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Comparative Efficacy of Ultrasound and Laser Therapy in Modulating Inflammatory Markers in a Rat Model of Testicular Inflammation

Ahmed Mamdouh Abdelkader[1*], Ahmed Ali Torad[2], Mohamed Ahmed Elbedewy[3], Nihal Mostafa[4], Amr Saadeldeen Mohamed Shalaby[5], Tayseer Saber Abdeldayem[6], Alaa Anwar Ahmed[7]

[1]Physiotherapy (Integumentary), School of Health and Social Work, University of Hertfordshire hosted by GAF (UH-GAF), Egypt
[2]Department of Physical Therapy, Clarkson University, NY, USA
[3]Department of Physical Therapy, Faculty of Allied Medical Sciences, Isra University, Amman, Jordan
[4]Lecturer of Biochemistry, Faculty of Science, Ain Shams University, Cairo, Egypt
[5]Department of Basic Sciences, Faculty of Physical Therapy, Cairo University, Cairo, Egypt
[6]Lecturer of Physical Therapy for Pediatrics, Department of Woman and Child Health, Faculty of Physical Therapy, Beni-Suef University, Beni Suef, Egypt
[7]Lecturer of Physical Therapy, Department of Physical Therapy for Integumentary, Egyptian Chinese University, Cairo, Egypt

***Correspondence to**
Ahmed Mamdouh Abdelkader,
Email: a.abdelkader@gaf.edu.eg

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Abstract

Introduction: All three degrees of inflammation (cellular, tissue, and systemic) are normal reactions that our bodies have to foreign substances. Cellular damage from bacteria, viruses, and even cancer can be warded off with the aid of these reactions. An efficient non-pharmaceutical method of treating inflammation is frequently seen as physiotherapy. In this study, the effects of ultrasonic treatment (US) and low-level laser therapy (LLLT) on the levels of C-reactive protein (CRP) in rats with inflamed testicles are investigated.

Methods: Three groups, each including eighteen male rats, were established: the control group (C), the US group (which received ultrasonic treatment), and the LLLT group (which received low-level laser therapy).

Results: The blood CRP levels in the US group were significantly lower than those in the control and LLLT groups.

Conclusion: Findings suggest that ultrasound might be more effective than LLLT in treating testicular inflammation, as shown by the decrease in blood CRP levels.

Keywords: C-reactive protein (CRP); Low-level laser therapy (LLLT); Ultrasound (US).

Introduction

Inflammation and C-Reactive Protein

Orchitis is quite simply an inflammation of the testicular tissue in progress. In our study, we observed a notable increase in the levels of C-reactive protein (CRP). The liver manufactures this specific Class II acute phase protein, meaning it serves as a marker during the initial stage of inflammation and other injuries concerning cell/tissue damage. Therefore, based on that kind of response to testicular inflammation, it appears plausible that CRP might give some indication or even be a marker to just how bad things may have gotten within the male reproductive system. These data suggest that further investigation is warranted to better understand the contribution of CRP in orchitis.[1]

An inflammatory response is a natural mechanism of the body to remove the injurious agent or start the healing process. Irritation is observed at the cellular level, where interstitial (between organs), vascular (blood or lymph circulation), and disorganization of brain tissue damage classes are grouped together. Inflammation occurs when irritation clears the way for defensive reactions and causes blood to flow into the injured region, thus producing redness. Macrophages or neutrophils, on the other hand, would limit pro-inflammatory cytokines and enable tissue/cell repair.[2]

Testicular irritation disrupts testicular function and causes a few serious diseases. The resistive framework and aging are two examples of close and/or distant natural changes that may affect testicular organs. Macrophage-secreted cytokines govern the resistant system's reaction and cerebral and vascular tone.[3]

