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Effects of phototherapy on blood pressure and hemodynamic status in women with rheumatoid arthritis

Angeles Leyda Aviles García[1], Mariana Guadalupe Pineda Gonzalez[1], María Jose Vargas Contreras[1], Irma Socorro Gonzalez Sanchez[2], Araceli Consuelo Hinojosa Juarez[1], Joel Alberto Vargas Hernandez[1], Hugo Mendieta Zeron[1,2]

[1]Faculty of Medicine, Autonomous University of the State of Mexico, Toluca, 50180, Mexico

[2]Maternal Perinatal Hospital "Monica Pretelini Saenz", Paseo Tollocan Pte. 201, Universidad, 50010, Toluca, Mexico,

Abstract

Objective: To evaluate the chronic effect of phototherapy on blood pressure and hemodynamic status in women with rheumatoid arthritis.

Methods: In this descriptive and retrospective study, hemodynamic variables of rheumatoid arthritis patients treated with phototherapy within a range between 425 and 650 nm, 11.33 J/cm2, 30 cm above the chest were registered for six months.

Results: Thirty-on patients (mean age 45.4 (16.2) years) were included. There was a significant reduction in heart rate (p=0.02912), cardiac output (p=0.0384), thoracic fluid content (p =0.00165) and thoracic fluid content index (p=0 .00049) from the basal point to the six-month period of follow-up.

Conclusions: Phototherapy could potentially affect the hemodynamic variables in a positive and beneficial effect in patients with rheumatoid arthritis.

Key words: Cardiac output, heart rate, hemodynamic status, phototherapy, rheumatoid arthritis, retrospective study, cohort study

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Introduction

Under physiological conditions, endothelial cells are the main regulators of arterial tone homeostasis and vascular growth, sensing and transducing signals between tissue and blood. Disease risk factors can lead to an imbalance in their homeostasis, known as endothelial dysfunction (1). Following this line of knowledge, red and near-infrared light can interact with the cells and modulate their metabolism by interacting with cytochromes in mitochondria, leading to increased oxygen consumption, adenosine tri-phosphate (ATP) and reactive oxygen species (ROS) production, as well as regulating nitric oxide (NO) release and intracellular Ca2+ concentration. This phenomenon is known as photobiomodulation (2).

Photobiomodulation can modulate endothelial dysfunction, improving inflammation, angiogenesis, and vasodilation. According to some studies, intracoronary irradiation of 808 nm and 18 J (0.2 W, 2.05 cm2) during percutaneous coronary interventions can prevent restenosis, as well as 645 nm and 20 J (0.25 W, 2 cm2) can stimulate angiogenesis (1). However, larger randomized controlled trials are needed.

Some studies have shown that low-level laser therapy is able to induce a photobiological response within cells that modifies the micro- and macrovascular response; this accompanies the evidence showing the systemic effects of intravascular laser blood irradiation (3). There has been satisfactory experience with the use of phototherapy in various autoimmune diseases (4, 5).

