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Effectiveness of Low Level Laser Therapy on Pain and Functional Status in Ankylosing Spondylitis

Ankilozan Spondilitte Düşük Doz Lazer Tedavisinin Ağrı ve Fonksiyonellik Üzerine Etkisi

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Summary

Objective: The aim of this study was to evaluate the effects of low-level laser therapy (LLLT) on pain, functional status and disease activity in patients with ankylosing spondylitis (AS).

Materials and Methods: A randomized, double-blind, placebo-controlled trial was performed on 37 patients. Group 1 (n=19) was treated with LLLT for 10 sessions (1.2J, 30 mW), group 2 received placebo laser. LLLT was applied on the L3 to S1 supraspinous ligaments and sacroiliac joints bilaterally with a skin-contact method. Evaluation parameters were Visual Analogue Scale (VAS), at rest and during movements, the Bath Ankylosing Spondylitis Disease Activity İndex (BASDAI), Bath Ankylosing Spondylitis Functional İndex (BASFI), and the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire.

Results: Compared with the pre-therapy, LLLT group showed significant improvement in VAS ($p<0.05$), ASQoL ($p<0.01$) and BASDAI ($p<0.001$) scores during movement at the end of the treatment and at the second month ($p<0.05$). However, there was no statistically significant difference between treatment and placebo groups.

Conclusion: This is the first study to assess the effects of LLLT in patients with AS. The results show LLLT seemed to improve pain and functional status in patients with AS.

Key Words: Low-level laser therapy, low back pain, inflammation, ankylosing spondylitis

Özet

Amaç: Bu çalışmanın amacı, ankilozan spondilit (AS) hastalarında düşük doz lazer tedavisinin (DDLT) ağrı, fonksiyonel durum ve hastalık aktivitesi üzerine etkisinin araştırılmasıdır.

Gereç ve Yöntem: Çift kör randomize placebo kontrollü olarak düzenlenen çalışmaya 37 hasta alındı. On seans boyunca 1. gruba (n=19) DDLT (1,2 J, 30 mW), 2. gruba (n=18) plasebo lazer uygulandı. DDLT uygulaması L3-S1 arasında supraspinöz ligamanlar üzerine ve bilateral sakroiliak eklemler üzerine deri ile temas halinde yapıldı. Değerlendirme parametreleri olarak, istirahat ve harekette Vizüel Analog Skala (VAS), Bath Ankilozan Spondilit Hastalık Aktivitesi Ölçeği (BASDAI), Bath Ankilozan Spondilit Fonksiyonel İndeksi (BASFI) ve Ankilozan Spondilit Yaşam Kalitesi Ölçeği (ASQoL) kullanıldı.

Bulgular: Tedavi öncesi ile kıyaslandığında DDLT grubunda hareket sırasında VAS ($p<0,05$), ASQoL ($p<0,01$) ve BASDAI'de ($p<0,001$) tedavi sonunda ve tedavi sonrası 2. ayda anlamlı düzelme gözlendi ($p<0,05$). Ancak tedavi ve placebo grupları arasında istatistiksel olarak anlamlı farklılık tespit edilemedi.

Sonuç: AS hastaları üzerinde DDLT'nin etkisini inceleyen bu ilk çalışmada DDLT'nin ağrı ve fonksiyonellik üzerine olumlu etkileri olduğu gözlendi.

Anahtar Kelimeler: Düşük doz lazer tedavisi, bel ağrısı, enflamasyon, ankilozan spondilit

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Introduction

Ankylosing spondylitis (AS) is a chronic, inflammatory rheumatic disease characterized by inflammation of the pelvis and spine, leading to limitation of spinal mobility. Its prevalence is 0.2-0.9% in the population, and is three times more common in males than in females (1). The condition usually starts in the third decade of life and the most common initial symptoms include back pain and stiffness.

The main clinical phenomena in AS are pain and body limitation that effect daily activities and quality of life. Patients describe their pain in one or both buttocks, also occasionally in the mid lumbar region. Additionally, morning stiffness and loss of spinal mobility are debilitating symptoms which are explained by spinal inflammation, structural damage or both.