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The majority of obsessive and physiochemical elements influencing blood tests are due to barriers and work. Blood test limits, like blood-brain borders, are the most unusual and baffling aspects of the sexual organ and brain blockage. They play a critical role in maintaining the testis environment. The unique ultrastructure of the blood-testis barrier is composed of endothelial cell-rich vasculature and tight junctions that prevent actin from passing between Sertoli cells and their stem cells. This obstacle includes transmembrane proteins and junctional sticky atoms. When these obstructions are broken, the conveyance and substance of intracellular proteins change, resulting in crucial damage to the gonads and generating inflammation.[4]

CRP is most commonly used in clinical settings as a measure of irritation. With its use, incendiary diseases may be distinguished from noninfective clutters that have similar severe stage responses. Furthermore, various reactions that are commonly associated with elevated CRP and the acute stage reaction are also associated with increased overall mortality. When an irresistible or noninfectious offense occurs, elevated CRP levels in the circulation usually rise early, and they develop in proportion to the degree of damage that hastened them.[5]

Ultrasound Therapy

The restorative ultrasound application employs a frequency of less than 3 MHz, and the ultrasound frame has both warm and non-thermal consequences. Warm impacts are used to reduce swelling, improve cell layer penetration, speed up chemical supply, increase the local digestive system, reduce solid fitful impacts, and provide pain-relieving advantages. Non-thermal impacts are often preferred due to their good effects on healing and recovery, which are more particular in physical therapy patients and can regulate biochemical and physical changes. This is because they inevitably provide support to tissues that are undergoing repairing activities.[6]

Phonophoresis can be performed via non-thermal impact. The cavitation impact is observed in useful ultrasonic applications when a sound wave interacts with a tissue containing gas atoms. According to studies, this type of cell partition accelerates lymph flow and cell recovery, making these forms critical for the healing process. This method also includes tissue recovery and emission. This ultrasonic feature is used for bone-tissue and tendon-ligament mending treatments.[7]

Laser Therapy

The laser therapy hypothesis is founded on the modifying effect of the application of vitality in the location of the emission. Lights are characterized as close- or far-infrared based on the framework being used. Power and light periods also shift. The action is non-invasive, and the superficial interchange of vitality frequently results in increased tropism, alterations in the atomic makeup of the damaged tissue, and a speeding up of responses to tissue aggravation. Safeguards are essential to safeguard the animal's safety during laser therapy. To acquire useful results, a few variables must be addressed. A few pieces of experimental data, which include an increase in microcirculation, an increase in the speed of the cellular reaction and collagen generation, an increase in supplement delivery, and an increase in anti-inflammatory activity, have been provided for the laser parameters that were used. The data show how the influence of the laser is filtered by different fabric levels, which might apply to tissues.[8]

Chromophores absorb laser light and convert it into natural movement. Photochemical forms accelerate and stimulate collagen production, which also includes phagocytic, endothelial, and fibroblast cells. Laser hits are inhibitory. It is often used to treat musculoskeletal structural disorders. Torment administration, irritation reduction, tissue and cell mending and repair employing circulation acceleration, immunological and provocative impact reduction, enzymatic activation, inhibition of cell division, and irresistible specialist obliteration are examples of beneficial applications.[9]

Experimental Design

Eighteen young adult male-skinned rats weighing between 150 and 200 g were used in this test as part of a kindling testicular exploratory rodent exhibition. They were uncovered to the identical bacterial media enhanced by direct injection to provide the appearance of an aroused testis. Following the formation of the flaming gonad, the rats were divided into three groups. These are the bunches for ultrasound and laser therapy, as well as the kindled testicular control bunch. All of the rats' blood tests were extracted, and samples from both solid and stimulated testicular tissues were homogenized. Rodent blood plasma was tested for biochemical analysis and quantitative CRP levels as this method complements the biochemical measurement of serum CRP levels by offering a localized assessment of inflammatory changes within the testicular tissue.[10]

CRP is a marker of systemic inflammation, which is linked to cancer progression and survival outcomes in urological cancers. CRP was selected as a primary endpoint due to its established role as a systemic marker of inflammation in acute and chronic conditions.[11]

Serum Analysis

Rodent ELIZA Packs CRP was obtained from Elabscience Biotechnology Co. Ltd, Building 4, Room 403, Guandong Science and Innovation Industry, Wu Han, PRC.

