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HITS magnetic stimulation of large skeletal muscles reduces the expression of serum TNF-α in patients with chronic inflammation symptoms associated with muscle disuse atrophy

Adrian Gaspar[1], Marcelo Tettamanti[2], Irena Hreljac[2,3], Matjaž Lukač[2,3,4,5]
[1] Espacio Gaspar Clinic, Mendoza, Argentina
[2]Laser and Health Academy, Ljubljana, Slovenia
[3]Fotona d.o.o.., Ljubljana, Slovenia
[4]Institut Josef Stefan, Light and Matter Dept., Ljubljana, Slovenia
[5]University of Ljubljana, Faculty of Mathematics and Physics, Ljubljana, Slovenia

ABSTRACT

The aim of this pilot study was to investigate the efficacy of High-Intensity Tesla Magnetic Stimulation (HITS™) in managing symptoms of chronic inflammation. Treatment resulted in significant reductions in TNF-α and fasting insulin levels, accompanied by improvements in the impact of clinical symptoms on patients' quality of life. Notably, HITS™ therapy targeted large muscle groups, promoting muscle activation and potentially modulating inflammatory pathways. These findings suggest that HITS™ therapy holds promise as a non-invasive and effective intervention for addressing chronic inflammation-related symptoms, particularly those associated with muscle disuse atrophy.

Key words: High-Intensity Tesla Magnetic Stimulation (HITS™), muscle atrophy, chronic inflammation, TNF-α.

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I. INTRODUCTION

Human biology is inherently adapted for a balanced lifestyle that includes both low-intensity activities and occasional bursts of high intensity [1]. However, in today's modern world, many people spend most of their time in sedentary activities, leading to significant health implications such as an increase in muscle atrophy, metabolic disorders, and cardiovascular disease [2].

The combination of a sedentary lifestyle and the consumption of processed foods high in sugar leads to constant excessive activation of inflammatory signaling pathways [3]. These molecular inflammatory cascades involve cytokines such as Tumor Necrosis Factor alpha (TNF-α), which plays a pivotal role in chronic inflammation, perpetuating inflammatory responses [4]. TNF-α is implicated in various chronic conditions such as rheumatoid arthritis, inflammatory bowel disease, and obesity-related inflammation [4]. Interestingly, myokines, proteins released by contracting skeletal muscles during exercise, have been found to regulate TNF-α levels. For instance, interleukin-6 (IL-6), a prominent myokine, has anti-inflammatory properties and can inhibit TNF-α production, contributing to the anti-inflammatory effects of exercise [5].

Fasting insulin levels have also been linked to chronic inflammation, particularly in the context of metabolic disorders such as insulin resistance and type 2 diabetes [3]. Insulin resistance is associated with increased levels of pro-inflammatory cytokines, contributing to a state of chronic low-grade inflammation. Regular exercise has been shown to modulate fasting insulin levels by improving insulin sensitivity and glucose uptake in skeletal muscles [6]. This effect of exercise not only helps to regulate blood glucose levels but also contributes to the reduction of chronic inflammation associated with insulin resistance.

The inflammatory responses are integral parts of the normal innate immune response, conferring protection to infection and initiating mechanisms of repair and regeneration of damaged tissues [7]. Under acute inflammatory conditions, recognition receptors activate several signaling cascades, leading to the release of pro- and anti-inflammatory mediators, which orchestrate the recruitment of neutrophils and

monocytes/macrophages to the damaged tissues while at the same time initiate the lysis of inflammation and the process of repair [8]. In the case of acute inflammation, such as in response to minor physical trauma or an infection, the process usually lasts for a few hours or a few days.

Long-term, persistent infections, autoimmune diseases, and increased daily inflammatory signaling due to lifestyle factors, such as physical inactivity, unhealthy diet and obesity, can overwhelm the anti-inflammatory processes of the immune system and results in chronic, sub-clinical inflammation [9]. Common symptoms of chronic inflammation include persistent fatigue, joint stiffness, tendonitis, muscle pain, gastrointestinal complications, weight fluctuations, skin rashes, and persistent infections [10]. These symptoms can range from mild to severe and last for several months or years.