Subchondral bone marrow inflammation in the sacroiliac joints and at the entheses is a characteristic histopathologic feature of the disease. Chronic inflammation of the entheses leads to new bone formation in the form of syndesmophytes, and ankylosis of the vertebrae and joints, primarily in the axial column. These active inflammatory spinal lesions are detected by magnetic resonance imaging and sacroiliac biopsies (2). Tumor necrosis factor-alpha (TNF-α) plays a key pro-inflammatory role in AS. The immunohistological findings suggest a role for TNF-α and interleukin-6 (IL-6) in early, active lesions, and for transforming growth factor-beta 1 (TGF-β1) at the time of secondary cartilage and bone proliferation (3,4). Inhibition of TNF-α was found to substantially improve signs and symptoms of AS (5,6). Hence, recent attention has been focused on new treatment modalities which can provide TNF-β blockage.

Low-level laser therapy (LLLT) is thought to be useful in the treatment of various musculoskeletal pain disorders (7-9). The exact mechanisms of action have not been well defined. One of the suggested mechanisms is releasing local neurotransmitters, such as serotonin and endorphins (10,11). Additionally, the analgesic effect of LLLT is thought to be related to its anti-inflammatory action (12-15). Many experimental and clinical studies have shown that LLLT can reduce or modulate TNF-α levels (13,15).

When analgesic and anti-inflammatory effects of LLLT are taken into consideration, the purpose of this study was to evaluate the effects of LLLT on clinical symptoms and quality of life in patients with AS. In the literature, there was no randomized controlled trial investigating the effects of LLLT in AS patients.

Materials and Methods

A randomized controlled trial was conducted. Thirty-seven patients, who satisfied the Modified New York Criteria for AS, were recruited from our outpatient clinic. Exclusion criteria were: presence of malignancy, infection at or near the treatment site, and pregnancy. The study was approved by the Human Research Ethics Committee of Marmara University. Written informed consent was obtained from all patients prior to inclusion to the study.

A total of 37 patients were randomly assigned to treatment and divided into two groups. The patients in Group 1 (n=19) received LLLT (1.2 J, 30 mW), and Group 2 (n=18) received placebo laser with an inactive probe. The therapy was applied to the patients for ten sessions (i.e. working days of following 2 weeks). Laser irradiation was performed with a Gallium-Aluminum-Arsenide (GaAlAs) λ=810 nm, 30 mW (MedArt Uni-laser 201 product, Asah Medico A/S, Hvidovre, Denmark). Continuous wave in skin-contact mode was chosen. Application of the laser beam was designed to include L3 to S1 supraspinous ligaments and sacroiliac joints bilaterally. Stimulation time of 40 seconds was used for each point to produce 1.2 J radiant energy with 30 mW power. Both the investigator and the participants wore protective goggles during the laser treatment sessions. Each session took approximately 20 minutes for each patient. Placebo LLLT was applied in the same manner with the same device which was deactivated.

Assessments were performed before, immediately after the treatment and at the end of week 8, by an investigator who was blind to the treatment. Both groups were evaluated for pain, disease activity, functionality and quality of life. Evaluation parameters were a visual analogue scale (VAS) for pain at rest and during movements, duration of morning stiffness, the Bath Ankylosing Spondylitis Disease Activity İndex (BASDAI), Bath Ankylosing Spondylitis Functional İndex (BASFI), and the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire. VAS scores were taken as an average of what the patient normally suffered one week before the evaluation. The BASDAI is a patient-reported measure of disease activity in patients with AS. The functional status of patients with AS was assessed by the BASFI. Ruof et al. (16) suggested a good discriminative capacity of the BASFI in physical therapy clinical trials. All these questionnaires are valid in Turkish patients.

All appointments of the patients were arranged at the same time period of the day to standardize the treatments and the assessments. For the duration of the study, the patients received their usual medication and were advised to maintain their usual activities.

Statistical Analysis

This study was designed to enroll 32 patients so that it would have at least 80% power to detect a treatment group difference of 1.0 point in pain severity as measured by VAS. The use of a 1.0 point difference in VAS was based on the result of a study by Salaffi et al. (17). Statistical analyses were done using SPSS version 10.0 for Windows. The results were expressed as means±standard deviations. For comparing the two groups before therapy, demographic data was analyzed using a student's t-test and the Mann-Whitney U test. Comparisons of the outcomes pre-therapy, weeks 2 and 8 in the groups were done by using the Friedman test and Wilcoxon-signed rank test, as appropriate. Statistical significance between the two groups was tested by the Mann-Whitney U test. The level of statistical significance was set at a two tailed p-value of 0.05.

