IMPACT OF WHOLE BODY CRYOTHERAPY ON THE BLOOD PLASMA VISCOSITY AND FIBRINOGEN CONCENTRATION IN WOMEN WITH RHEUMATOID ARTHRITIS

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Abstract

Aim: The aim of this study was to assess the effects of whole body cryotherapy on the plasma viscosity and fibrinogen concentration in women with rheumatoid arthritis.

Basic procedures: The study groups consisted of 10 women with rheumatoid arthritis, aged 57.2 ± 9.4, who underwent systemic cryotherapy treatments (3 min treatment time, -120°C chamber temperature, 10 treatment sessions, 5 times a week). Their average body height was 165.5 ± 4.6 cm, weight 68.5 ± 4.9 kg and BMI 24.8 ± 2.2 kg/m². In order to analyse plasma parameters, venous blood samples were drawn from the participants of the study twice. The first study was held on the day of beginning treatments and the second test was conducted after a series of 10 treatments. The viscosity of the blood plasma was determined in the viscometer (type D-52159 Roetgen, Myrenne Co., Germany). Determination of plasma fibrinogen was performed using the Bio-Ksel, Chrom – 7 camera.

Results: Analysing the average values of plasma viscosity and fibrinogen in women with rheumatoid arthritis before and after whole body cryotherapy, no statistically significant differences were found.

Conclusions: Regular usage of cryotherapy treatments (whole body cryotherapy) not affect the levels of fibrinogen and plasma viscosity in women with rheumatoid arthritis.

Introduction

Rheumatoid arthritis (RA) is a chronic, autoimmune, systemic connective tissue disease whose etiology is not fully understood, that leads to progressive joint damage, disability, deterioration in quality of life, and shortened life expectancy. Even mild inflammation may result in irreversible damage and permanent disability. RA is more frequently observed in women and elderly people [1]. The consequences of ongoing RA are pain, impaired

Authors’ contribution:
A. Study design/planning
B. Data collection/entry
C. Data analysis/statistics
D. Data interpretation
E. Preparation of manuscript
F. Literature analysis/search
G. Funds collection
physical function, and fatigue, which cause limitations in physical functioning and work disabilities, and finally adversely affect the health-related quality of life [2]. 50% of the risk for development of rheumatoid arthritis is attributable to genetic factors. Smoking is the main environmental risk. In industrialised countries, rheumatoid arthritis affects 0.5–1.0% of adults, with 5–50 per 100 000 new cases annually [3]. Although the prospects for most patients are now favourable, many still do not respond to current therapies. Accordingly, new therapies are urgently required.

In an arthritic joint, the temperature increases [4, 5]. Local cryotherapy e.g. with cold packs, is widely used to alleviate pain in inflammatory diseases, injuries and overuse symptoms [6]. Whole-body cryotherapy (WBC) is currently used to alleviate inflammation and pain in arthritis and osteoarthritis, and for pain relief in fibromyalgia. WBC has been found useful in neurological diseases in reducing spasticity, as a method of kinesitherapy in rheumatic diseases and multiple sclerosis, and for its sedative effect in psoriasis and neurodermatitis [7, 8, 9].

The usage of systemic cryotherapy is one of the ways to reduce pain threshold or cause its abolition. WBC creates favorable conditions to improve cardiovascular health, can help to decrease skeletal muscle tension, reduce the size of edema, increase muscle strength, improve metabolism, and well-being, accelerate regenerative processes and repair and improve mobility in treated joints. The use of systemic cryotherapy is a way of increase the threshold of pain perception or its endurance [10, 11, 12].

Morphological and biochemical research carried out after application of cryotherapy is indicative of an increase in levels of haemoglobin, leucocytes and blood platelets compared to baseline values. There is also an increase in serum concentrations of epinephrine, norepinephrine, acetylcholinesterase, cortisol, and a reduction of inflammatory parameters such as ESR (erythrocyte sedimentation rate), Waaler-Rose reaction and seromucoid [13, 14].

The aim of this study was to assess the effects of whole body cryotherapy on the plasma viscosity and fibrinogen concentration in women with rheumatoid arthritis.

Study design

The study group consisted of 10 women with rheumatoid arthritis (RA type II - classification criteria RA according to American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) - 2010) – patients of the Malopolska Cryotherapy Centre in Krakow (preliminary research — without calculation), aged 57.2 ± 9.4, who underwent systemic cryotherapy treatments (3 min treatment time, -120°C chamber temperature, 10 treatment sessions, 5 times a week). Their average body height was 165.5 ± 4.6 cm, weight 68.5 ± 4.9 kg and BMI 24.8 ± 2.2 kg/m². Illness duration 6 - 41 years. Most of the respondents were also treated Methotrexate and NSAID (nonsteroidal anti-inflammatory drugs). Additionally, the subjects were screened for the following exclusion criteria: diabetes mellitus, use of β-blockers or anxiety medication, and consumption of more than four cups of coffee each day or more than two alcoholic drinks each day. In order to analyse plasma parameters, venous blood samples were drawn from the study participants twice. The first study was held on the day of beginning treatments and the second test was conducted after a series of 10 treatments. Methodology was the same as in previous studies [15].

