sciendo

Original Study • DOI: 10.2478/ahem-2022-0023 • AHEM • Vol. 76 Issue 1/2022 • 199-208

AHEM

Advances in Hygiene and Experimental Medicine
Postępy Higieny i Medycyny Doświadczalnej

Is combined physical therapy more effective than topical hyperbaric oxygen therapy in the treatment of venous leg ulcers? Preliminary study

Original Study

Mikołaj Pietrzak[1], Jarosław Pasek[1,2]*, Sebastian Szajkowski[3], Karol Szyluk[4], Grzegorz Cieślar[1]

[1] *Department of Internal Medicine, Angiology and Physical Medicine, Faculty of Medical Sciences in Zabrze, Medical University of Silesia in Katowice, Poland*
[2] *Faculty of Health Sciences, Jan Długosz University in Częstochowa, Poland*
[3] *Department of Osteopathic Medicine, Department of Physiotherapy, Medical University of Mazovia in Warsaw. Warszawa, Poland*
[4] *District Hospital of Orthopedics and Trauma Surgery, Piekary Śląskie, Poland*

Received 23 August, 2021, Accepted 9 December, 2021

Abstract

Introduction. Recently, increased frequency of chronic leg ulcers has been observed. The aim of the study was to compare therapeutic efficacy of combined physical therapy to topical hyperbaric oxygen therapy in the treatment of venous leg ulcers.
Materials and Methods. Participants included 36 patients (14 females and 22 males) between 18 and 80 years of age with chronic venous leg ulcers. They were randomly divided into two study groups. Group I underwent topical hyperbaric oxygen therapy; group II underwent combined physical therapy. Before and after the therapeutic cycle (15 procedures) measurement of ulceration size by planimetry and analysis of laboratory parameters of blood was performed.
Results. In both groups, a statistically significant reduction of ulcer surface area was obtained (25.11±17.8cm^2 to 16.93±13.89cm^2, p=0.000196) vs. (34.17±14.82cm^2 to 23.99±15.15cm^2, p=0.004337). Blood morphology revealed a statistically significant reduction in patients from group II who underwent combined physical therapy (p=0.01). In both groups, statistically significant reduction of fibrinogen level (p=0.01 and p<0.001), and total protein level (p=0.01) was achieved. In group II reduction of the inflammation marker C-reactive protein (CRP) was noted.
Conclusions. Topical hyperbaric oxygen therapy and combined physical therapy had statistically significant effects on the reduction of surface area of treated venous leg ulcers. The changes in morphological and biochemical parameters may indicate the anti-inflammatory and anti-clotting action effects of combined physical therapy.

Keywords

biochemical blood parameters • venous leg ulcers • hyperbaric oxygen therapy • combined physical therapy • treatment

1. Introduction

Lower leg ulceration poses a serious interdisciplinary medical problem. Whatever the etiology, the disease is related to significant reduction of patients' Quality of Life (QoL) and steep costs of treatment. In the United States, nearly 5 million people suffer from problems concerning chronic wounds, to which category lower limb ulceration belongs, while the costs of their treatment reach nearly $3 billion a year. In developed countries, the problem of chronic wounds concerns some 1–2% of the entire population. Recent statistics indicate that some 15% of ulcerations do not heal completely, or recur (once or many times), even in 65% of patients, which requires continuous search for new methods of therapy, which may influence the ultimate result of treatment [1, 2].

In topical treatment of lower limb ulceration, the so-called TIME system is used (T, tissue debridement; I, infection and inflammation control; M, moisture balance; and E, epidermization stimulation), incorporating surgical or mechanical debridement (using water jet method), removal of necrotic tissue from the ulceration area, combating infection and inflammatory conditions, maintenance of correct moisturizing in the ulceration area, as well as pharmacological stimulation of epidermization. At present, specialist hydrocolloid dressings are widely used, as well as foam dressings and dressings containing silver. In patients with lower extremity ulcers of venous etiology, compression treatment appears to be an indispensable element of treatment [3, 4].

The healing process may be disturbed by topical or systemic factors. The former include: wound effusion (its excess causes maceration, whereas its scarcity causes drying of tissues), infection, disturbances in the composition of bacterial flora, as well

* *E-mail: jarus_tomus@o2.pl*

as repeated traumas connected with abrasion and tissue compression. Systemic factors, in turn, comprise: elderly age (over 65 years of age); gender; concomitant diseases such as arterial hypertension, diabetes, neoplasms, hepatic impairment, renal insufficiency, heart insufficiency, immunosuppression-related conditions, prolonged immobilization; as well as tobacco smoking. Wound healing time is extended, particularly in case of co-occurrence of two or more diseases from those listed above [5, 6]. Moreover, hypoxia of tissues, which is related to ischemia and disturbances described above, in the course of lower limb ulcerations, may lead to halting the healing process and increased risk of wound infection by reduced antibacterial activity of leukocytes. In turn, infection and the resulting necessity of antibiotic therapy in the course of treatment are factors which negatively affect the healing prognosis [2, 6].