Results

The basic characteristics of patients included in the study are shown in Table 1. There was no significant difference between the groups in demographic parameters and baseline scores for the assessment scales.

Baseline, week 2 and week 8 values of VAS at rest and during movements, morning stiffness, patient global assessment (PGA),

Table 1. Summary of demographics and baseline disease characteristics.

Characteristic	Placebo (n= 18)	LLLT (n=19)
Sex (Male/Female), #	10/8	15/4
Age, years±SD	41.3±13.4	38.9±10.7
Years since symptoms first occurred	12.1±7.5	11.2±7.7
Years since diagnosis of AS	8.7±7.1	6.6±6.1
Patients taking medications, no (%)	14 (87.8)	13 (68.4)
Patients smoking, no (%)	6 (33.3)	5 (26.3)
Patients doing regular exercises, no (%)	5 (27.8)	6 (31.6)

No significant difference between groups (Chi-square test when the variable is non- parametric).
LLLT: Low level laser treatment.

Table 2. Median values (range) of outcome variables for changes in clinical signs and symptoms from baseline to week 2 and week 8 in LLLT group (n=19).

Outcomes	Pre-treatment	Week 2	Week 8
Morning stiffness, minute	30 (5-60)	30 (5-30)	15 (5-60)
VAS at rest (0-10 scale)	5.5 (2.0-6.8)	2.4 (1-5.6)[b]	3.5 (1.2-6)
VAS during movement (0-10 scale)	5.6 (1.0-7.0)	2.4 (0-6.5)[b]	3.4 (1.0-6.5)[a]
BASFI	3.1 (1.9-5.8)	1.6 (0.9-4.5)	2.0 (1.1-6.9)
BASDAI	5.4 (3.4-7.1)	2.8 (0.6-4.5)[c]	3.3 (1.2-5.5)[a]
ASQoL	9.0(3.0-12)	4.0 (1.0-9.0)[b]	5.0 (2.0-11.0)[a]

[a]p<0.05 versus pre.treatment, [b]p<0.01 versus pre.treatment, [c]p<0.001 versus pre.treatment
VAS: Visual Analogue Scale, BASFI: Bath Ankylosing Spondylitis Functional Index, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index

Table 3. Median values (range) of outcome variables for changes in clinical signs and symptoms from baseline to week 2 and week 8 in placebo group (n=18).

Outcomes	Pre-treatment	Week 2	Week 8
Morning stiffness, minute	30 (13.7-60)	22.5 (3.7-37.5)	30 (13.7-60)
VAS at rest (0-10 scale)	46.0 (31.7-70.5)	27.5 (13.7-45.5)a	32.5 (20-52.7)a
VAS during movement (0-10 scale)	5.7 (2.3-8)	4.1 (2.0-5.2)	4.5 (1.0-5.9)
BASFI	2.9 (1.6-5.8)	2.6 (1.5-5.2)	4.4 (1.2-5.3)
BASDAI	4.8 (1.9-5.5)	3.0 (1.6-5.0)	4.7 (1.9-5.3)
ASQoL	9.5 (3.7-13)	7.0 (2.7-10)	5.5 (1.7-10.2)b

[a]p<0.05 versus pre.treatment, [b]p<0.01 versus pre.treatment, [c]p<0.001 versus pre.treatment
VAS: Visual Analogue Scale, BASFI: Bath Ankylosing Spondylitis Functional Index, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index

BASDAI, BASFI, and ASQoL scores were compared between the two groups and no statistically significant differences were found (p>0.05).

Immediately after the treatment VAS at rest improved in both groups, but LLLT group got more significant result as shown in Table 2 and Table 3. Likewise, VAS during movement improved in LLLT group after the treatment and this improvement lasted until the end of 8th week.

Compared with the pre-therapy, LLLT group showed significant improvement in ASQoL (p<0.01) and BASDAI (p<0.001) at the end of the treatment and at the second month (p<0.05).

We did not observe any complication nor an adverse effect during the study.

Discussion

The earliest forms and the most typical findings of AS result from sacroiliitis and enthesitis. Thus, suppression of inflammation at the early stages may slow progression of the disease. Various types of anti-inflammatory medications are being used in clinical practice today. In the past decade, new treatment modalities, aimed at specific neutralization of proinflammatory cytokines such as TNF-α and interleukin 1, seem the most promising. However, these biological agents have various side effects that limit the clinical use (18). From this aspect, LLLT can be considered as an alternative noninvasive treatment with its potential anti-inflammatory and analgesic effects (12,13,18-21).