The parameters obtained in the cryo-chamber:
- • aerial temperature: -60°C
- • chamber temperature: -120°C

The time of a single treatment for the group of males was 1.5 min (1st treatment), 3 min (2nd-10th treatment) - 10 treatment sessions, 5 times a week. 3 ml of blood were drawn from the vein inside the elbow from the participants on an empty stomach in the morning, into EDTA tubes. Blood samples were drawn by a qualified nurse under medical supervision, in accordance with applicable standards of the Pathology of Locomotion Laboratory at the University School of Physical Education in Krakow, where plasma parameters were determined. The study was approved by the Bioethics Committee at the Regional Medical Chamber in Krakow.

Measurement of plasma viscosity

After centrifugation of cellular blood components, the obtained 0.5 ml of plasma was put into the measurement capillary of the viscometer. The viscosity of the blood plasma was determined in the viscometer (type D-52159 Roetgen, Myrenne Co., Germany).

Determination of plasma fibrinogen

50 µl of plasma was used for the study. Determination was performed using the Bio-Ksel, Chrom – 7 camera.

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) or median and interquartile range, depending on the normality of distribution. The normality of distribution was tested using the Shapiro-Wilk test. To assess changes between the beginning and after cryotherapy, we used the t-test for dependent samples or the Wilcoxon signed-rank test. Calculations were performed using the Statistica 12 (StatSoft®, USA) software. All p-values were two-tailed, statistical significance was defined as p≤0.05.
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Results

Analysing the average values of plasma viscosity and fibrinogen in women with rheumatoid arthritis before and after whole body cryotherapy, no statistically significant differences were found: fibrinogen – increase 4.62% and plasma viscosity – increase 2.88%. (Tab. 1).

*Table 1. Mean values ± standard deviations of the plasma viscosity and fibrinogen at the beginning of the study and after 10 whole-body cryotherapy sessions in rheumatoid arthritis patients. N = 10 subjects.*

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After cryotherapy</th>
<th>p</th>
<th>change %</th>
<th>normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>fibrinogen [g/L]</td>
<td>3.25 ± 0.86</td>
<td>3.40 ± 1.03</td>
<td>0.373</td>
<td>4.62</td>
<td>1.50 – 4.00</td>
</tr>
<tr>
<td>plasma viscosity [mPa x s]</td>
<td>1.04 ± 0.07</td>
<td>1.07 ± 0.08</td>
<td>0.110</td>
<td>2.88</td>
<td>1.12 – 1.27  (reported at 37°C)</td>
</tr>
</tbody>
</table>

Discussion

The research presented in this paper is intended to show changes in the plasma viscosity and levels of fibrinogen in women with rheumatoid arthritis who underwent a series of 10 systemic cryotherapy treatments at -120°C. A review of literature indicates a lack of detailed data on the effects of systemic cryotherapy on rheological properties of the blood in patients with RA.

In our research, analysing the average values of plasma viscosity and fibrinogen, no statistically significant differences were found in the women undergoing cryotherapy treatments in relation to the measurements made on the day of beginning the cryotherapy treatment.

The results of the research carried out so far (very little) are difficult to interpret or compare because of differences in their research protocols. Lubkowska and Szygula [16] showed that the number of cryotherapy sessions (3 min at -130°C) has significant impact on changes in morphological indices [16].

After a few days of stimulation by cryogenic temperatures, an increase in the level of haemoglobin, platelet count and creatinine concentration as well as severity of glycaemia was observed [16, 17]. Some reports indicate a decrease in erythrocytes [18, 19, 20, 21, 22] and an increase in leukocyte number [23, 24], while others declare no changes in the number of erythrocytes and/or white blood cells, most likely due to the low number of sessions [17, 18, 20, 21, 25].

The aim of study by Lange et al. was to compare the effect of whole-body cryotherapy in the criostream on pain reduction, disease activity and pro-inflammatory cytokines (tumor necrosis factor-TNF-α and interleukin-IL-1), and improvement in functional scores. There was a significant reduction in TNF-α and IL-1 [26].

Among the patients with Rheumatoid Arthritis, the progress of disease and impact of treatment on pain is usually the subject of evaluation. The study conducted by Istrati et al. [27] showed the effect of cryotherapy on changes in fibrinolytic activity of patients with rheumatoid arthritis. After applying ten cryotherapy treatments, they noticed that the t-PA (tissue plasminogen activator) parameter decreased, and PAP complexes (plasmin-α2-antiplasmin) were increased in the serum. All patients experienced an improvement in mood and a decrease in pain intensity [27]. The research carried out by Braun et al. [28] involved 48 patients with RA. They used cryotherapy treatments twice a day. The researchers observed a reduction in pain after the application of treatments [28].

