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Exploring the Role of Magnetotherapy, Laser Therapy, Electrotherapy, and Cryotherapy in Rheumatoid Arthritis Treatment: A Review

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Abstract

Rheumatoid arthritis (RA) is a chronic systemic autoimmune connective tissue disorder that leads to disability, impairment and premature mortality. As non-pharmacological approaches that do not interfere with existing treatments, magnetotherapy, laser therapy, electrotherapy and cryotherapy present promising supplemental options. Although they are employed in the treatment of RA patients,their mechanisms of action and advantages are not fully understood and remain an area of ongoing research.

Aim of the Study: This review explores the mechanisms of magnetotherapy, laser therapy, electrotherapy and cryotherapy and evaluates their effects on inflammation, oxidative stress, pain, and functional outcomes in RA, providing insights into their potential as a complementary treatment and identifying potential risks.

Materials and Methods: A review of research literature was conducted through databases such as PubMed, Google Scholar, ResearchGate, and the Cochrane Library

Results: The studied methods effectively reduced pain and disease activity in RA patients.

Conclusions: These methods can complement conventional treatments, but further research is needed to standardize protocols and assess risks.

Keywords: rheumatoid arthritis, cryotherapy, magnetotherapy, PEMF, electrotherapy, TENS, laser therapy, photobiomodulation, whole body cryotherapy

Introduction

Rheumatoid arthritis is a relatively common condition and affected approximately 0.46% of the population from 1980 to 2018. (1)(2) It is more frequently observed in females than males, particularly in the elderly. (3) The underlying cause of rheumatoid arthritis is multifactorial, involving genetic predisposition, environmental influences, and immune system abnormalities. The disease is characterized by persistent inflammation of the synovial joints, leading to progressive joint damage, disability, and significant impacts on quality of life. Typically, the peripheral synovial joints are affected, including the metacarpophalangeal joints, ankles, and wrists. However, the knee, shoulders, elbows, and hips may also be involved. (4) (5) The most common symptoms include persistent joint swelling, tenderness, fatigue and prolonged morning stiffness. Extra-articular manifestations of rheumatoid arthritis affect about 40% of patients, involving various organs. Common issues include rheumatoid nodules, lung disease (e.g., interstitial lung disease), cardiovascular complications, eye problems (e.g., scleritis), and systemic conditions like anaemia and peripheral neuropathy. (6) One of the primary mechanisms of the disease is the activation of the immune system, particularly T cells and B cells. Self-reactive T cells, often initiate an inflammatory cascade that involves the release of pro-inflammatory cytokines such as tumor necrosis factor (TNF), interleukins (IL-1, IL-6), and interferon-gamma (IFN-γ). These cytokines, in turn, recruit other immune cells to the joint, promoting sustained inflammation B cells are producing rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA), which leads to immune complex formation and perpetuate the inflammatory response in the synovium which further contributes to the destruction of cartilage and bone.(7) (8) (9) Various scales are used to assess rheumatoid arthritis (RA), but for the purposes of this review, it is necessary to describe two of the most widely used: the Disease Activity Score 28 (DAS28) and the Health Assessment Questionnaire (HAQ). The DAS28 measures disease activity based on joint tenderness, swelling, and inflammatory markers while the HAQ evaluates functional disability and quality of life through a patient's ability to perform daily tasks. (10) (11)

Disease-modifying antirheumatic drugs (DMARDs), including conventional synthetic DMARDs (csDMARDs), biologic DMARDs (bDMARDs), and targeted synthetic DMARDs (tsDMARDs), help to slow RA progression by suppressing the immune system. Methotrexate (MTX), a csDMARD, is the preferred first-line treatment. The symptomatic treatment of rheumatoid arthritis (RA) mainly includes nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids (CS). (12) (13) Non-

pharmacological approach to treating rheumatoid arthritis consists of kinesiotherapy, magnetotherapy, ultrasound therapy, laser therapy, electrotherapy, cryotherapy and others . Although these methods are used in practice, scientific research on their effectiveness is still ongoing. (14) (15) (16) (17) (4) (18) (19)