This study included patients with pain or moderate disability and discomfort during daily activities on baseline examination, associated with AS. Our results did not show any statistically significant improvement between the groups. Detailed analyses of the results from LLLT group have shown clear differences between pre-therapy and post-therapy outcomes. The most prominent ones are the results on reduction in pain intensity, disease activity and quality of life.

In a previous study that followed up 825 patients with chronic musculoskeletal pain to determine the minimal clinically important difference (MCID) of changes in pain and its association with the numerical rating scale (NRS), the authors observed that on average a reduction of one point or a reduction of 15% in the NRS represented a MCID for the patients. Additionally, they determined that a NRS change score of -2.0 and a percent change score of -33% were best associated with the concept of "much better" improvement (17). In our study, both groups reached the MCID cut-off point in VAS at rest and during movement but not the much better improvement. In LLLT group, the improvement in pain status during movement was significant and permanent when compared with pain at rest. This would be related to the nature of the inflammatory pain which worsens at rest. Considering disease activity, previous literature suggested a BASDAI change of 1 cm is the MCID for AS patients (22). In our study, more than 1 cm decrement was observed in both groups at the end of the treatment, but LLLT group had a more significant decrease and this effect lasted to the end of the 8th week.

There was a lack of literature on the effectiveness of LLLT in patients with AS. However, LLLT has been reported to reduce low back pain (LBP) of various causes (23-27). Yousefi-Nooraie et al. (24) conducted a meta-analysis in an attempt to define the effect of LLLT on LBP. They concluded that there are insufficient data to draw consistent implications. A number of clinical studies have used LLLT for nonspecific LBP, however, the results are very heterogenic and nature of pain in these studies are not only caused by inflammatory and structural changes, but also by neurophysiologic and psychological mechanisms (23,25,26). Konstantinovic and colleagues (27) conducted a study to investigate additional anti-inflammatory effect of LLLT on acute LBP. The results suggest that 904-nm LLLT at a dose of 3 J/point could be used as an additional therapy to nonsteroidal anti-inflammatory drugs. Although, the study population and the laser beam parameters differ from ours, this study supports the possible clinical anti-inflammatory effects of LLLT on LBP.

There have been supportive data regarding the effectiveness of LLLT on other rheumatologic conditions. A Cochrane review (28) about the effect of LLLT on rheumatoid arthritis patients included five placebo-controlled trials and revealed LLLT reduced pain by 1.10 points on VAS relative to placebo, reduced morning stiffness duration by 27.5 minutes and increased tip to palm flexibility by 1.3 cm. The authors indicated no significant differences between subgroups based on LLLT dosage, wavelength, site of application or treatment length. In accordance with our short-term benefit, this review concludes that LLLT could be considered as a short-term treatment for relief of pain and morning stiffness in rheumatoid arthritis patients. Contrary to the results of this Cochrane review, several authors found similar outcomes to ours regarding pain, which include improvements in both groups from beginning to the end of the treatment, but no statistically significant differences between them (29-31).

Our study certainly has limitations. Firstly, the number of patients included is small. Secondly, the additional therapies and medications of patients were heterogenic. However, there was no statistically significant difference between the groups in terms of disease activity when assessed by the BASDAI. In addition, we had difficulty in choosing the laser irradiation parameters. There was a lack of literature related to the use of laser therapy in patients with AS. We analyzed the trials evaluating effectiveness of LLLT on LBP and rheumatoid arthritis. However, there was no standard opinion about the exact dosage, duration and type of the laser therapy. We observed good results in PGA, ASQoL and BASDAI in the placebo group. This fact emphasizes the importance of psychosocial factors in perception of pain and quality of life.

Conclusion

In this 8-week, randomized, double-blind, placebo-controlled trial, LLLT at the dosage of 1.2 J, 30 mW was not found superior to placebo, however, it was found to be efficacious on most in-group outcome measures in patients with AS, from beginning to the end of the treatment. Addition of LLLT to the management of AS may contribute towards improving treatment of patients with AS.

Conflict of Interest
Authors reported no conflicts of interest.

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