Treatments for chronic inflammation include anti-inflammatory drugs (NSAIDS, corticosteroids, immunosuppressants and biologics) and lifestyle modifications such as exercise, diet and methods for stress relief. Among the latter, exercise holds an especially important role as it improves both muscle function and blood circulation [11-12].

Muscle is the most abundant organ in the human body, representing 30 to 50% of the total corporal weight. Functions classically attributed to skeletal muscle include movement and maintenance of posture, protection of vital organs, stimulation of blood and lymphatic circulation, and activation of metabolic pathways because of the large amount of energy consumed. In muscle atrophy, normal blood circulation to the muscle is impaired, which further advances the state of chronic inflammation [13].

Muscle contraction activates skeletal muscular fibers, which produce and release several cytokines called myokines, including myostatin, musclin, irisin, interleukin-6 (IL-6), interleukin-1 (IL-1), and many others [15]. These myokines are released into bloodstream and act to stimulate an anti-inflammatory systemic environment, acting on different organs including brain, adipose tissue, bone, liver, gut, pancreas, vascular bed and skin [16-19]. This is one of the- main reasons behind several beneficial systemic biological effects of physical exercise.

Recent studies have shown that electrical muscle stimulation can induce myokine release in a manner similar to exercise [20]. HITS™ magnetic muscle stimulation stimulates muscles in a similar manner as electric stimulation, with an advantage of being able to stimulate larger volume of muscles due to its deeper penetration and better patient comfort.

The aim of this pilot study was to investigate the efficacy of High-Intensity Tesla Magnetic Stimulation (HITS™) in managing symptoms of chronic inflammation associated with muscle disuse atrophy.

II. MATERIALS AND METHODS

Sixteen patients (12 women and 4 men) presenting with a confirmed inflammatory profile, as indicated by laboratory testing for serum levels of pro-inflammatory cytokine TNF-α levels, along with corresponding clinical symptoms, were enrolled in this study. Fasting insulin serum levels were also assessed for all patients prior to treatment. The primary clinical symptoms reported by patients included persistent fatigue, insomnia, and low libido, with some patients (N=7) experiencing a combination of these symptoms.

Average patient age was 56.7 (47-68) years old with an average BMI of 26.1 (22-29).

Patients underwent treatment using the StarFormer® device (Fotona, Slovenia), employing High-Intensity Tesla Magnetic Stimulation (HITS™) technology. Treatment consisted of two weekly sessions over a six-week period, totaling twelve sessions. The HITS™ stimulation targeted the largest muscles in the body capable of exerting the most force.

Treatment targeted the following muscle groups:

- Gluteus muscles, including the gluteus maximus, gluteus medius, and gluteus minimus.
- Quadriceps muscles.

For each session, two radial applicators with a coil diameter (d) of 110 mm and a coil windings number (n) of 19 were positioned on top of clothing, maintaining an average distance of 8 mm from the skin surface. The applicators were applied bilaterally to the gluteus

muscles for 45 minutes, followed by the same duration of treatment on the quadriceps. Software presets mimicking intense resistance training were utilized, with the total power emission gradually increased for patient comfort until reaching 100% of the system's maximum power.

Figure 1. The experimental setup showing applicators applied to gluteus muscles.

Comfort levels during treatment and any side effects experienced during and after treatment were assessed for all patients.

Patient questionnaires, utilizing a 0 to 10 Visual Analog Scale (VAS) to assess the impact of clinical symptoms on quality of life (0 indicating no impact and 10 indicating extreme impact), were completed. The results from patient questionnaires are summarized in Table 1 and Figure 2.