Continued search for new possibilities to support treatment of chronic wounds, including treatment of lower leg ulceration, is among the prominent tasks that contemporary medicine faces. Among them are physical methods, which improve and stimulate natural mechanisms responsible for the efficient course of healing process [7]. Such methods include hyperbaric oxygen therapy, magnetotherapy, and low-energy light therapy.

Hyperbaric oxygen therapy (HBO) is a physical method utilizing pure oxygen or mixture of gases with oxygen concentration close to 100%, under pressure exceeding atmospheric pressure. Oxygen is indispensable for correct wound healing process at each of its stages – proliferation of cells, synthesis of collagen, re-epithelization, and fighting infections – both in case of physiological healing and in case of chronic wounds. Among the primary/original mechanisms of HBO treatment action in case of skin ulceration, of significant importance is the hyper-oxygenation of tissues caused by increased partial pressure of oxygen, which results in increased diffusion force and oxygen solubility in plasma, as a result of which more oxygen dissolved in plasma reaches tissues, where physiologically – due to low diameter of blood vessels or their contraction – the supply of oxygen may be limited. On the other hand, secondary mechanisms of therapeutic action include, among others, stimulation of angiogenesis and fibroblast proliferation [8, 9].

Magnetotherapy is a physical method which is characterized by frequencies of less than 100Hz, magnetic induction in the range of 0.1-20mT, as well as sinusoidal – rectangular or triangular – shape of impulse. In case of that method, the electric field strength amounts to about 130V/m and is comparable with that of the Earth [10]. As a result of applying low frequency magnetic fields, the process of tissue regeneration and healing of chronic wounds is driven by improved micro-circulation, formation of new blood vessels, development of collateral circulation, and vaso-dilatation, as a result of which perfusion of arterial blood as well as drainage of venous blood and lymph are improved. Also, the process of oxygen utilization on tissues and internal respiration is stimulated as a result of increased capture of oxygen by hemoglobin and cytochromes. The influence of magnetic fields also pushes the inhibition of infectious processes; also after a transient hyper-coagulation phase it induces a strong and well-established anticoagulation effect [10, 11].

Another physical procedure which demonstrates beneficial effects in patients with lower leg ulceration is light therapy with the application of low energy light emitted by semiconductor LEDs (light emitting diodes). The results of experimental and clinical studies conducted so far prove that the most pronounced biostimulating action at cell level is that of light radiation in the red portion of the spectrum, with the wavelength of 632.8nm. The irradiation procedures lead, among others, to stimulation of collagen production by the activated fibroblasts. The improved blood supply to tissues, resulting from the activity of low energy light radiation in the vicinity of ulceration areas is due to vasodilatation activity and improved lymphatic drainage. The light beam, reaching cellular structures, increases the synthesis of proteins and influences changes in membrane potential and release of neurotransmitters [11, 12].

1.1 Aim of the study

The aim of the study was to compare the treatment efficiency of physical combined therapy with the use of topical hyperbaric oxygen therapy, magnetotherapy, and low-energy light therapy vs. topical hyperbaric oxygen therapy alone, in the treatment of venous leg ulcers.

2. Materials and Methods

2.1 Study design

Participants included 36 patients (14 female and 22 male ones) ranging in age from 18 to 80 years (average age: 68.9±9.6 years), who suffered from chronic venous ulcers of the lower leg without positive effects of previous treatment. They were enrolled and randomized alternately 1:1 to two comparative groups.

The first study group consisted of 18 patients treated with the use of the OXYBARIA-S device (FASER S.A., Tarnowskie Góry, Poland) applied in procedures of topical hyperbaric oxygen therapy. The second group consisted of 18 patients, who underwent treatment with the use of the multifunction device LASEROBARIA-S (INVENTMED, Świętochłowice, Poland) applied for procedures of combined physical therapy with simultaneous use of topical hyperbaric oxygen application in combination with extremely-low-frequency variable magnetic field and low-energy light.

The criteria for inclusion were as follows: the occurrence of venous lower leg ulcers, age range from 18 to 80 years, written consent for participation in the study, no contraindications for undergoing procedures with the use of both devices in physical treatment, while the exclusion criteria were as follows: absence

of written consent for participation in the study, age under 18 years or over 80 years, acute limb ischemia, venous leg ulcers due to diabetes, arterial or mixed ulcerations, pregnancy, presence of electronic implants, thyrotoxicosis, active pulmonary tuberculosis, bleeding from the alimentary tract, neoplastic disease, condition after organ transplantation, sepsis or active infection requiring systemic therapy with antibiotics, NYHA III/IV heart failure, hypersensitivity to light.

Before the beginning of therapeutic cycle every patient attended a surgical consultation, while in case of the presence of necrotic tissue or purulent infiltration in the ulceration area, surgical wound debridement was also performed.

The therapeutic cycles for both groups comprised a total of 15 procedures, each lasting 30 minutes, performed every day at the same time in the morning hours, and applied for 5 days a week, with weekend breaks (on Saturday and Sunday).