Equipment

- Stat Fax®2100 - Microplate Peruser (Mindfulness

Innovation, Inc.), PO Drawer 1679, Palm City, FL 34991.

- Ultrasound (Primo Combination 860 treatment equipment acquired from S.A.G. Worldwide for Therapeutic Equipment, Nasr City, Cairo, Egypt).
- Chattanooga Judgment Skills Versatile Laser 2779 - Lesson 3B: Moo Level Laser. The treatment had the following parameters: Type of laser: Diode laser, Emission mode: Continuous wave, Time on/Time off: Continuous operation, Delivery system: Handpiece with fiber optic cable, Energy distribution: Uniform, Peak power: 1600 mW, Average power: 200 mW, Spot diameter at the focus: 3 mm, Focus spot area: 7.07 mm^2, Spot diameter at the tissue: 4 mm, Focus-to-tissue: 1:1.33, Spot area at the tissue: 12.57 mm^2, Peak power density at spot area: 226.8 W/cm^2, Peak power density at the tissue: 127.2 W/cm^2, Average power density at spot area: 28.3 W/cm^2, Average power density at the tissue: 15.9 W/cm^2, Beam divergence: 9 degrees, Water irrigation: Not applicable and Air and aspirating airflow: Not applicable. (Main Control: 120-240 VAC, 50-60 Hz purchased from Servomed Universal Co., Cairo, Egypt, 1, Abdel Wahab Selim Al-Beshryst., Sheraton-Heliopolis).

Experimental Animal Grouping

The Animal Core Facility at the Faculty of Agriculture, Minya University, provided us with eighteen adult male albino rats weighing between 150 and 200 g. The rats were housed at the College of Veterinary Medicine's Physiology Laboratory for one week before the experimental protocol began at Minya University. The rats were kept in cages with a 12-hour light-dark cycle at a temperature of 25 °C. They had all the food and water. Therefore, we had these three groups of rats, each with six: (1) the control group (C); (2) Ultrasound (US): those who received underwater ultrasound therapy for 8 minutes at a smooth 1 MHz frequency, with a 3 cm square region on their heads receiving a mild 1.5 W of power per square centimeter. It seemed they were getting a gentle, circular, rhythmic massage from the ultrasound pulses.[12] The statistician performing the data analysis was blinded to the group assignments to minimize bias in the interpretation of results. This study was conducted in accordance with the Declaration of Helsinki, ensuring compliance with ethical principles for research involving animals and adherence to institutional guidelines for animal welfare; (3) low-level laser therapy (LLLT) groups received LLLT therapy for 20 seconds at 850 nm (Chattanooga), with a power output of 200 mW, a fluence of 3.6 J/cm^2, and a frequency of 16 Hz.[13]

Ten sessions total—two to three times per week for four weeks—were allocated to the application of US and Laser.[10]

Statistical Methods

We completed all of the numbers crunching for our experiment using the useful program GraphPad Prism 6.07 from GraphPad Software Inc., which is based in La Jolla, California, USA. Outliers were identified using boxplots and the interquartile range (IQR) method. No outliers were detected in the dataset. Additionally, data normality was assessed using the Shapiro-Wilk test, which revealed that the data followed a normal distribution. Based on these findings, parametric statistical tests were applied to compare the groups. We looked at the average scores (the mean) and their range (the standard deviation) to get a sense of how dispersed things are. We used One-Way ANOVA and Tukey's HSD test to see whether there were any significant differences between our data groups. A significance threshold of $P < 0.05$ was used to indicate statistical significance.