Further evaluation of physical therapies in rheumatoid arthritis (RA) is essential, as these methods have the potential to not only improve quality of life, reduce symptoms, and slow disease progression, but also to decrease reliance on medications By doing so, they may lower the risk of pharmacotherapy-related side effects such as those caused by NSAIDs (e.g., gastric ulcers, kidney damage), steroids (e.g., osteoporosis, weight gain, and diabetes), biologics (e.g., increased infection susceptibility), and DMARDs (e.g., liver toxicity, bone marrow suppression). (20)

Magnetotherapy

Magnetotherapy is a therapeutic approach that uses magnetic fields to influence physiological processes in the body. Magnetic fields (MFs) affect cellular processes by altering ion flow, leading to hyperpolarization of cell membranes. This enhances metabolism, energy production, and oxygen use, stimulating processes like cell growth and apoptosis, crucial for tissue repair. MFs also influence signaling pathways, promoting collagen production and reducing inflammation, which aids in the healing of bone and connective tissues. (21) (22) (23) (24) Research shows that magnetotherapy can alleviate pain. (25) (26) Magnetic fields are categorized into different types based on their characteristics and mechanisms: Static Magnetic Fields (SMFs) are constant, non-varying fields, Low-Frequency Magnetic Fields (LFMFs),Pulsed Electromagnetic Fields (PEMFs) which use short bursts of electromagnetic energy and High-Frequency Magnetic Fields which have rapidly changing frequencies, mainly used for diagnostics- like MRI. (27) (24) (28) (29) The type and intensity of magnetotherapy in RA are customized based on the patient's condition and disease stage. (14) A study by Hong et al. explores the impact of PEMF on murine model collagen-induced arthritis. PEMF treatment significantly reduced paw inflammation and cartilage destruction. Serum IL-1β levels were lower in the PEMF-treated group, in comparison to untreated group, and tissue levels of inflammatory markers such as IL-1β, IL-6, TNF-α, were also reduced. These results suggest that PEMF helps preserve joint cartilage and could be a promising adjuvant therapy to slow rheumatoid arthritis progression. (30) Zwolińska et al. conducted a double-blind, randomized trial comparing static magnetic fields (SMF) and pulsed

electromagnetic fields (PEMF) in patients with rheumatoid arthritis (RA). Over three weeks, patients underwent 10 physiotherapy sessions, including magnetotherapy and hand exercises. Both SMF and PEMF therapies significantly improved hand function, pain, morning stiffness, and swelling. While SMF was more effective in reducing morning stiffness, PEMF showed greater improvements in functional status and swelling reduction. The study highlights magnetotherapy, particularly PEMF, as a valuable complementary treatment to pharmacotherapy for enhancing hand function and alleviating RA symptoms. (31) A study conducted by Eldoushy et al. (2022) on 100 rheumatoid arthritis patients compared the effects of mild magnetic compression gloves with built-in static magnets that apply a weak magnetic field (Group I) to massage therapy (Group II). Patients using the gloves experienced significantly greater relief from hand-joint symptoms—pain, stiffness, swelling, and tenderness—than those receiving massage therapy. (32) Magnetotherapy is generally considered safe- clinical trials have not identified significant side effects from magnetotherapy in RA patients. However, some individuals may experience hypersensitivity reaction, including skin redness, tingling, blurred vision, or other vegetative symptoms. Low-frequency electromagnetic fields are classified as potentially carcinogenic, and ongoing research continues to explore their long-term effects. Occupational risks for physiotherapists exposed to these fields also should be further investigated. (14) (31)