The procedures were performed in semi-reclining position. The treated limb was placed in the cylindrical therapy chamber, which was then closed at thigh level by means of a flexible sealing flange. In patients treated with the OXYBARIA-S device, the oxygen applied was introduced to the chamber from an external cylinder, the oxygen concentration was about 95%, its pressure amounted to 1.5mBa, the applied flow rate was about 5 l/min., whereas in patients treated with LASEROBARIA-S device the following physical factors were applied simultaneously: oxygen supplied to the chamber from an external cylinder, at a concentration of about 90%, pressure of 1.5mBa and flow rate of some 5 l/min., alternating magnetic field with sinusoidal impulse waveform, frequency of 40 Hz and magnetic induction of 15mT generated by induction coil located in the housing of the cylindrical therapy chamber, as well as low-energy light emitted by semiconductor diodes (LEDs) installed in the internal surface of the therapeutic chamber, with energy density of 10 J/cm^2 and light wavelength of 635 nm in the first half of the procedure and 410 nm throughout the remaining part of the procedure [13].

Each time the procedure was completed, both using the OXYBARIA-S device and the LASEROBARIA-S, the therapy chambers and flexible sealing flanges of both devices were disinfected using Desam OX.

After completion of each procedure, the protective hydrocolloid dressing Granuflex (ConvaTec) was applied. Compression therapy with the use of bandaging was applied by medical personnel, to ensure sound application and proper pressure distribution. In the course of the study, patients continued the pharmacological treatment introduced before.

Before the beginning and after the completion of the therapeutic cycle, in order to verify the healing results obtained, planimetric assessment of ulcer surface area was performed in both groups, with the use of a computer software developed by Michał Senejko, MSc. Planimetric assessment of ulcer surface area with the use of computer software was performed in manual mode. In the first stage, a doctor loaded the analyzed picture from a digital photo of a leg ulcer, with a subsequent selection of ulcer contours, by moving the mouse cursor continuously along the contour of the target area, and subsequent double-clicking the mouse cursor, that resulted in automatic closing of the drawn contour and creating a closed curve. When the selection stage was completed, the software automatically calculated the surface area within the previously defined contour. The surface area was represented in pixels or, after adequate calculation, in square centimeters. In order to maintain high accuracy, all planimetric measurements were performed by only one specialist experienced in this method, who did not know which physical method has been applied in the treatment of particular patients.

In both study groups, the assessment of a set of laboratory examinations has been performed, which included determination of selected markers of inflammation (CRP, leukocytosis) both in blood serum and in whole blood, CBC parameters with peripheral blood smear, selected parameters of blood clotting (fibrinogen concentration, activated partial thromboplastin time [aPTT], prothrombin time, INR), as well as selected biochemical markers of the metabolism of carbohydrates, lipids, proteins, and electrolytes, and indicators of renal function (total cholesterol level, level of LDL and HDL cholesterol, concentration of triglycerides, glucose, protein, sodium, potassium, creatinine, urea, and uric acid) in blood serum. The laboratory examinations were performed before starting the cycle of therapy and after its completion.

In order to perform laboratory tests, all patients' blood was collected from the ulnar vein, in aseptic conditions, by means of disposable equipment. 10 ml of venous blood was collected from each patient. Blood for determination of concentration of inflammatory condition markers, as well as selected parameters of carbohydrate, lipid, protein, and electrolyte metabolism, as well as indicators of renal function, were collected to test tubes without anticoagulant. Subsequently, after centrifugation of blood serum, specific biochemical parameters were determined (concentration of CRP, glucose, total cholesterol, LDL and HDL cholesterol, triglycerides, glucose, protein, sodium, potassium, creatinine, urea, and uric acid). The blood samples for CBC parameters, with peripheral blood smear and clotting parameters (fibrinogen concentration, activated partial thromboplastin time [aPTT], prothrombin time, and INR) were collected to a test tube with anticoagulant. All tests were performed in the central laboratory of Specialist Hospital No. 2 in Bytom, by means of automatic diagnostic device Cobas IT 3000.

The study was conducted in accordance with the principles of Helsinki Declaration (1964), and its protocol was approved by the Bioethical Committee of the Medical University of Silesia Medical University of Silesia in Katowice (Resolution No. KNW/0022/KB1/102/16). All qualified patients signed a written consent for participation in this study.

2.2 Statistical analysis

Statistical analysis of collected data has been performed with the use of the following software: MS Excel 97-2003 and Statistica 13 (Statsoft, Poland). The obtained results were presented in the form of mean values and standard deviation. For verification of statistical significance of differences between parameters studied, U Mann Whitney test was applied for independent variables, and Wilcoxon test in case of dependent variables. $p<0.05$ was assumed as the threshold of statistical significance.

3. Results

Study groups did not differ significantly in terms of age and had a similar distribution of occurrence of specific etiologic factors, as well as frequency of contamination of ulcerations (Table 1).

In all patients from study group I, treated with the use of OXYBARIA-S device, the mean ulcer surface area after the completion of therapeutic cycle underwent statistically significant reduction, in comparison with the initial size before the beginning of therapy (25.11±17.8cm^{2}to16.93±13.89cm^2) (p=0.000196). Also, in all patients from group II, treated by means of LASEROBARIA-S device, the mean ulcer surface area after the completion of therapeutic cycle underwent statistically significant reduction, in comparison with the initial size before the beginning of therapy, 34.17±14.82cm^2 to 23.99±15.15cm^2 (p=0.004337) (Table 2).