Results

Serum CRP levels were significantly reduced in the US and increased significantly in the LLLT groups compared to the control group ($P < 0.05$). The US group showed a reduction in CRP levels, indicating its superior anti-inflammatory efficacy. These findings are summarized in Table 1 and illustrated in Figure 1.

The comparative analysis of CRP levels suggests that ultrasound therapy is more effective than LLLT in mitigating inflammation and promoting tissue repair. Statistical analysis confirms a significant difference between the US and LLLT groups ($P < 0.05$), as shown in Table 2.

These findings provide robust evidence for the potential of ultrasound therapy as a superior non-pharmacological intervention for testicular inflammation. The advancement and specificity of this research will greatly aid in understanding the components of light therapy action.[14]

Discussion

As a result, empowering outcomes may be achieved by improving therapy-related evidence-based rules. The purpose of this work is to discern key biophysical and biochemical correlations in models of inflammation.[15]

Oxidants are subjected to increasing inflammation, resulting in increased CRP and scrotal hypertrophy. Ultrasonic and laser treatments, like inflammation, improve the conjunction and dissociation of light therapy and acute inflammation development. The employment of cell intelligence will make it easy to clarify the effect of pathways on testicles.[16]

These findings may also have an impact on the development of cancer preventive drugs. It is important to keep in mind that the oxidative push edge differs depending on the application and type of tissue.[17]

Because of these observations, academic research

Table 1. One-way ANOVA analysis results of control, US and Laser groups.

ANOVA						
Source of Variation	**SS**	**df**	**MS**	**F**	***P* Value**	**F crit**
Between groups	1.574	2	0.787	66.84	0.000	4.96
Within groups	0.177	15	0.012			
Total	1.751	17				

Note: F crit, Critical F value; MS, mean squares; SS, sum of squares.

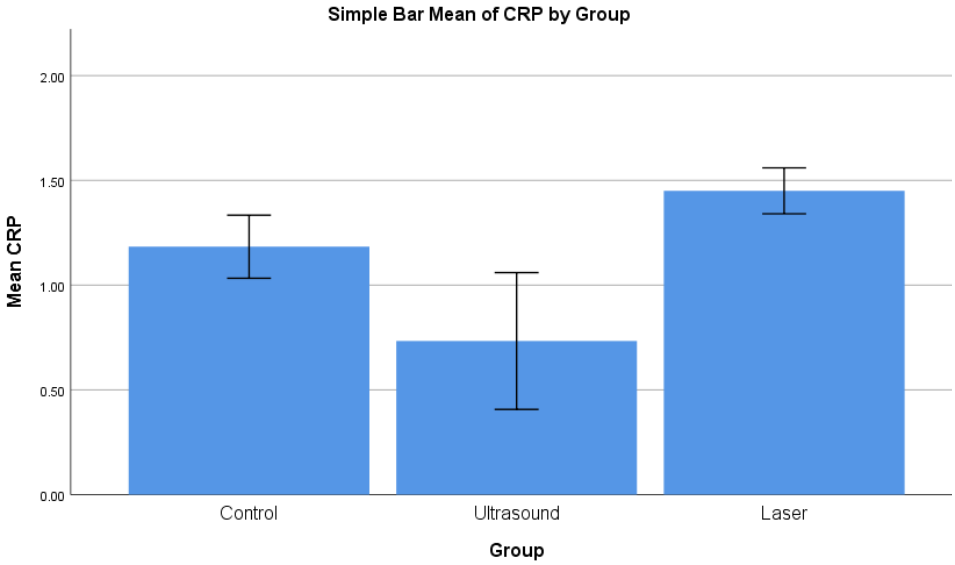

Figure 1. Normal Values for the Mean and Standard Deviation Within the Control, Ultrasound, and Low-Level Laser Groups. Data represents SD

into the application of ultrasound technology for the assessment of CRP levels may be enhanced. The main findings of the study indicate that CRP might be a useful biomarker in the context of ultrasonic mild hyperthermia therapy regimens. This suggests that including CRP measurement in ultrasound-based symptomatic norms may provide crucial therapeutic advice for identifying and monitoring provocative circumstances.[18]