Laser therapy

Low-level laser therapy (LLLT), is a non-invasive therapeutic approach that employs specific wavelengths of light within the visible and near-infrared (NIR) spectra. These wavelengths typically range from red light (620–700 nm) to near-infrared light (700–1440 nm). (33) When low-level lasers (LLL) or light-emitting diodes (LEDs) are applied, they penetrate the tissue and interact with cellular components, particularly mitochondria. The light energy is absorbed by chromophores, such as cytochrome c oxidase in the mitochondria, leading to increased ATP production. This enhances cellular metabolism, which accelerates tissue repair and regeneration. Additionally, laser therapy stimulates the production of reactive oxygen species (ROS), which act as signaling molecules to activate various intracellular pathways. These pathways are involved in inflammation reduction, cell proliferation, and tissue healing. The application of laser light also influences blood circulation. It can induce vasodilation,

improving nutrient and oxygen delivery to tissues, further accelerating the healing process. (34) (35) (36) The aim of N. Zhuravleva et al. study was to evaluate the effectiveness of laser therapy in addition to standard treatment for rheumatoid arthritis (RA). 114 RA patients were randomly assigned to two groups, one receiving methotrexate 15 mg intramuscularly once a week and NSAIDs on demand, and the other receiving the same regimen along with low-intensity laser therapy. After 6 months, the laser therapy group showed significant improvements in pain, morning stiffness, and reduced NSAID use compared to the control group. The study concludes that laser therapy is an effective adjunct treatment in RA. (37) Yamaura et al. aimed to evaluate the effects of 810 nm radiation on pro-inflammatory cytokine production in rheumatoid arthritis (RA) synoviocytes. The cells were treated either before or after the addition of tumor necrosis factor-α (TNF-α), and cytokine mRNA levels (TNF-α, IL-1β, IL-6, IL-8) were measured using RT-PCR. The results showed that 810 nm radiation reduced TNF-α, IL-1β, and IL-8 levels, suggesting that low-level light therapy may help reduce inflammation in RA. (38) Thirty RA patients in a study conducted by Kostro et al. were divided into two groups: one group received laser therapy and the other received low-frequency magnetic field therapy, with both groups undergoing 10 treatment sessions. Pain was assessed using the VAS scale and Laitinen questionnaire, while hand joint range of motion and functionality were evaluated using the MHQ, DASH, and AIMS-2 questionnaires. The results showed that both therapies reduced pain, but magnetotherapy was more effective in improving hand joint mobility and enhancing the patients' quality of life and functional abilities compared to laser therapy. (39) Research conducted by Ruaa A. Thajeel involved forty-eight male rats to examine the effects of low-level laser therapy (LLLT) on rheumatoid arthritis, which was induced by injecting Complete Freund’s adjuvant (CFA) into the right hind paw of each rat. The rats were divided into six groups: a negative control, RA positive control, RA treated with LLLT at 650 nm, 910 nm, or 1064 nm, and RA treated with methotrexate (RA+MTX). After four weeks of treatment, paw swelling and biochemical markers (IL-6, IL-1β, TNF-α, MDA) were measured. The results indicated that LLLT effectively reduced paw swelling and lowered levels of IL-6, IL-1β, TNF-α, and MDA, with the 1064 nm LLLT showing the most significant effect. (40) Studies indicate that photobiomodulation is a safe treatment option for arthritis, with no significant side effects reported in both human and animal models. (41) (42)

Electrotherapy

Electrotherapy is a treatment that uses electrical impulses to stimulate muscles and nerves. It has been clinically tested that it influences cell migration, proliferation, and division orientation, activates key cellular signaling pathways while also promoting stem cell regenerative responses and guiding their differentiation. (43) A type of electrotherapy called Transcutaneous Electrical Nerve Stimulation (TENS) is thought to produce analgesia according to the gate control theory. It is applied by placing electrodes on the skin near the area of pain. (44) (45) TENS stimulates large diameter sensory fibers. This sensory input is transmitted to the central nervous system to trigger descending inhibitory pathways, helping to alleviate hyperalgesia. Research shows that High Frequency TENS increases the levels of β-endorphins in bloodstream and cerebrospinal fluid and reduces pain by activating opioid, GABA, and muscarinic receptors in the spinal cord and brain. (46) Although TENS is commonly used to alleviate pain in rheumatoid arthritis (47), studies on its impact in patients with RA are limited. A study by Abelson et al., which investigated acupuncture-like TENS (a type of TENS where electrodes are placed on acupuncture points), reported a statistically significant reduction in resting pain in patients with hand rheumatoid arthritis (RA) after three weeks of treatment, compared to placebo. The acupuncture-like TENS was applied once a week for 15 minutes. Although the methodology of the study is considered poor. (48) (47) However there are studies testing TENS in another rheumatoidal condition- osteoarthritis and the results strongly indicate that it can provide considerable pain relief, improve functional capacity, and enhance walking ability in individuals with knee osteoarthritis. (49) It is evident that these diseases involve distinct mechanisms (50) ; however, this could serve as an additional indicator and motivation to expand research on RA. These findings suggest that VNS could represent a novel therapeutic approach for patients with difficult-to-treat rheumatoid arthritis. Another interesting form of electrotherapy explored in recent years in RA is a short-term transcutaneous non-invasive vagus nerve stimulation. It is applied by a portable stimulator that delivers transcutaneous electrical stimulation to the cervical vagus nerve using steel contact electrodes, emitting sine-wave electric pulses with a 25 Hz frequency and adjustable voltage. Research supports the idea that the stimulation of vagus nerve, via the cholinergic anti-inflammatory pathway, helps to reduce the production of pro-inflammatory cytokines like TNF-α, IL-1, and IL-6. This process occurs when acetylcholine (ACh) is released from the vagus nerve and binds to specific receptors on immune cells,