Both before and after the completion of the therapeutic cycle the average ulcer surface area in patients from both groups did not differ significantly. Similarly, mean ulcer surface areas in group I and in group II showed no statistically significant differences (35.3% vs 30.2%, respectively) (p=0.837).

The results of blood morphology parameters determined in both study groups before the beginning and after completion of the therapeutic cycle are presented in Table 3.

In patients from group I, treated by means of topical hyperbaric oxygen therapy, after the completion of the therapeutic cycle, a statistically significant increase of the proportion of monocytesin peripheral blood smear was found, in comparison with initial values (7.73±2.19 % vs 8.47±2.68 %, respectively) (p=0.01). On the other hand, the mean values of other blood morphology parameters for patients from that group after completion of the therapeutic cycle were not statistically significantly different from initial values. In patients from group II, then, who were treated by means of combined physical therapy, at the end of the therapeutic cycle a statistically significant decrease in white blood cells has been noted (8.30±2.33 G/l to 7.26±1.56 G/l, respectively) (p=0.01), as well as reduced percentage of neutrophils in peripheral blood smear (63.10±10.32% to 56.64±9.86%, respectively) (p=0.01), and also a statistically significant increase of the proportion of monocytes (7.00±2.05% vs 7.71 ± 1.97%, respectively) (p=0.01) and eosinophils (3.30±2.39%vs3.77±1.79%,

Table 1. Clinical characteristics of the studied population of patients

Parameter	Group I treated with OXYBARIA-S device	Group II treated with LASEROBARIA-S device	Statistical significance
Women	7 (38.9%)	7 (38.9%)	p=1.000
Men	11 (61.1%)	11 (61.1%)	
Age	70.94 ± 10.86	66.83 ± 7.20	p=0.055
Diabetes	7 (38.9%)	9 (50.0%)	p=0.170
Venous insufficiency	9 (50.0%)	8 (44.4%)	p=0.740
Atherosclerosis	15 (83.3%)	17 (94.4%)	p=0.280
Bacterial contamination	16 (88.9%)	14 (77.8%)	p=0.365

Table 2. Comparison of ulceration surface areas measured by means of planimetric method (mean ± SD) in patients from both study groups before the beginning of therapeutic cycle and after its completion, with statistical assessment

Group	Surface area before the therapeutic cycle (average± SD)	Surface area after the therapeutic cycle (average± SD)	Statistical significance
Group I treated with OXYBARIA-S device	25.11 ± 17.8	16.93 ± 13.89	p=0.0002
Group II treated with LASEROBARIA-S device	34.17 ± 14.82	23.99 ± 15.15	p=0.004
Statistical significance Group I vs. Group II	p=0.071	p=0.169	

respectively) (p=0.01) in peripheral blood smear, in comparison with initial values. On the other hand, the mean values of the remaining blood morphology parameters for patients from that group after completion of the therapeutic cycle showed no statistically significant differences from initial values.

The results for selected parameters of the blood coagulation system in both study groups before starting the therapeutic cycle and after its completion are presented in Table 4.

In both study groups, after completion of the therapeutic cycle a statistically significant reduction of fibrinogen level in blood has been achieved, in comparison with initial values, (p=0.01) and (p<0.001). The mean values of other blood coagulation parameters for patients from both study groups, however, were not statistically significantly different after the completion of the therapeutic cycle from the initial values.

The results concerning selected biochemical parameters (markers of carbohydrate, lipid, protein, and electrolyte metabolism, as well as indicators of renal function, and CRP as marker of inflammatory condition) in the blood serum of patients from both study groups, before the beginning of the therapeutic cycle and after its completion, are presented in Table 5.

In patients from group I, treated by means of topical hyperbaric oxygen therapy after completion of the therapeutic cycle, statistically significant reduction of glucose level was detected (105.45±7.55 mg/dl to 91.50±9.45 mg/dl, respectively) (p=0.04), as well as reduced level of total protein (7.22±0.60 g/dl to 6.69±0.46 g/dl, respectively) (p=0.01) in comparison with initial values. On the other hand, the mean concentration values for laboratory parameters in blood serum in case of patients from that group were not statistically significantly different from the initial values. As regards patients from study group II, treated by means of associated physical therapy, statistically significant reduction was detected in total cholesterol (146.33±38.82 to 138.5±27.58 mg/dl, respectively) (p=0.04), HDL cholesterol (51.26±12.42 mg/dl to 43.6±8.22 mg/dl, respectively) (p=0.03), total protein (7.00±0.71 g/dl to 6.60±0.65 g/dl, respectively) (p=0.03), and C-reactive protein (CRP) (20.66±25.79 mg/l to8.21±7.68 mg/l, respectively) (p=0.05). The mean values of remaining laboratory parameters in blood serum of patients from that group, however, were not statistically significantly different from initial values.