The purpose of the evaluation was to explore the use of low-intensity and ultrasonic laser therapy on a certain incendiary worldview. After organizing both low-intensity and ultrasonic laser mediations, the test subjects, especially the rats, were subjected to the effects of non-pharmacological incendiary markers.[19]

Several pathophysiological viewpoints detect testicular irritation, one of which is the onset of aggravation, which results in an increase in proinflammatory cytokines.[20]

Previous research has demonstrated that both LLLT and US are effective strategies for reducing irritation. US is very important for its medicinal and preventive effects. More thought is needed to have a better grasp of the aspects that sustain the US's viability in this regard.[21]

Ultrasound, particularly low-intensity pulsed ultrasound (LIPUS), improves microcirculation, facilitating nutrient and oxygen delivery to damaged tissues. Acoustic streaming and radiation forces generated by ultrasound promote fluid flow, redistributing essential signaling molecules and nutrients.[22]

Low-intensity ultrasound has been shown to reduce pro-inflammatory cytokines, promoting anti-inflammatory gene expression and enhancing the activity of immunosuppressor cells. The induction of exosome biogenesis and docking further aids in the delivery of anti-inflammatory mediators to target cells, mitigating inflammation.[23]

Furthermore, LLLT provides a compelling therapy technique by regulating the production of incendiary cytokines.[24]

The current research indicated that ultrasonic therapy was more effective than laser treatment in relieving testicular discomfort, with CRP levels falling considerably. Despite obvious differences in both treatment groups when compared to the control group, the significant difference in outcomes suggests that ultrasonic treatment is more practical than laser treatment. The study reveals that in addition to their mechanical effects, ultrasound and laser vitality have a restorative influence, which includes the increased success of ultrasonic therapy in this situation.[25]

At this point, we may infer that halting all other pathogenic cascades may be considerably facilitated by the ability of US and LLLT to reduce CRP levels and

Table 2. Post hoc Tukey's HSD test analysis results of all group pairs.

Group Pairs		MD (LL-UL)	*P* Value
Control	Ultrasound	0.45 (0.316-0.58)	0.000
Control	Laser	-0.27 (-0.4--0.13)	0.001
Ultrasound	Laser	-0.72 (-0.85--0.58)	0.000

LL, Lower Limit; MD, Mean Difference; UL, Upper Limit.

diminish inflammatory symptoms.[26]

For the following reasons, therapy in the present trial provided during the inflammatory period may be more successful in decreasing CRP: CRP is less accurate at identifying non-bacterial inflammation. The benefits and drawbacks of using CRP must be carefully considered for each unique scenario. Gathering strong and weak evidence could help academics and decision-makers in the field of global health have more objective conversations in an often-divisive field.[27]

To our knowledge, no prior study has studied the influence of conventional US or LLLT on CRP levels in the blood during testicular inflammation in rats.[28]

Because of these concerns, treatment options may play an important role in reducing CRP levels and enhancing testicular healing throughout the inflammatory process. However, their efficacy may differ when compared to their performance in treating other inflammatory conditions, perhaps generating less favorable consequences for testicular recovery.[29]

One possible explanation for the effectiveness of the therapy in decreasing CRP levels might be connected to the timing of the study treatment; all medicines should be provided at the proper time to avoid worsening regulation rather than maximizing pathway balance.[30]

In contrast to this study, it was found that 50 mW laser therapy reduced the expression of TNF-α, IL-6, and IL-1β, while 100 mW lowered the quantity of inflammation-causing TNF-α.[31]

Others have seen a dose-dependent decrease in TNF-alpha in acute lung injury caused by an intravenous injection of 10 mg ovalbumin in 0.5 ml, with LLLT starting at 0.11 Joules and given at a power density of 31.3 mW/cm^2 in 42 seconds. This apparent disparity may be resolved by employing a different animal model, modifying the LLLT parameters or altering the number and duration of therapeutic sessions.[32]