Address for Correspondence: Hugo Mendieta Zeron. Faculty of Medicine, Autonomous University of the State of Mexico, Paseo Tollocan, s/n, Moderna de la Cruz, 50180, Toluca, Mexico
E-mail: drmendietaz@yahoo.com **Phone:** +52- 722 217 4831
ORCID: Angeles Leyda Aviles García - 0000-0003-4167-686X; Mariana Guadalupe Pineda Gonzalez- 0000-0003-1013-9500; María Jose Vargas Contreras - 0000-0001-5390-5362; Irma Socorro Gonzalez Sanchez - 0009-0003-1659-4042; Araceli Consuelo Hinojosa Juarez - 0000-0002-9100-9259; Joel Alberto Vargas Hernandez -0000-0001-7404-3132; Hugo Mendieta Zeron - 0000-0003-3492-8950
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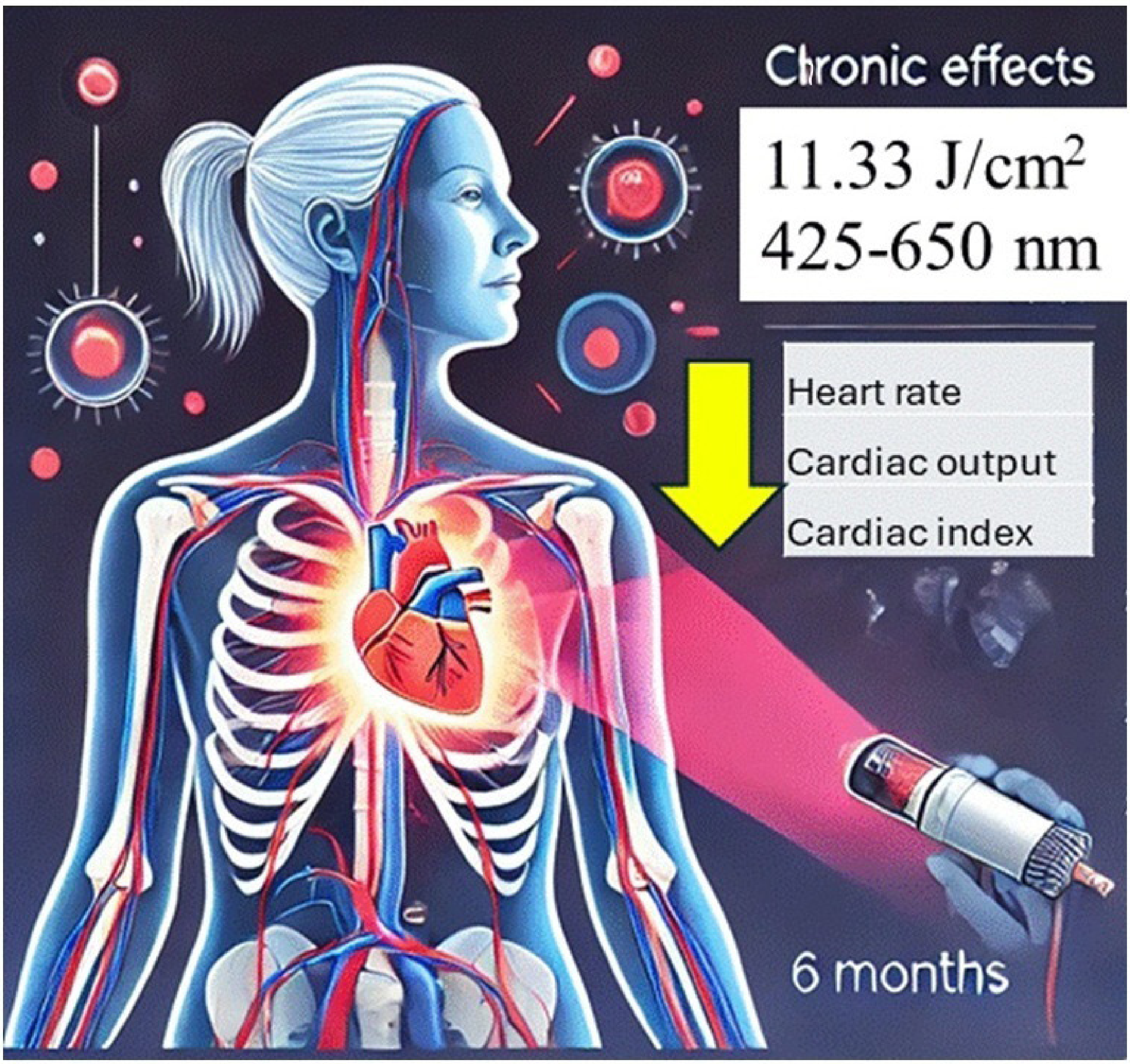
Graphical abstract

Effects of phototherapy on blood pressure and hemodynamic status in women with rheumatoid arthritis