inhibiting the NF-κB pathway that typically triggers inflammation. A regulation of hypothalamic-pituitary-adrenal (HPA) axis by vagus nerve also takes part in such anti-inflammatory response. (51) Koopman's study was the first to investigate whether stimulating the inflammatory reflex using an implanted electronic device could influence TNF and other cytokines in humans. The researchers repurposed a VNS device originally designed for epilepsy and tested it on two groups of rheumatoid arthritis patients: one with early-stage disease resistant to methotrexate, and another with inadequate responses to at least two biological treatments targeting different pathways. The results showed significant improvements in disease activity, measured by the DAS28-CRP score, along with substantial reductions in TNF and IL-6 levels, which aligned closely with the patients' clinical responses. (52) The most frequently reported side effect of TENS is minor skin irritation at the site of electrode application. (53) Researchers also evaluated the safety of a miniaturized vagus nerve stimulation (VNS) device for rheumatoid arthritis. The study found no serious device-related or treatment-related adverse events, though surgery-related issues such as Horner's syndrome and vocal cord paralysis occurred but resolved without significant effects. (54)

Cryotherapy

Cryotherapy involves subjecting the body to extremely low temperatures, either in targeted areas or across the entire body. It was proven, that it works by causing vasoconstriction, which decreases blood flow, helping to limit swelling and reduce inflammation in the treated area. Once the cold stimulus is removed, a reflexive vasodilation, known as the "hunting response," occurs, which leads to an increase in blood flow and the delivery of oxygen and nutrients to the tissue. Cold exposure also reduces nerve conduction velocity, which decreases the transmission of pain signals. Additionally it decreases tissue oxygen demand, lowering metabolic activity and reducing the production of pro-inflammatory cytokines. (55) Study conducted by Peyronnel et al. tested the effects of local cryotherapy on joint damage in a rat model of arthritis. Rats were treated with cold spray or ice for 14 days, and both treatments significantly reduced arthritis progression and joint damage. Swelling was reduced more by ice. However, no changes in cytokine levels were observed compared to control group. These results suggest that cryotherapy could help reduce joint damage in early rheumatoid arthritis, potentially supporting traditional DMARD treatments but its potential effects on decreasing cytokine levels still need to be investigated. (56) Another study by Peyronnel et al. explored