4. Discussion

In the study groups, statistically significant reduction of the surface area of treated venous lower leg ulcers after completion of the cycle of procedures has been demonstrated. This applies both to the cycle in the form of monotherapy (topical hyperbaric oxygen therapy, HBO), and combined physical therapy. This confirms the efficiency of regenerative action of both physical methods compared, which leads to activation of healing processes for ulcerations. The experimental and clinical studies conducted so far lead to the conclusion that one of the basic mechanisms behind the regenerative effect of topical HBO is proper saturation of tissues with oxygen, which is indispensable for proper course of all wound healing stages, which has also been demonstrated in our study with the use of the OXYBARIA-S device [14, 15]. In the case of the LASEROBARIA-S device, the regeneration effect of HBO was additionally supplemented by low-frequency magnetic fields having physical parameters used in magnetotherapy, as well as low-emission light emitted by LEDs [16]. It is also of significance that procedures carried out with the use of both those devices may be applied jointly with pharmacotherapy and compression therapy.

The results of these studies also point out the fact that physical procedures should constitute a valuable addendum to complex therapies to treat lower limb ulceration. These are non-invasive methods, well tolerated by patients, and are characterized by very low incidence of adverse reactions, and relatively low cost of therapy. The efficacy of those methods is particularly stressed in the aspect of regenerative effects, as well as reduced intensity of pain experienced by patients [9, 17, 18, 19, 20].

The study results demonstrated a statistically significant reduction in the number of leucocytes and percentage of neutrophils in peripheral blood smear from patients undergoing cycles of combined physical therapy procedures. In that group of patients, also statistically significantly reduced concentration of fibrinogen and C-reactive protein, as markers of inflammation, have been noted. The above changes may indicate beneficial anti-inflammatory and anti-coagulation activity of physical agents used in this method of therapy. The reduced level of inflammation markers influenced by physical procedures may indicate extensive impact of such procedures upon the immunological system, thus its stimulation to protect the body against infections and diseases, providing cellular protection by generation of free radicals and a whole range of proteins with bactericidal and bacteriostatic properties. High concentrations of fibrinogen increase the risk of thrombo-embolic complications, which may result in a serious life-threatening condition, hence the result obtained supports the supposition of beneficial effects of the above physical procedures. It may thus be concluded that significant reduction of inflammation markers may positively influence faster treatment of chronic wounds, through the mechanism of the healing effects of the two compared methods of physical therapy.

In case of the remaining blood morphology parameters, no statistically significant changes were observed, which may be connected with relatively short duration of the entire therapeutic cycle.

The results of clinical studies published in available literature, in which HBO procedures have also been applied in the treatment of lower limb ulceration, are inconclusive and similar to the results of the studies discussed [17].

Table 3. Comparison of selected blood morphology parameters (mean± SD) in patients from both study groups, before the beginning of therapeutic cycle and after its completion, with statistical evaluation

Parameter	Group I treated with OXYBARIA-S device	Group II treated with LASEROBARIA-S device	Statistical significance Group I vs. Group II
Leukocytes [G/l] before treatment after treatment	8.02±2.63 6.81±2.15	8.30±2.33 7.26±1.56	p=0.709 p=0.484
Statistical significance before treatment vs after treatment	p=0.35	p=0.01	
Erythrocytes [T/l] before treatment after treatment	4.28±0.65 4.13±0.70	4.40±0.54 4.17±0.49	p=0.660 p=0.846
Statistical significance before treatment vs after treatment	p=0.23	p=0.21	
Hemoglobin [g/dl] before treatment after treatment	12.22 ± 1.79 11.82 ± 1.96	12.70 ± 1.59 12.10 ± 1.87	p=0.425 p=0.666
Statistical significance before treatment vs after treatment	p=0.08	p=0.22	
Haematocrit [%] before treatment after treatment	37.71 ± 5.40 36.81 ± 6.07	39.70 ± 5.07 37.38 ± 5.65	p=0.259 p=0.769
Statistical significance before treatment vs after treatment	p=0.52	p=0.19	
MCV [fl] before treatment after treatment	88.57 ± 6.89 89.37 ± 5.75	91.10 ± 5.01 89.43 ± 6.75	p=0.222 p=0.977
Statistical significance before treatment vsafter treatment	p=0.53	p=0.72	
MCH [pg] before treatment after treatment	28.78 ± 3.02 28.69 ± 1.85	29.10 ± 2.00 29.97 ± 2.71	p=0.698 p=0.722
Statistical significance before treatment vs after treatment	p=0.63	p=0.80	
MCHC [g/dl] before treatment after treatment	32.44 ± 1.16 32.13 ± 1.14	32.00 ± 1.39 32.36 ± 1.14	p=0.264 p=0.561
Statistical significance before treatment vs after treatment	p=0.63	p=0.87	
RDW-CV [%] before treatment after treatment	13.77 ± 1.65 13.56 ± 1.29	13.70 ± 1.53 13.51 ± 1.85	p=0.942 p=0.926
Statistical significance before treatment vs after treatment	p=0.90	p=0.36	
Platelets [tys./μl] before treatment after treatment	271.3 ± 157.7 248.6 ± 208.2	248.9 ± 75.8 229.5 ± 67.9	p=0.591 p=0.713
Statistical significance before treatment vs after treatment	p=0.39	p=0.54	
MPV [fl] before treatment after treatment	6.75 ± 1.29 6.86 ± 1.23	7.00 ± 0.91 6.72 ± 0.86	p=0.434 p=0.685
Statistical significance before treatment vs after treatment	p=0.61	p=0.66	
Neutrophils [%] before treatment after treatment	67.11 ± 8.01 58.88 ± 10.26	63.10 ± 10.32 56.64 ± 9.86	p=0.199 p=0.509
Statistical significance before treatment vs after treatment	p=0.73	p=0.01	
Lymphocytes [%] before treatment after treatment	21.81 ± 6.50 26.24 ± 9.95	25.90 ± 9.72 31.02 ± 9.75	p=0.150 p=0.155