This study has several limitations. Firstly, while CRP is a widely used marker for systemic inflammation, it lacks specificity for orchitis, which limits its utility as a sole diagnostic tool; future studies should consider additional biomarkers. Secondly, the use of an animal model, while providing controlled experimental conditions, may not fully replicate the complexity of human testicular inflammation, necessitating further validation in human studies. Thirdly, the sample size, though sufficient for detecting significant differences, could be expanded in future research to enhance the robustness of the findings. Additionally, the study explored only specific parameters for ultrasound and laser therapies; varying intensities, frequencies, and durations should be investigated for a more comprehensive understanding. Lastly, the study did not evaluate the long-term effects of these therapies on testicular health and systemic inflammation, which highlights the need for follow-up studies to determine the durability of the therapeutic effects. It is worth noting that this research is part of a larger-scale investigation, which includes the study by Mahmoud et al examining the effects of ultrasound and laser therapy on a levofloxacin-induced rat model of knee osteoarthritis.[10] The insights from that study helped inform our approach and interpretation of findings in the current investigation.

Conclusion

This study looked at three groups of experimental subjects: a control group, an US treatment group that got 1 MHz ultrasonic intervention, and an LLLT group that was exposed to an 850 nm wavelength. The empirical findings presented here demonstrate that US treatment was more successful in reducing testicular inflammation in rat models. For example, the US treatment resulted in a considerable decline in CRP levels, a known predictor of inflammation, when compared to both the control and LLLT groups. Given these findings, the authors advocate ultrasonic therapy as a better option for treating testicular inflammation in these animal models.

Authors' Contribution

Conceptualization: Ahmed Mamdouh Abdelkader.
Data curation: Ahmed Ali Torad.
Formal analysis: Nihal Mostafa.
Funding acquisition: Amr Saadeldeen Mohamed Shalaby.
Investigation: Alaa Anwar Ahmed.
Methodology: Nihal Mostafa.
Project administration: Tayseer Saber Abdeldayem.
Resources: Alaa Anwar Ahmed.
Software: Mohamed Ahmed Elbedewy.
Supervision: Tayseer Saber Abdeldayem.
Validation: Mohamed Ahmed Elbedewy.
Visualization: Amr Saadeldeen Mohamed Shalaby.
Writing–original draft: Ahmed Mamdouh Abdelkader.
Writing–review & editing: Ahmed Ali Torad.

Competing Interests

The authors declare no conflict of interest.

Ethical Approval

All research investigations were approved by the Cairo University Faculty of Physical Therapy's Ethical Committee and the Local Ethical Committee of the Faculty of Medicine, Minya University in accordance with the Ethical Guidelines for Scientific Research in Conscious Animals.