the potential of cryotherapy to reduce vascular inflammation in rheumatoid arthritis (RA), which, as mentioned before, increases cardiovascular risk due to long-term inflammation contributing to atherosclerosis and endothelial dysfunction. (57) In this study, ice cryotherapy was applied for 14 days in a rat model of rheumatoid arthritis (AIA). The researchers assessed immune cell infiltration in the aorta as well as the expression of cytokines and adhesion molecules. The results showed that cryotherapy significantly reduced the infiltration of various lymphocyte subsets (CD4+ T cells, CD8+ T cells, and Tc17 cells), suggesting a decrease in vascular inflammation. These findings indicate that ice cryotherapy could help reduce vascular comorbidities, making it a promising adjunctive therapy for managing RA. A study by Wojtecka-Lukasik et al. found that whole-body cryotherapy significantly lowered histamine levels in the blood of rheumatoid arthritis (RA) patients, with the effect lasting for at least three months. No such changes were observed in patients with osteoarthritis (OA) or those receiving other forms of physiotherapy. This indicates that the therapeutic effects of cryotherapy in RA patients may be, at least in part, attributed to its influence on histamine regulation. (58) A research by Zerjavic was conducted measuring the potential advantage of local versus systemic cryotherapy. The study found that a single application of cold air therapy or ice massage results equally in notable pain relief in individuals with active rheumatoid arthritis, with the benefits persisting for approximately one hour. (59) A randomized trial was conducted Klemm et al. to assess the effects of whole-body cryotherapy (WBC) in patients with active rheumatoid arthritis. One group of patients received standard multimodal rheumatologic therapy (MRCT), while the other group received MRCT combined with WBC - 6 sessions over 16 days. The results showed a significant reduction in pain in the WBC group compared to the control group, and this pain reduction was maintained at the 12-week follow-up. Additionally, 58% of patients in the WBC group either reduced or stopped using analgesics. WBC also led to a significant decrease in TNF and IL-6 levels.

The intervention group experienced a significant improvement in disease activity – measured by DAS 28 and functional capacity (measured by HAQ) compared to the control group right after the treatment, though this difference was not maintained at 12-week follow-up. However, DAS28 in the intervention group after 12 weeks remained significantly lower than starting level. (60) A study conducted by Księżnopolska-Orłowska et al. compares the effectiveness of rehabilitation in patients with rheumatoid arthritis (RA) with and without cryotherapy. Sixty-four women with RA were divided into two groups. Over three weeks, one group received traditional rehabilitation, including

electromagnetic and instrumental therapy, as well as individual and pool-based non-weight-bearing kinesiotherapy. The other group underwent cryogenic chamber therapy and local cryotherapy, along with non-weight-bearing, instrumental, and individual kinesiotherapy. Disease activity (DAS-28), functional impairment (HAQ-DI), pain severity (VAS), and overall well-being were assessed three times: before rehabilitation, after three weeks, and at a three-month follow-up. Results showed improvements in both groups. However, the group that received cryotherapy experienced greater improvements primarly in disease activity (DAS-28) and locomotor function (HAQ-DI). Improvements in this group were not only more significant immediately after the rehabilitation period but also lasted for longer – they sustained over the three-month follow-up. The conclusion of the study is that the rehabilitation program incorporating cryotherapy surpasses other forms of rehabilitation included in the study (16). In contrast, a study conducted by Giziska et al. 44 RA patients were split into two groups: 25 received whole-body cryotherapy and 19 received traditional rehabilitation (magnetotherapy, electrotherapy, ultrasound, and laser therapy). Both groups showed improvements in pain, disease activity, fatigue, and walking ability. Inflammatory markers (IL-6 and TNF-α) decreased similarly in both groups. (61)

A study done by Julita Israti concludes that the therapy of RA patients in cryogenic chamber can disturb hemostatic-fibrinolytic balance and potentially in some patients may lead to thrombosis and cardiovascular events. (62) Other potential side effects of cryotherapy in rheumatoid arthritis patients may include respiratory infections, frostbite, headache, hypertension, dizziness, urticaria, malaise, joint or muscle pain, and nervousness. (62)

Conclusion

Magnetotherapy, laser therapy, electrotherapy, and cryotherapy have shown the potential to effectively reduce pain, thereby decreasing the reliance on NSAID medications, reduce inflammation, improve quality of life, and slow disease progression in rheumatoid arthritis (RA) patients. However, there is still a limited number of studies focusing on these therapies for this specific group of patients, with many studies facing methodological challenges such as small sample sizes, lack of standardization, and short follow-up periods.While clinical evidence suggests positive outcomes, further research is essential to refine treatment protocols and fully understand their long-term benefits and potential risks. Studies, including those by Gizynska et al., support the idea that rehabilitation, in any form, can offer substantial benefits to RA patients.

Disclosure

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