Parameter	Group I treated with OXYBARIA-S device	Group II treated with LASEROBARIA-S device	Statistical significance Group I vs. Group II
Statistical significance before treatment vs after treatment	p=0.79	p=0.05	
Monocytes [%] before treatment after treatment	7.73 ± 2.19 8.47 ± 2.68	7.00 ± 2.05 7.71 ± 1.97	p=0.289 p=0.083
Statistical significance before treatment vs after treatment	p=0.01	p=0.01	
Eosinophils [%] before treatment after treatment	2.51 ± 3.34 4.26 ± 2.65	3.30 ± 2.39 3.77 ± 1.79	p=0.427 p=0.516
Statistical significance before treatment vs after treatment	p=0.15	p=0.01	
Basophils [%] before treatment after treatment	0.70 ± 0.15 0.96 ± 0.35	0.80 ± 0.20 0.87 ± 0.24	p=0.346 p=0.364
Statistical significance before treatment vs after treatment	p=0.58	p=0.43	

Table 4. Comparison of selected blood coagulation parameters (mean ± SD) in patients from both study groups, before the beginning of therapeutic cycle and after its completion, with statistical evaluation

Parameter	Group I treated with OXYBARIA-S device	Group II treated with LASEROBARIA-S device	Statistical significance Group I vs Group II
Fibrinogen [g/l] before treatment after treatment	4.22±1.28 3.39 ± 0.68	4.05±1.36 3.5 ± 0.71	p=0.708 p=0.569
Statistical significance before treatment vs after treatment	p=0.01	p<0.001	
Kaolin-cephalintime (aPTT)[s] before treatment after treatment	33.76±9.77 37.19 ± 11.97	31.85±9.42 31.4 ± 10.17	p=0.554 p=0.130
Statistical significance before treatment vs after treatment	p=0.16	p=0.45	
Prothrombin time[s] before treatment after treatment	11.75±0.90 11.75 ± 0.90	11.80±1.10 12.0 ± 0.60	p=0.704 p=0.287
Statistical significance before treatment vs after treatment	p=0.19	p=0.29	
International Normalized Ratio (INR) before treatment after treatment	1.15±0.25 1.20 ± 0.20	1.10±0.15 1.21 ± 0.12	p=0.751 p=0.282
Statistical significance before treatment vs after treatment	p=0.20	p=0.35	

In the study by Erdal Gunes A. et al. the authors have assessed hyperbaric oxygen (HBO) therapy in140 patients on the basis of blood parameters in complete blood count (CBC) over a long term. Patients were treated for 55.5±41 days. The results of the present study showed that a number of alterations occurred in CBC values in patients who received HBO, such as reduction of the number of platelets, but this was not clinically significant. According to the results, HBO does not have any effect on hemoglobin, hematocrit, red blood cell count, mean corpuscular volume, mean corpuscular hemoglobin, red blood cell distribution width, mean corpuscular hemoglobin concentration, platelet count, platelet distribution width, and mean platelet volume [21].

In another study, by Sinan M. et al., the authors investigated the effect of HBO on hemo-rheological and hematological parameters. Red blood cell (RBC) deformability and aggregation,

Table 5. Comparison of selected biochemical parameters (mean ± SD) in blood serum of patients from both study groups, before the beginning of therapeutic cycle and after its completion, with statistical evaluation