Ángeles Leyda Avilés García, Mariana Guadalupe Pineda González, María José Vargas Contreras, Irma Socorro González Sánchez, Araceli Consuelo Hinojosa Juárez, Joel Alberto Vargas Hernández, Hugo Mendieta Zerón, Toluca, Mexico



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Rheumatoid arthritis is an autoimmune inflammatory disease with complex pathogenesis and with a variable response to different pharmacological management regimens. Due to this and drug cost aspects, there is increasing discussion about phototherapy as a sole or complementary alternative to treat this disease (6). As a matter of fact, phototherapy has been used throughout the history of medicine with various spectrums of ultraviolet (UV) light, laser photodynamic therapy, light-emitting diodes, etc. (7). By contrast, in healthy individuals, a single irradiation with 20 J/cm2 of UVA mobilizes NO from skin stores into the circulation, causes arterial vasodilation, and results in a transient fall in blood pressure (8).

On the other hand, impedance is defined as the resistance to a flow of alternating electric current through a segment. Bioimpedance is dependent on a conductive tissue, which is formed by the intravascular volume composed of the fluids and electrolytes contained in the blood. The impedance in the chest is inversely proportional to the fluid content in the chest (9).

Previous studies with bioimpedance have shown that, in cases of preeclampsia, the following variables are elevated: systolic blood pressure (BP), diastolic BP, mean BP, vascular resistance index, and thoracic flow content (10).

The purpose of this study was to evaluate the chronic effect of phototherapy on hemodynamic status in women with rheumatoid arthritis.

Methods

Study design and population

This was a retrospective cohort study. The medical files of female patients diagnosed with rheumatoid arthritis, treated in the Research Service of the Maternal-Perinatal Hospital "Monica Pretelini Saenz" (HMPMPS), Health Institute of the State of Mexico, in Toluca, Mexico, were reviewed.

The inclusion criteria were files of patients who received phototherapy sessions between 2011 and 2023 and who had undergone the same regimen with complete baseline and three- and six-month evaluations. Patients with another autoimmune disease, cancer, or kidney disease were excluded.

Ethical approval has been granted by the local IRB. Patients provided consent for phototherapy. Informed consent of patients for study participation has been waived by the IRB due to the retrospective nature of the study.

Clinical variables and vital signs

Vital signs such as BP heart rate, respiratory rate, and temperature, as well as weight and height, body mass index (BMI), were recorded for all patients at the beginning of the study, at three months, and at six months.

We also collected information on medical therapy and comorbidities as diabetes and hypertension.

Phototherapy

The phototherapy lamp (registration number: 1694E95) was placed within a range between 425 and 650 nm, 11.33 J/cm2, 30 cm above the chest. The phototherapy schedule was as follows: a) daily 45-min sessions from Monday to Friday for 2 months; b) three 45-min sessions per week for 2 months; c) 45-min sessions twice a week for 1 month, and d) one session per week for 1 month.

With the patient in the supine position, after recording vital signs (BP, heart rate, respiratory rate, and temperature, as well as weight and height), the phototherapy lamp was placed 30 cm above the chest. The Rheumatoid Arthritis Quality of Life (RAQoL) and the Quality of Life-Rheumatoid Arthritis Scale (QOL-RA) questionnaires were applied to monitor the patients' clinical evolution.

Thoracic bioimpedance monitoring

It was measured using the Non Invasive Continuous Cardiac Output Monitor (Niccomo) (Medis, Germany), through four bimodal devices, two located on each side of the neck and two on the lateral and inferior side of the thorax. The transmitter emits a high-frequency (60 kHz) and low-amplitude (4 mA) alternating electric current. Blood has the highest electrical conductivity, so the electric current passes primarily through the aorta and then returns to the receiver.