Patients' TNF-α and fasting insulin serum levels were measured before treatment initiation and sixty days following the final HITS™ session. Additionally, a follow-up questionnaire was administered to evaluate patients' perceptions of their clinical symptoms post-treatment completion. Wilcoxon signed rank test was used for statistical comparison of the baseline and follow-up values. P value larger than 0.05 was considered statistically significant. Results are summarized in Table 1 and Figure 3.

Prism software (GraphPad, USA) was used for statistical analysis and graphical representation.

III. RESULTS

All patients comfortably tolerated the treatment which in no case needed to be interrupted. No undesirable side effects were recorded during or after the treatment.

The results of the patient questionnaires before and 60 days following the treatment are represented in Figure 2 below.

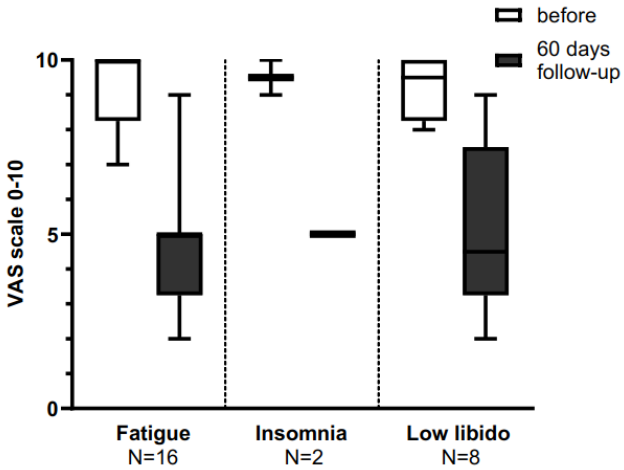

Figure 2. Patient's evaluation on the extent that clinical symptoms associated with chronic inflammation affected their quality of life evaluated before and 60 days following HITS treatment (0 - not affected to 10 - extremely affected). Box limits indicate the range of the central 50% of the data, with a central line marking the median value. Bars indicate minimum and maximum values.

Figure 3 shows the quantified values of serum TNF-α and fasting insulin before and 60 days following the final HITS™ session.

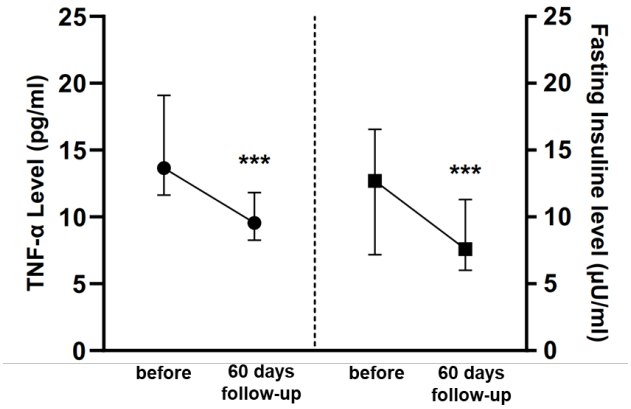

Figure 3 Graph showing the serum values of TNF-α and fasting insulin before starting treatments and 60 days following treatment. Values present median +/- interquartile range. *** - $p<0.0005$, Wilcoxon signed rank test

Table 1. The summary of study results. Values are represented for subgroups of patients that presented with one or more clinical symptoms. All patients complained of fatigue (N=16), 2 of those also presented with insomnia and 8 with low libido. P values were calculated using Wilcoxon signed rank test. In the insomnia subgroup, the number of patients (2) was too low for statistical comparison. P value <0.05 was considered statistically significant.

