group								
	Normotensive			Treated hypertension			Untreated hypertension		
	Mean	SD	Valid, *n*	Mean	SD	Valid, *n*	Mean	SD	Valid, *n*
Syspre	114.21	4.41	13	127.33	12.83	5	129.71	7.78	5
Syspost	118.85	4.15	13	133.28	13.44	5	134.00	4.34	5
Diastpre	72.62	4.64	13	80.47	6.77	5	80.57	2.31	5
Diastpost	74.69	3.09	13	82.62	6.19	5	80.91	3.81	5

n number, *syspre, syspost, diastpre, diastpost* systolic and diastolic blood pressure before and after WBC

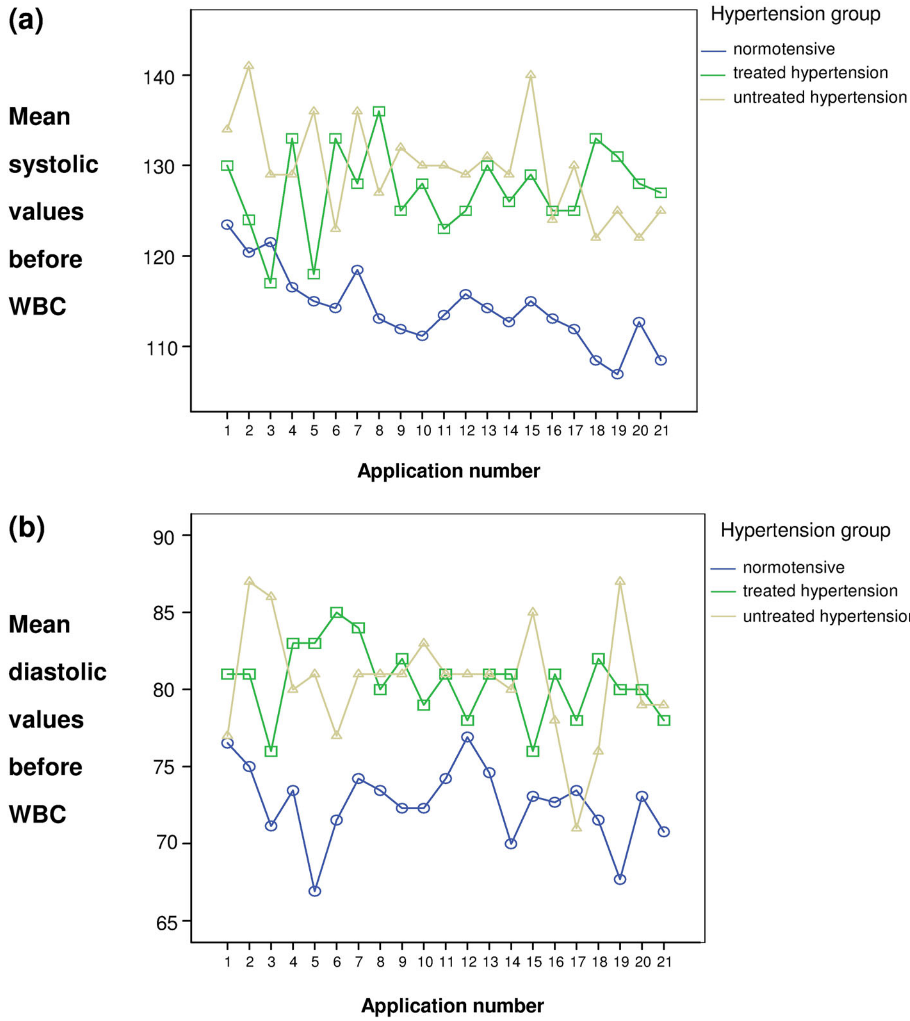

Fig. 2 **a** Mean systolic values of the three hypertension groups before each application of WBC (mmHg). **b** Mean diastolic values of the three hypertension groups before each application of WBC (mmHg)

Table 3 Paired sample tests of blood pressure values in the three hypertension groups before and after WBC

Group		Paired differences		*t* value	*df*	Sig. (two-tailed)
		Mean	SD			
Normotensive						
Pair 1	Syspre–syspost	−4.63462	3.54956	−4.708	12	0.001
Pair 2	Diastpre–diastpost	−2.06923	2.37036	−3.148	12	0.008
Treated hypertension						
Pair 1	Syspre–syspost	−5.95000	3.72402	−3.573	4	0.023
Pair 2	Diastpre–diastpost	−2.14800	1.51282	−3.175	4	0.034
Untreated hypertension						
Pair 1	Syspre–syspost	−4.28600	4.14910	−2.310	4	0.082
Pair 2	Diastpre–diastpost	−0.33600	1.93700	−0.388	4	0.718