The Niccomo equipment classifies the next parameters: Flow (heart rate, cardiac output, cardiac index, stroke volume, stroke index, systolic BP, diastolic BP, mean arterial pressure), Contractility (velocity index, acceleration index, heather index, pre-ejection period, left ventricular ejection time, systolic time ratio), Fluid (thoracic flow content, thoracic fluid content index), Work (left cardiac work, left cardiac work index) and Vascular (systemic vascular resistance, systemic vascular resistance index, total arterial compliance, total arterial compliance index). Oxygen delivery was also registered.

Statistical analysis

The statistical analyses were carried out using the free online Social Science Statistics (https://www.socscistatistics.com/).

Quantitative variables are represented by measures of central tendency. First, the Kolmogorov- Smirnov test was performed to determine the normality of the variables. Student's t-tests or the Mann Whitney U tests were used to do multiple comparisons between groups for all the variables. The I p-value was ≤ 0.05 was accepted as significant.

Results

Information of 31 patients (all women) was recorded (mean age 45.4 (16.2) years). The average time of rheumatoid arthritis progression before starting phototherapy was between 1 and 3 years. The changes in body mass index (BMI), QOL-RA scale and RAQoL scale are shown in Table 1.

Table 1. Changes in body mass index, and rheumatoid arthritis scales QOL-RA and RAQoL

Variables	**Basal**	**Final**
BMI, kg/m2	25.22 (4.5), 19.2-39.9	24.74 (4.6) 17.8-38.2
QOL-RA scale, points	13.4 (4.7), 8-30	72.6 (9.7), 50-80
RAQoL scale, points	28.6 (1.7), 25-30	10.5 (9.5) 0-27

Data are presented as mean (SD), (range)
BMI- Body Mass Index, QOL-RA quality of life-rheumatoid arthritis scale, RAQoL - rheumatoid arthritis quality of life, SD - standard deviation

In order of frequency, the medications most used by patients were methotrexate (13), diclofenac (12), folic acid (9), prednisone (8), sulfasalazine (8), celecoxib (4), sulindac (3), deflazacort (3), hydroxychloroquine (3), diacerein (2) and al the rest patients with only one case each one: azathioprine, chloroquine, cyclosporine, leflunomide and meloxicam. In three patients, phototherapy was the only treatment. As comorbidities, systemic arterial hypertension was referred by two patients and type 2 diabetes mellitus was confirmed in one case.

Table 2 shows the mean and standard deviation of all the variables included in the follow-up. After performing the Kolmogorov test it was confirmed a normal distribution of the variables, so the t-test for dependent means was used. According to how the Niccomo classifies the variables, there were three of them that showed statistical changes in the parameter of Flow: reduction of heart rate ($p = 0.01294$ at three months vs six months and $p = 0.02912$ baseline vs six months) reduction of cardiac output ($p = 0.03177$ three months vs six months and $p = 0.0384$ baseline vs six months) and decrease in cardiac index ($p = 0.02395$ three months vs six months).; two in the parameter of Fluid – increase in thoracic fluid content rate ($p=0.0352$ baseline vs three months and $p=0.00165$ baseline vs six months] and increase in thoracic fluid content index ($p=0.04157$ baseline vs three months and $p=0.00049$ baseline vs six months) and two in the parameter of Work – reduction in left cardiac work ($p=0.01356$ three months vs six months) and left cardiac work index ($p=0.01369$ three months vs six months) (Table 3).

Discussion

It has already been suggested that phototherapy including photodynamic therapy and photothermal therapy has demonstrated distinctive potential in rheumatoid arthritis treatment. The suggested mechanism is that under light irradiation, phototherapy can convert light into heat or generate ROS to promote necrosis or apoptosis of rheumatoid arthritis inflammatory cells, thus reducing the concentration of related inflammatory factors and relieving the symptoms of rheumatoid arthritis (11). Besides, there is a clear efficacy of phototherapy in patients who remained non-responsive to previous immunosuppressive therapies (12).