		Clinical symptom effect on life quality				TNF-α Level (pg/ml)				Fasting Insulin level (μU/ml)			
	patient N	Before mean (SD)	60 days follow up mean (SD)	% change	p value	Before mean (SD)	60 days follow up mean (SD)	% change	p value	Before mean (SD)	60 days follow up mean (SD)	% change	p value
FATIGUE	16	9.3 (1)	4.7 (1.7)	-51%	**0.0004**	60.7 (176.8)	16.9 (27.2)	-32%	**0.0005**	12.6 (6.8)	9.0 (4)	-22%	**0.002**
INSOMNIA	2	9.5 (0.5)	5.0 (0)	-47%	NA	23.2 (3.8)	7.5 (1.5)	-68%	NA	10.6 (6.5)	8.7 (3.4)	0%	NA
LOW LIBIDO	8	9.5 (0.8)	5.1 (2.3)	-46%	**0.014**	13.2 (3)	9.2 (1.8)	-26%	**0.014**	11.0 (6.3)	7.8 (3.4)	-19%	**0.014**

IV. DISCUSSION

The results of this study demonstrate a marked reduction in TNF-α and fasting insulin levels following High-Intensity Tesla Magnetic Stimulation (HITS™) treatment, accompanied by a decrease in the impact of clinical symptoms associated with chronic inflammation on patients' quality of life. These findings suggest that HITS™ therapy may offer a promising approach for managing chronic inflammatory conditions.

The observed decrease in TNF-α levels is particularly important, as TNF-α plays a central role in maintaining chronic inflammatory responses. Reduction in TNF-α levels has been associated with improvements in inflammation-related symptoms and overall health outcomes [4]. Similarly, the decrease in fasting insulin levels following HITS™ treatment is consistent with previous research linking physical activity and exercise to improved insulin sensitivity and glucose metabolism [6]. The findings suggest that HITS™ therapy may help mitigate insulin resistance, a common feature of chronic inflammatory conditions.

The improvement in patients' quality of life as reflected by the reduction in the impact of clinical symptoms is consistent with the known benefits of exercise and physical activity in managing chronic inflammation [5]. Previous studies have shown that exercise can attenuate inflammatory responses and improve symptoms associated with chronic inflammatory conditions [19]. The release of myokines, such as interleukin-6 (IL-6), may contribute to these beneficial effects [14-19].

Lack of exercise and sedentary lifestyle result with accumulation of more visceral fat, further enhancing inflammation [21]. However, some individuals are not capable of optimal physical exercise in terms of adequate duration, intensity, or muscles involved, and therefore they may be virtually deprived of at least some of the physiological benefits induced by exercise [22]. HITS™ magnetic stimulation can provide those patients with a powerful, effective, non-invasive, , and safe method to obtain very high muscle contraction activity without the need for patient exertion and with all the benefits of intense muscle activation – including release of myokines, prevention of disuse atrophy and increase in blood circulation. In order to maximize the production of myokines, large skeletal muscle groups, such as located in the arms, thighs, abdomen and buttocks were targeted in the treatment sessions.

To our knowledge, this is the first paper showing anti-inflammatory effects of magnetic muscle stimulation. Our findings support the notion that HITS™ therapy, by stimulating muscle contractions and potentially inducing the release of myokines, can modulate inflammatory pathways and improve metabolic function. The non-invasive nature of HITS™ therapy, along with its ability to target large muscle groups, makes it a promising therapeutic option for individuals with chronic inflammatory conditions who may have limitations with traditional exercise modalities.

While the results of this study are promising, further research is warranted to elucidate the underlying mechanisms by which HITS™ therapy exerts its anti-inflammatory effects and to explore its long-term efficacy and safety. Additionally, larger-scale clinical trials are needed to confirm these findings and to assess

the potential role of HITS™ therapy as part of a comprehensive treatment approach for chronic inflammatory conditions.

V. CONCLUSIONS

Magnetic stimulation has demonstrated efficacy in reducing serum TNF-α levels and ameliorating the impact of chronic inflammation symptoms on quality of life. These findings highlight the potential of High-Intensity Tesla Magnetic Stimulation (HITS™) as a promising therapeutic intervention for managing symptoms associated with chronic inflammation, particularly those linked to muscle disuse atrophy. By targeting inflammatory pathways and promoting muscle stimulation, HITS™ therapy could offer a non-invasive and effective approach to mitigating the negative effects of chronic inflammation on physical well-being.

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