SD standard deviation, *df* degree of freedom, *sig.* significance, *syspre–syspost, diastpre–diastpost* systolic and diastolic blood pressure before and after WBC

study, in our study only normotensive subjects showed significant blood pressure differences after 21 WBC applications. In another study an increase of systolic blood pressure of 21 mmHg, and of diastolic blood pressure of 9 mmHg was observed, which was higher than in our sample (Lubkowska and Suska 2011). In contrast to our study, their sample consisted of a group of 40 young, healthy men, and no subjects with hypertension.

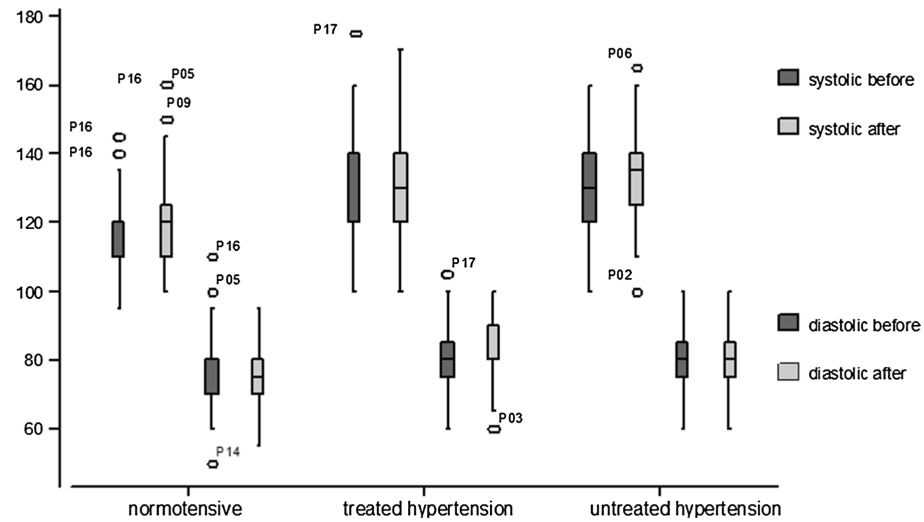

Fig. 3 Box-and-whisker plot (following the method of Tukey) of systolic and diastolic values of the three BP groups before and after WBC (in mmHg), showing *boxes* with values between 25th and 75th percentile, *whiskers* with a maximum length equal to 1.5 times the interquartile range, and outliers

After the first application of WBC, the average systolic measurements were lower [−1.09 (±15.45) mmHg] than before WBC. After further applications, a systolic rise of different degrees was observed. This is in contrast to the findings of Taghawinejad et al. (1989) and Westerlund et al. (2004). We cannot entirely explain these differences, but they may be attributable more likely to different levels of stress and anxiety of the subjects at the beginning of WBC than to possible neuro-muscular adaptation (Westerlund et al. 2009) after only one application of WBC. Except for this, no habituation reaction of the other BP values occurred, which is also in contrast to the study cited above (Koczorowska et al. 2008).

In accordance with previous studies, we assumed that subjects of a higher age and with a pre-existing arterial hypertension might have limited ability to cope with extreme external thermal stimuli (Antony et al. 1994; Koczorowska et al. 2008; Zalewski et al. 2014). The results of this study show not only the mean blood pressure values of the three sub-groups alone, but also the occurrence of individual extreme BP values, which were not discussed in detail in the herein cited studies. In clinical practice, such extreme BP values deserve consequent attention due to their potentially harmful impact on subjects with limited regulatory capacity.

In conclusion, when subjects with known risk factors are excluded, WBC appears to be safe with respect to unwanted BP alterations for adult persons under 70 years. This is also true for patients with pre-existing pharmacologically treated or untreated mild arterial hypertension. In this study, no undesirable side effects occurred after 483 applications of WBC. Factors such as gender or a pre-existing arterial hypertension only slightly influenced blood pressure readings before and after WBC. In some cases, systolic rises of more than 20 mmHg, diastolic rises of more than 10 mmHg, and in one case a rise of MAP up to 128.3 mmHg were observed. This means that extreme BP rises, which may be harmful to the individual, occur in some subjects. We, therefore, suggest mandatory blood pressure readings before and after each WBC application throughout WBC therapy, as extreme events can be observed especially in elderly subjects.

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