The clinical meaning of reduction of hemodynamic parameters for patients with rheumatoid arthritis

There is a plenty of information about hemodynamic changes with phototherapy treatment in neonates, and they show changes mainly in cardiac output (decrease in cardiac systolic volume and blood pressure) (13, 14). Especially in preterm newborns, when they receive phototherapy, the decrease in stroke volume leads to a reduction in the cardiac output. The heart rate variability is slightly reduced (as the sympathetic activity predominates). Systemic blood pressure is decreased and heart rate is elevated in both preterm and term newborns during phototherapy (14).

By contrast, there is so little information about hemodynamic changes in adult patients treated with some variant of phototherapy. For example, a previous publication showed that intravascular laser irradiation of blood therapy applied to the primitive carotid artery induces a reduction in blood pressure and, more notably, heart rate in mastectomized women using the tamoxifen or aromatase inhibitors (15).

It is well known that the impedance in the thorax is inversely proportional to the fluid content in the thorax. For example, with each heartbeat, the heart pumps blood into the aorta, which increases the fluid content in the thorax, producing a

Table 2. Mean, standard deviation and range of the included variables

Parameter	Variables	Baseline	Three months	Six months
Flow	Heart rate, beats/min	70.8 (12.0) (51 - 100)	69.3 (7.7) (53 - 83)	65.2 (8.8) (47 - 83)
	Cardiac output, L/min	5.3 (1.1) (2.3 – 7.1)	5.3 (1.2) (3 - 8.1)	5.0 (1.1) (2.7 - 6.7))
	Cardiac index, L/min/m^2	3.4 (5.9) (1.8 – 4.3)	3.4 (0.6) (1.9 - 4.3)	3.2 (0.6) (1.7 - 4.3)
	SV, mL	76.9 (19.4) (27 – 107)	77.3 (18.1) (45 – 119)	77.4 (19.7) (37 – 112)
	SI, mL/m^2	48.6 (10.5) (21 – 64)	49.2 (8.6) (29 – 67)	49.7 (10.2) (24 – 62)
	SBP, mmHg	109.4 (20.6) (68 – 168)	109.4 (18.3) (74 – 150)	110.3 (21.3) (73 – 172)
	DBP, mmHg	68.3 (11.5) (44 – 89)	68.6 (11.7) (43 - 91)	66.1 (9.8) (46 – 86)
	MBP, mmHg	78.6 (13.1) (50 – 105)	79.3 (12.3) (52 – 103)	77.5 (10.9) (60 – 110)
Contractility	VI, 1/100 s	67.2 (22.6) (28 – 116)	68.3 (19.1) (24 - 104)	68.9 (21.4) (24 – 109)
	AI, 1/100 s^2	110.7 (43.0) (40 – 223)	115.4 (36.0) (43 - 189)	116.1 (40.4) (42 – 200)
	Heather index, ohm/s^2	19.2 (6.3) (6.5 - 34.7)	17.8 (6.6) (1.6 - 31.9)	17.9 (5.7) (5.4 - 29.3)
	PEP, ms	98.5 (26.3) (53 – 215)	97.9 (26.6) (37 - 199)	97.5 (18.0) (55 - 126)
	LVET, ms	325.6 (41.8) (207 – 396)	327.2 (36.9) (264 – 404)	331.6 (40.4) (251 – 402)
	STR	0.4 (0.3) (0.1 - 1.3)	0.3 (0.1) (0.1 - 0.5)	0.3 (0.1) (0.2 - 0.5)
	FTc, ms	4.8 (1.2) (2.4 – 7.6)	4.8 (0.9) (3.4 – 7.0)	5.2 (1.2) (3.5 – 8.3)
Fluid	TFC, kOhm	30.0 (5.2) (23.5 - 49.1)	34.3 (11.6) (26.1-87.1)	32.1 (6.2) (21.7 - 52.4)
	TFCI, 1/kΩ*m^2	19.2 (4.0) (12.1 - 30.6)	21.9 (7.0) (13.8 - 52.5)	20.9 (4.6) (13.3 - 31.4)
Work	LCW, kg* m^2	5.2 (1.3) (3.1 - 8.1)	5.3 (1.6) (2.3 - 9.4)	4.8 (1.2) (2.6 - 6.9)
	LCWI, kg*m/m^2	3.3 (0.8) (2.2 - 4.8)	3.4 (0.9) (2.0 - 5.8)	3.1 (0.8) (1.7 - 4.4)
Vascular	SVR (dyn • s • cm^{-5})	1177.3 (505.4) (508 - 3317)	1166.3 (371.0) (681 – 2352)	1220.7 (374.2) (754 – 2134)
	SVRI, dyn*s/cm^5*m^2	2014.4 (1170.1) (874 – 7332)	1792.5 (543.9) (1116 – 3671)	1860.9 (588) (1051 – 3331)
	TAC, mL/mm Hg	2.1 (0.8) (0.4 - 4.1)	2.1 (0.9) (0.7 - 4.7)	2.0 (0.9) (0.6 - 4.8)
	TACI, mL m^2/mm Hg	1.3 (0.5) (0.3 - 2.4)	1.3 (0.5) (0.5 - 2.8)	1.3 (0.6) (0.4 - 2.9)
Others	DO2, ml O2/min/m^2	533.7 (108.7) (213 - 703)	551.8 (95.0) (311 – 701)	518.7 (98.7) (281 - 690)