Parameter	Group I treated With OXYBARIA-S	Group II treated with LASEROBARIA-S	Statistical significance Group I vs Group II
Glucose [mg/dl] before treatment after treatment	105.45 ±7.55 91.50±9.45	101.60± 12.55 100.1± 12.43	p=0.880 p=0.067
Statistical significance before treatment vs after treatment	p=0.04	p=0.08	
Total cholesterol[mg/dl] before treatment after treatment	140.83±33.31 134.39±34.40	146.33±38.82 138.5±27.58	p=0.842 p=0.695
Statistical significance before treatment vs after treatment	p=0.59	p=0.04	
Cholesterol-LDL[mg/dl] before treatment after treatment	85.78±33.35 81.33±33.19	107.56±31.41 84.2±25.10	p=0.052 p=0.770
Statistical significance before treatment vs after treatment	p=0.68	p=0.06	
Cholesterol-HDL[mg/dl] before treatment after treatment	45.89±9.97 41.22±9.53	51.26±12.42 43.6±8.22	p=0.162 p=0.424
Statistical significance before treatment vs after treatment	p=0.22	p=0.03	
Triglycerides [mg/dl] before treatment after treatment	107.72±32.09 117.44±39.83	119.06±55.01 114.6±39.13	p=0.455 p=0.831
Statistical significance before treatment vs after treatment	p=0.50	p=0.80	
Total protein[g/dl] before treatment after treatment	7.22±0.60 6.69±0.46	7.00±0.71 6.60 ±0.65	p=0.319 p=0.585
Statistical significance before treatment vs after treatment	p=0.01	p=0.01	
Sodium [mmol/l] before treatment after treatment	139.44±2.57 137.89±4.59	138.94±3.02 139.8±3.45	p=0.596 p=0.160
Statistical significance before treatment vs after treatment	p=0.24	p=0.69	
Potassium [mmol/l] before treatment after treatment	4.83±0.53 4.64±0.55	4.58±0.50 4.40 ±0.38	p=0.149 p=0.122
Statistical significance before treatment vs after treatment	p=0.23	p=0.09	
Creatinine [mg/dl] before treatment after treatment	0.93±1.94 0.88±0.15	0.96±0.13 1.00 ±0.16	p=0.776 p=0.281
Statistical significance before treatment vs after treatment	p=0.82	p=0.74	
Urea [mg/dl] before treatment after treatment	43.45±11.1 45.55±15.04	34.85±12.40 38.90 ±5.42	p=0.704 p=0.248

Parameter	Group I treated With OXYBARIA-S	Group II treated with LASEROBARIA-S	Statistical significance Group I vs Group II
Statistical significance before treatment vs after treatment	p=0.46	p=0.70	
Uricacid [mg/dl] before treatment after treatment	6.28±1.29 6.29±1.93	6.03±2.09 5.90 ±2.10	p=0.676 p=0.529
Statistical significance before treatment vs after treatment	p=0.97	p=0.82	
C Reactive Protein (CRP) [mg/l] before treatment after treatment	14.99 ± 16.20 11.26±14.31	20.66 ± 25.79 8.21±7.68	p=0.790 p=0.765
Statistical significance before treatment vs after treatment	p=0.52	p=0.05	

blood and plasma viscosity, and superoxide dismutase activity were investigated in patients who underwent 20 sessions of HBO. The results showed that HBO did not cause any significant changes in hemo-rheological parameters, thereby not causing any problems for the patients [22].

Li Y et al., in turn, have assessed the influence of HBO therapy on vascular endothelial function in SCF in 98 patients diagnosed with SCF by coronary artery angiography. The patients were divided into two groups according to the following: HBO therapy group (n = 48) and control group (n = 50). There were no significant differences in plasma levels (p>0.05). However, comparing with the control group, FMD, plasma NO, and CGRP levels were significantly increased in the HBO group after treatment (p<0.01), whereas hsCRP and ET-1 levels decreased dramatically. The authors indicate that HBO treatment provided in addition to conventional therapy may significantly improve the vascular endothelial function in SCF patients [23].

5. Conclusions

The application of topical hyperbaric oxygen therapy and combined physical therapy results in comparable statistically significant reduction of surface areas of treated ulceration, confirmed by objective planimetric assessment. The changes in morphological and biochemical parameters of blood obtained as a result of applying mainly combined physical therapy may indicate anti-inflammatory and anticoagulant action of physical agents applied by means of that method. It seems necessary to carry out randomized studies on more clinical material in order to unambiguously verify the effects of treatment.

Abbreviations

CRP – C-reactive protein, **INR** – International Normalized Ratio, **MCH** – mean corpuscular hemoglobin, **MCV** – mean corpuscular volume, **MMP-2** – matrix metalloproteinase, **MPV** – mean platelet volume, **NO** – nitricoxide, **RDW-CV** – red cell distribution width.

Authors' Contribution

M.P.: research concept and design, supervising the project, carrying out the experiments, acquisition of data, data analysis and interpretation, writing: original draft preparation, writing: review and editing, final proofreading and approval of the version for publication, funding acquisition; **J.P.**: research concept and design, supervising the project, carrying out the experiments, data analysis and interpretation, writing: original draft preparation, writing: review and editing, visualization, literature review, final proofreading and approval of the version for publication, funding acquisition; **S.S.**: acquisition of data, writing: review and editing, literature review, final proofreading and approval of the version for publication, funding acquisition; **K.S.**: data analysis and interpretation, writing: review and editing, final proofreading and approval of the version for publication, funding acquisition; **G.C.**: research concept and design, supervising the project, data analysis and interpretation, writing: review and editing, final proofreading and approval of the version for publication, funding acquisition

ORCID

Mikołaj Pietrzak https://orcid.org/0000-0003-4395-9070
Jarosław Pasek https://orcid.org/0000-0001-6181-337x
Sebastian Szajkowski https://orcid.org/0000-0003-4983-8018
Karol Szyluk https://orcid.org/0000-0002-0853-9014
Grzegorz Cieślar https://orcid.org/0000-0003-2210-8744

Conflict of Interest

The authors have no potential conflicts of interest to declare.

Ethics Approval

The study was conducted in accordance with the principles of Helsinki Declaration (1964), and its protocol was approved by the Bioethical Committee of the Medical University of Silesia Medical University of Silesia in Katowice (Resolution No. KNW/0022/

KB1/102/16). All qualified patients signed a written consent for participation in this study.