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References

1. Dutta S, Sengupta P, Slama P, Roychoudhury S. Oxidative stress, testicular inflammatory pathways, and male reproduction. Int J Mol Sci. 2021;22(18):10043. doi: 10.3390/ijms221810043.
2. Bumbasirevic U, Bojanic N, Simic T, Milojevic B, Zivkovic M, Kosanovic T, et al. Interplay between comprehensive inflammation indices and redox biomarkers in testicular germ-cell tumors. J Pers Med. 2022;12(5):833. doi: 10.3390/jpm12050833.
3. Sun L, Yang X, Yuan Z, Wang H. Metabolic reprogramming in immune response and tissue inflammation. Arterioscler Thromb Vasc Biol. 2020;40(9):1990-2001. doi: 10.1161/atvbaha.120.314037.
4. González-Barrio D, Diezma-Díaz C, Tabanera E, Aguado-Criado E, Pizarro M, González-Huecas M, et al. Vascular wall injury and inflammation are key pathogenic mechanisms responsible for early testicular degeneration during acute besnoitiosis in bulls. Parasit Vectors. 2020;13(1):113. doi: 10.1186/s13071-020-3959-9.
5. Mackiewicz A, Kushner I, Baumann H. Acute Phase Proteins Molecular Biology, Biochemistry, and Clinical Applications. CRC Press; 2020. doi: 10.1201/9781003068587.
6. Uddin SM, Komatsu DE, Motyka T, Petterson S. Low-intensity continuous ultrasound therapies—a systematic review of current state-of-the-art and future perspectives. J Clin Med. 2021;10(12):2698. doi: 10.3390/jcm10122698.
7. Bracciano A. Physical Agent Modalities: Theory and Application for the Occupational Therapist. New York: Routledge; 2024. doi: 10.4324/9781003525677.
8. Yaseen SD, Hasan JA, Musawi MS. Influence of low-level laser irradiation on C-reactive protein in patients with COVID-19 in vitro. AIP Conf Proc. 2024;3079(1):060028. doi: 10.1063/5.0202137.
9. Ansari MA, Erfanzadeh M, Mohajerani E. Mechanisms of laser-tissue interaction: II. Tissue thermal properties. J Lasers Med Sci. 2013;4(3):99-106.
10. Mahmoud GS, Elbedewey M, Abdelkader AM, Bekheet AB, El-Kossy DM, Sabbahi SA. Effects of ultrasound versus low level laser therapy in levofloxacin-induced rat model of knee osteoarthritis. IOSR J Dent Med Sci. 2017;16(6):78-85. doi: 10.9790/0853-1606017885.
11. Saito K, Kihara K. C-reactive protein as a biomarker for urological cancers. Nat Rev Urol. 2011;8(12):659-66. doi: 10.1038/nrurol.2011.145.
12. Nazer B, Ghahghaie F, Kashima R, Khokhlova T, Perez C, Crum L, et al. Therapeutic ultrasound promotes reperfusion and angiogenesis in a rat model of peripheral arterial disease. Circ J. 2015;79(9):2043-9. doi: 10.1253/circj.CJ-15-0366.
13. Koo HM, Yong MS, Na SS. The effect of low-intensity laser therapy (LILT) on cutaneous wound healing and pain relief in rats. J Phys Ther Sci. 2015;27(11):3421-3. doi: 10.1589/jpts.27.3421.
14. Mancilla-Galindo J, Kammar-García A, Mendoza-Gertrudis ML, García Acosta JM, Nava Serrano YS, Santiago O, et al. Regional moderate hyperthermia for mild-to-moderate COVID-19 (TherMoCoV study): a randomized controlled trial. Front Med (Lausanne). 2023;10:1256197. doi: 10.3389/fmed.2023.1256197.
15. Kölükçü E, Atılgan D, Uluocak N, Deresoy FA, Katar M, Unsal V. Milrinone ameliorates ischaemia-reperfusion injury in experimental testicular torsion/detorsion rat model. Andrologia. 2021;53(8):e14128. doi: 10.1111/and.14128.
16. Mobaraki F, Momeni M, Barghbani M, Farasati Far B, Hosseinian S, Hosseini SM. Extract-mediated biosynthesis and characterization of gold nanoparticles: Exploring their protective effect against cyclophosphamide-induced oxidative stress in rat testis. J Drug Deliv Sci Technol. 2022;71:103306. doi: 10.1016/j.jddst.2022.103306.
17. Breitenbach M, Eckl P. Introduction to oxidative stress in biomedical and biological research. Biomolecules. 2015;5(2):1169-77. doi: 10.3390/biom5021169.