Data are presented as mean (SD), (range)
AI- acceleration index, DBP- Diastolic blood pressure, DO2- oxygen delivery, FTc- corrected flow time, LCW- left cardiac work, LCWI- left cardiac work index, LVET- left ventricular ejection time, MBP- mean blood pressure, PEP- pre-ejection period, SBP- systolic blood pressure, SI- stroke index, STR- systolic time ratio, SV- stroke volume, SVR- systemic vascular resistance, SVRI- systemic vascular resistance index, TAC- total arterial compliance, TACI- total arterial compliance index, TFC- Thoracic Fluid Content, TFCI- Thoracic Fluid Content Index, VI- Velocity Index

Table 3. Statistical analysis in six months of follow up

Parameter	Variable	Baseline vs three months	Baseline vs six months	Three months vs six months
Flow	Heart rate, beats/min	t = -0.74, p = 0.4655	t = -2.29, p = 0.02912	t = -2.64, p = 0.01294
	Cardiac output, L/min	t = -0.17, p =.86561	t = 2.14, p = 0.0384	t = -2.25, p = 0.03177
	Cardiac index, L/min/m2	t = -0.94, p =.35539	t = -1.14, p =.26199	t = -2.38, p =.02395
	SV, mL	t = 0.16, p = 0.87784	t = 0.17, p = 0.86734	t = 0.17, p = 0.86734
	SI, mL/m2	t = 0.44, p = 0.66246	t = 0.58, p = 0.56303	t = 0.34, p = 0.73556
	SBP, mmHg	t = 0, p = 1	t = 0.31, p = 0.76028	t = 0.31, p = 0.75977
	DBP, mmHg	t = 0.14, p = 0.88716	t = -1.32, p = 0.195	t = -1.60, p =.12042
	MBP, mmHg	t = 0.33, p = 0.74664	t = -0.59, p = 0.56124	t = -1.13, p = 0.26679
Contractility	VI, 1/100 s	t = 0.45, p = 0.65543	t = 0.52, p = 0.60726	t = 0.23, p = 0.82065
	AI, 1/100 s2	t = 1.01, p = 0.32215	t = 1.00, p = 0.32266	t = 0.16, p =.8751
	Heather index, ohm/s2	t = -1.41, p = 0.16844	t = 1.53, p = 0.13555	t = 0.15, p = 0.88014
	PEP, ms	t = -0.1, p = 0.92113	t = -0.16, p = 0.8763	t = -0.07, p = 0.94365
	LVET, ms	t = 0.204507, p = 0.83934	t = 0.707668, p = 0.48461	t = 0.593902, p = 0.55703
	STR	t = -1.41, p = 0.17023	t = -1.25, p = 0.22185	t = -0.09, p = 0.93168
	FTc, ms	t = -1.17, p = 0.9158	t = -1.62, p = 0.11561	t = 1.89, p = 0.06827
Fluid	TFC, kOhm	t = 2.20, p = 0.0352	t = 3.46, p = 0.00165	t = -1.15, p = 0.2606
	TFCI, 1/kΩ*m2	t = 2.13, p = 0.04157	t = 3.91, p = 0.00049	t = -0.83, p = 0.41516
Work	LCW, kg* m2	t = 0.41, p = 0.68676	t = -1.65, p = 0.1096	t = -2.62, p = 0.01356
	LCWI, kg*m/m2	t = 0.75, p = 0.45718	t = -1.18, p = 0.2487	t = -2.62, p = 0.01369
Vascular	SVR (dyn • s • cm-5)	t = -0.16, p = 0.87543	t = 0.60, p = 0.55518	t = 1.20, p = 0.2396
	SVRI, dyn*s/cm5*m2	t = -1.02, p = 0.31418	t = -0.69, p = 0.49305	t = 0.93, p = 0.36012
	TAC, mL/mm Hg	t = 0.262593, p = 0.79466	t = 0.298206, p = 0.7676	t = -0.546877, p = 0.58851
	TACI, mL m2/mm Hg	t = 0.492137, p = 0.6262	t = 0.043639, p = 0.96548	t = -0.49699, p = 0.62282ñ
Others	DO2, ml O2/min/m2	t = 1.06, p = 0.29631	t = -0.89, p = 0.38213	t = -2.34, p =0.02617