References

[1] Augustin M, Brocatti LK, Rustenbach SJ, Schäfer I, Herberger K. Cost-of-illness of leg ulcers in the community. Int Wound J. 2014; 11: 283-292.

[2] Wittens C, Davies AH, Bækgaard N, R Broholm R, Cavezzi A, Chastanet S, de Wolf M, Eggen C, Giannoukas M Gohel M, et al.: Editor's Choice - Management of chronic venous disease: Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). Eur. J. Vasc. Endovasc. Surg. 2015; 49: 678-737.

[3] Bowers S, Franco E. Chronic wounds: Evaluation and management. Am Fam Physician. 2020; 101: 159-166.

[4] Leaper DJ, Schultz G, Carville K, Fletcher J, Swanson T, Drake R. Extending the TIME concept: What have we learned in the past 10 years? Int Wound J. 2012; 2: 1-19.

[5] McDaniel JC, Browning KK. Smoking, chronic wound healing, and implications for evidence-based practice. J Wound Ostomy Continence Nurs. 2014; 41: 415-423.

[6] Scotton MF, Miot HA, Abbade LP. Factors that influence healing of chronic venous leg ulcers: a retrospective cohort. An Bras Dermatol. 2014; 89: 414-422.

[7] Pasek J, Stanek A, Pasek T, Sieroń A. Physical medicine as an opportunity for improving the health state of patients with vascular diseases (angiopathies). Acta Angiol. 2012; 18: 93-98.

[8] Sieroń A, Cieślar G. Outline of hyperbaric medicine. Bielsko-Biała. α-Medica Press. 2007.

[9] de Smet GHJ, Kroese LF, Menon AG, Jeekel J, van Pelt AWJ, Kleinrensink GJ, Lange JF. Oxygen therapies and their effects on wound healing. Wound Repair Regen. 2017; 25: 591-608.

[10] Pasek J, Pasek T, Sieroń-Stołtny K. Electromagnetic fields in medicine: The state of art. Electro Biol Med. 2016; 35: 170-175.

[11] Sieroń A, Cieślar G. Magnetic fields and light therapy in medicine and physiotherapy. Bielsko-Biała: α-Medica Press. 2013.

[12] Noé C, Pelletier-Aouizerate M, Cartier H. LED en dermatologie LED lights in dermatology. Ann Dermatol Venereol. 2017; 144: 301-314.

[13] Pasek J, Szajkowski S, Pietrzak M, Cieślar G. Comparison of the efficacy of topical hyperbaric oxygen therapy alone versus a combination of physical methods including topical hyperbaric oxygen therapy, magnetotherapy and low-energy light therapy in the treatment of venous leg ulcers. Dermatologic Therapy. 2020; 10: 14474.

[14] Pasek J, Cieślar G, Pietrzak M, Jagodziński L, Sieroń A. The use of physical medicine procedures in the treatment of chronic wounds of palm fingers: case report. Pol Merk Lek. 2018; 44: 68-70.

[15] Pasek J, Majda D, Cieślar G, Sieroń A. Wound treatment after congenital syndactyly separation with 100% oxygen therapy: A case report. Surg Curr Res. 2015; 5: 1-3.

[16] Pasek J, Cieślar G, Pietrzak M, Sieroń A. Application local hyperbaric oxygen therapy with use a LASEROBARIA–S in the treatment of chronic wounds. Pol Hyp Res. 2016; 57: 29-38.

[17] Cieślar G. The basics of hyperbaric oxygen therapy. [In:] Ponikowska I, Kochański JW, red. Great book of balneology, physical medicine and heath resort. Konstancin-Jeziorna. Wydawnictwo Aluna. 2017: t. I, pp. 339-344.

[18] Cieślar G, Nowak M, Kawecki M. The application of magnetic fields in the treatment of wounds. Wound Treatment. 2005; 2: 99-106.

[19] Mallick R, Raju A, Campbell C, Rashad Carlton R, Wright D, Boswell K, Eaddy M. Treatment patterns and outcomes in patients with varicose veins. Am. Health Drug. Benefits. 2016; 9: 455-465.

[20] Pasek J, Pasek T, Sieroń A. Magnetostimulation in the treatment of crural vein ulceration. Int Wound J. 2012; 9: 566-569.

[21] Erdal Gunes A, Aktas S. Effect of hyperbaric oxygen therapy on complete blood count. Undersea Hyperb Med. 2017; 44: 357-364.

[22] Sinan M, Zeynep Ertan N, Mirasoglu B, Mirasoglu B, Yalcin O, Atac N, Toklu AS, Basaran-Kucukgergin C, Baskurt OK. Acute and long-term effects of hyperbaric oxygen therapy on hemorheological parameters in patients with various disorders. Clin Hemorheol Microcirc. 2016; 62: 79-88.

[23] Zhang G, Liu X, Li Y, Wang Y, Liang H, Li K, Li L, Chen C, Sun W, et al.: Effects of hyperbaric oxygen on vascular endothelial function in patients with slow coronary flow. Cardiol J. 2018; 25: 106-112.