18. Marghani BH, Fehaid A, Ateya AI, Ezz MA, Saleh RM. Photothermal therapeutic potency of plasmonic silver nanoparticles for apoptosis and anti-angiogenesis in testosterone induced benign prostate hyperplasia in rats. Life Sci. 2022;291:120240. doi: 10.1016/j.lfs.2021.120240.
19. Mantineo M, Pinheiro JP, Morgado AM. Low-level laser therapy on skeletal muscle inflammation: evaluation of irradiation parameters. J Biomed Opt. 2014;19(9):98002. doi: 10.1117/1.Jbo.19.9.098002.
20. Ru X, Chen S, Chen D, Shao Q, Shao W, Ye Q. Simulating the clinical manifestations and disease progression of human sepsis: a monobacterial injection approach for animal modeling. Virulence. 2024;15(1):2395835. doi: 10.1080/21505594.2024.2395835.
21. Ishibashi N, Uchiyama T, Tao S. Effect of photobiomodulation on lower urinary tract dysfunction in rat cystitis model. PLoS One. 2024;19(7):e0306527. doi: 10.1371/journal.pone.0306527.
22. Karthikesh MS, Yang X. The effect of ultrasound cavitation on endothelial cells. Exp Biol Med (Maywood). 2021;246(7):758-70. doi: 10.1177/1535370220982301.
23. Yang Q, Nanayakkara GK, Drummer C, Sun Y, Johnson C, Cueto R, et al. Low-intensity ultrasound-induced anti-inflammatory effects are mediated by several new mechanisms including gene induction, immunosuppressor cell promotion, and enhancement of exosome biogenesis and docking. Front Physiol. 2017;8:818. doi: 10.3389/fphys.2017.00818.
24. Oyebode OA, Jere SW, Houreld NN. Current therapeutic modalities for the management of chronic diabetic wounds of the foot. J Diabetes Res. 2023;2023:1359537. doi: 10.1155/2023/1359537.
25. Rajabi A, Mogheiseh A, Nazifi S, Ahrari-Khafi M, Dehghanian A, Vesal N, et al. Effect of direct therapeutic ultrasound exposure of ovaries on histopathology, inflammatory response, and oxidative stress in dogs. BMC Vet Res. 2023;19(1):88. doi: 10.1186/s12917-023-03657-6.
26. Parnham MJ. Inflammation research: modern design, more quality science. Inflamm Res. 2011;60(1):1. doi: 10.1007/s00011-010-0290-5.
27. Escadafal C, Incardona S, Fernandez-Carballo BL, Dittrich S. The good and the bad: using C reactive protein to distinguish bacterial from non-bacterial infection among febrile patients in low-resource settings. BMJ Glob Health. 2020;5(5):e002396. doi: 10.1136/bmjgh-2020-002396.
28. Mouliou DS. C-reactive protein: pathophysiology, diagnosis, false test results and a novel diagnostic algorithm for clinicians. Diseases. 2023;11(4):132. doi: 10.3390/diseases11040132.
29. Bernstein D, Coster D, Berliner S, Shapira I, Zeltser D, Rogowski O, et al. C-reactive protein velocity discriminates between acute viral and bacterial infections in patients who present with relatively low CRP concentrations. BMC Infect Dis. 2021;21(1):1210. doi: 10.1186/s12879-021-06878-y.
30. Leticia Fernandez-Carballo B, Escadafal C, MacLean E, Kapasi AJ, Dittrich S. Distinguishing bacterial versus non-

bacterial causes of febrile illness - a systematic review of host biomarkers. J Infect. 2021;82(4):1-10. doi: 10.1016/j.jinf.2021.01.028.

31. Alves AC, Vieira R, Leal-Junior E, dos Santos S, Ligeiro AP, Albertini R, et al. Effect of low-level laser therapy on the expression of inflammatory mediators and on neutrophils and macrophages in acute joint inflammation. Arthritis Res Ther. 2013;15(5):R116. doi: 10.1186/ar4296.
32. Aimbire F, Albertini R, Pacheco MT, Castro-Faria-Neto HC, Leonardo PS, Iversen VV, et al. Low-level laser therapy induces dose-dependent reduction of TNFalpha levels in acute inflammation. Photomed Laser Surg. 2006;24(1):33-7. doi: 10.1089/pho.2006.24.33.