t- t-value of the T-test (a t-value of 0 indicates that the sample results exactly equal the null hypothesis. As the difference between the sample data and the null hypothesis increases, the absolute value of the t-value increases).
Abbreviations – see Table 2.

dramatic decrease in the impedance to the flow of electric current. The behavior of these two variables followed this trend in our study, since while the thoracic flow content increased at three months, at six months it decreased to approach the baseline level, a situation exactly opposite to the impedance. Moreover, previous studies have shown that an increase in thoracic flow content is associated with diastolic dysfunction in patients with heart failure; the behavior shown by this variable in rheumatoid arthritis is not clear (16).

Considering the number of variables per parameter and the measurements in which there was significance, the Fluid parameter would be the most clearly influenced by phototherapy since out of six measurements, there were statistically significant changes in four. By contrast, the Vascular parameter shows no statistically significant change in any time point of measure. The variables that showed the most consistent changes were heart rate and cardiac output.

A strength of this study is that it shows consistency with reported benefits of phototherapy and that it offers an affordable and accessible alternative for most patients if it could be implemented widely.

Study limitations

The fact that this was a retrospective study is a clear limitation for generalizing the findings. It is also evident that the actions of each antirheumatic drug make it difficult to discern the true effect of phototherapy. Notwithstanding, with the results found (reduction in heart rate, cardiac output, cardiac index, O2 supply, left cardiac work and left cardiac work index), it can be suggested that phototherapy reduces the dynamic state of the patients with rheumatoid arthritis.

Conclusion

The hemodynamic status of the patients with rheumatoid arthritis treated with phototherapy within a range between 425 and 650 nm, 11.33 J/cm2, 30 cm above the chest is improved.

Ethics: Ethical approval has been granted by the local IRB. Patients provided consent for phototherapy.

Informed consent of patients to participate in the study has been waived by the IRB due to the retrospective nature of the study.

Peer-review- External and internal

Conflict of interest- None to declare

Authorship- A.L.A.G., M.G.P.G., M.J.V.C., I.S.G.S., A.C.H.J., J.A.V.H., and H.M.Z. contributed equally to the study and preparation of manuscript.

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Availability of data and material- Do not apply

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