Zagrobelska et al. [29] described WBC effect on selected hemodynamic indices. (63 patients with rheumatoid arthritis - 14 days, once daily - cooling the body for two-minute periods in cryogenic chamber with temperatures ranging from -110 degrees C to -160 degrees C) It was demonstrated that after a single session in the cryogenic chamber, after 7 and 14 days the level of ACTH, cortisol and beta-endorphins in blood serum rises. The level of TSH, T4, T3, GH and 6-keto-PGF1 alpha+, however, remains unchanged. The cryogenic chamber treatment 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 of arrhythmias and ischemic changes of the heart [29].

The interaction of coagulation factors with the perivascular environment affects the development of disease in ways that extend beyond their traditional roles in the acute hemostatic cascade. Key molecular players of the coagulation cascade like tissue factor, thrombin, and fibrinogen are epidemiologically and mechanistically linked with diseases with an inflammatory component. In particular, a proinflammatory role for fibrinogen has been reported in vascular wall disease, stroke, brain trauma, multiple sclerosis, Alzheimer's disease, rheumatoid arthritis, colitis, lung and kidney fibrosis, and several types of cancer. Genetic and pharmacologic studies have unraveled pivotal roles for fibrinogen in determining the extent of local or systemic inflammation. As cellular and molecular mechanisms for fibrinogen functions in tissues are identified, the
role of fibrinogen is evolving from a marker of vascular rapture to a multi-faceted signaling molecule with a wide spectrum of functions that can tip the balance between hemostasis and thrombosis, coagulation and fibrosis, protection from infection and extensive inflammation, and eventually life and death [30].

Increase in erythrocyte aggregation (EA) is pathognomonic for rheumatoid arthritis, and its estimation through erythrocyte sedimentation rate (ESR) is part of DAS 28-4 activity diagnosis, with low correlation with aggregation and that does not discriminate the contribution of cell factors that increase aggregation. Plasma factors, Igs and Fb increased aggregation, since rigidity index is altered, this reduces the process efficiency regarding aggregation. Patients with active RA present an increased EA, with values modifications associated with the activity index DAS 28-4, thus becoming an RA activity indicator [31].

Plasma viscosity is determined by water-content and macromolecular components. Plasma is a highly concentrated protein solution, therefore weak protein–protein interactions can play a role that is not characterized by electrophoresis. The effect of a protein on plasma viscosity depends on its molecular weight and structure. The less spheroid shape, the higher molecular weight, the higher aggregating capacity, and the higher temperature or pH sensitivity a protein has, the higher plasma viscosity results. Plasma is a Newtonian fluid, its viscosity does not depend on flow characteristics, therefore it is simple to measure, especially in capillary viscosimeters. In rheumatoid arthritis, its sensitivity and specificity are better than that of ESR or C-reactive protein. Plasma fibrinogen concentration and plasma viscosity are elevated in unstable angina pectoris and stroke and their higher values are associated with higher rate of major adverse clinical events. Elevation of plasma viscosity correlates to the progression of coronary and peripheral artery diseases. [32]

Blood rheology was studied in 130 consecutive RA outpatients. All rheological variables were significantly elevated in the RA patients compared with the controls. Painful joint count (PJC), morning stiffness (MS) and radiographic changes (RC) correlated significantly with plasma viscosity (PV), CRP, ESR and fibrinogen concentration (FC). RA patients with EAD (extra-articular disease) had higher PV, CBV (corrected blood viscosity) at 92/s and ESR than the RA patients without EAD. Differences in profiles of viscosity variables between subgroups of EAD in RA patients were observed. [33]

Cryotherapy used as an adjuvant therapy and applied using standardized and optimized protocols could help to spare corticosteroid and NSAID (nonsteroidal anti-inflammatory drugs) doses in these patients, and subsequently, decrease cardiovascular, infectious or gastrointestinal morbidity and mortality. This treatment option may be of special interest in an increasing number of patients with NSAID and/or corticosteroid contraindications (cardiovascular diseases, diabetes, kidney deficiency, and so on) [34].

In summary, these studies have reported that exposure to cold in the form of whole body cryotherapy not affect the levels of fibrinogen and plasma viscosity in women with rheumatoid arthritis. However, these studies require expansion to become acquainted with the body’s response under these conditions. Despite many studies on laboratory parameters changes in a variety of disorders, this study, as we know, is the first to have been conducted in patients with rheumatoid arthritis.

Conclusions

Regular usage of cryotherapy treatments (whole body cryotherapy) not affect the levels of fibrinogen and plasma viscosity in women with rheumatoid arthritis.

References

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