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Low-Level Laser Therapy in the Treatment of Autoimmune Thyroiditis

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Abstract

Introduction: Autoimmune thyroiditis (AIT) is an autoimmune disorder that is characterized by thyroid gland dysfunction. Low-level laser therapy (LLLT), as a safe and non-invasive intervention, has gained much attention in many clinical applications including pain relief, regenerative medicine, and autoimmune.

Methods: In this review, we discuss the effect of LLLT on cellular responses and its application in the treatment of AIT. Such keywords as "low-level laser therapy", "photobiomodulation" and "autoimmune thyroiditis" were used to find studies related to laser therapy in AIT in Google Scholar, PubMed and Medline databases.

Results: LLLT reduced thyroid gland inflammation and inhibited immune cell trafficking. LLLT modulated inflammatory responses and improved thyroid gland regeneration.

Conclusion: Investigations indicated that besides current treatment strategies, LLLT could be a promising therapeutic approach for the treatment of AIT.

Keywords: Low-level laser therapy (LLLT); Photobiomodulation; Autoimmune thyroiditis; Laser therapy; Autoimmune disease; Inflammation.

Introduction

Autoimmune thyroiditis (AIT) is the most common organ-specific autoimmune disorder characterized by thyroid gland auto-inflammatory situation and lymphocytic infiltration into the thyroid follicles.[1] This disorder includes Hashimoto thyroiditis (the common form of AIT) and Graves' disease (GD).[2] The exact etiology of the AIT has still remained elusive; however, a combination of the genetic predisposition which causes the loss of self-tolerance and environmental factors such as selenium deficiency, excess iodine intake, smoking, and viral infections has been identified. Autoimmune responses against the thyroid gland cause tissue destruction. As a result, insufficient thyroid gland function and hypothyroidism occur. Common treatment is symptomatic and focuses on thyroid hormone replacement.[1,3]

Low-level laser therapy (LLLT) is described as a special kind of laser (near-infrared light (600-1100 nm)) that affects cellular biology and signaling pathways. LLLT application leads to the inhibition of inflammation and pain relief, and it increases cell proliferation and induces tissue regeneration. LLLT has been used as a photo-bio-stimulation therapy in various diseases including low back pain, stroke, neurodegenerative disorders, rheumatoid arthritis, and wound healing.[4-7] Recent data have indicated that LLLT is safe and might have beneficial effects in hypothyroidism patients. The hypothesis of combining the LLLT therapy and current medication has widely been used in many countries such as Russia. About 400 000 laser devices are used in various healthcare clinics, and they have been very successful in various diseases.[7] In the present review, we discuss the effects of low-level laser irradiation on AIT.

Immunopathogenesis of AIT

Hashimoto thyroiditis is generally identified with the infiltration of immune cells including antigen-presenting cells, macrophages, plasma cells, and lymphocytes in the thyroid parenchymal tissue.[1,3] Immune responses lead to the production of thyroglobulin (Tg) and thyroid peroxidase auto-antibodies (TPO). T cells and autoantibodies cause damage and destruction of thyroid cells.[8,9]

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Similarly, immune cells such as T cells and B cells play a major role in the GD pathogenesis. However, GD is mainly characterized by autoantibodies produced by B cells infiltrated into the thyroid gland against the thyroid follicular cell thyrotropin receptor (TSH-R).[10-12]

It was also shown that TH1 cells and their related chemokine receptors r (C-X-C)R3 receptor have a pivotal role in the pathogenesis of GD.[13] Tumor necrosis factor-alpha (TNF-α) and interferon-gamma (IFN-γ) inflammatory cytokines play a part in inflammatory immune responses.[14,15]

Low-Level Laser Therapy and its Biological Effects

LLLT or photobiomodulation is a non-invasive treatment that produces no heat or vibration, and it is used as a single wavelength of light. A near-infrared laser beam with a wavelength from 600 to 1100 nm and power of 1-500 mW with low energy density is used for treatment.[16,17] The first LLLT was used as a treatment approach for pain relief, wound healing and inflammation reduction. However, in recent years, it has become a more popular treatment approach in various conditions including dentistry, multiple sclerosis, stroke, traumatic brain disorders, and regenerative medicine.[18-20] LLLT could act at different cellular and molecular levels. LLLT at wavelengths from 632 to 1064 nm could stimulate cellular responses.[21,22] Laser irradiation at a specific wavelength affects cellular biochemistry and could change the whole cellular metabolism and cell fate. Studies indicate that LLLT could induce adenosine triphosphate (ATP) production and DNA synthesis in stem cells and also in various cell lines.[22] It was shown that LLLT markedly stimulated cell division and proliferation of cells, including immune cells, mesenchymal stromal cells, fibroblasts, and keratinocytes, through chromophores and activation of the mitochondrial respiratory chain.[23] At the end of this process, the synthesis of DNA, RNA and cellular proteins increased and proliferation and/or differentiation occurred.[24,25] LLLT also could protect cells from NO mediated apoptosis.[26] Moreover, LLLT possesses photo-biomodulation effects, and it could decrease inflammatory responses and modulate the immune system.[27,28] Studies showed that LLLT reduced inflammation, pain and edema. LLLT could induce collagen synthesis and accelerate the tissue remodeling process.[29,30]

Different parameters could affect the laser properties. These parameters, including laser light wavelength, mode of laser irradiation, power of laser irradiation, exposure time, targeted area, and course of the laser therapy should be taken into consideration due to the probable inhibitory effects.[7]

Due to the biological effects of the LLLT, it has been widely used in different therapeutic approaches.[31-33]

Low-Level Laser Therapy in Autoimmune Thyroiditis

Animal studies indicated that in healthy thyroid tissue, LLLT caused a significant improvement in blood microcirculation and modulated T3 and T4 hormones.[34,35] LLLT on hypothyroidism-induced male rats showed that laser irradiation could affect the shape and structure of thyrocytes and thyroid follicles. It was also indicated that LLLT changed the size and volume of the thyroid gland and improved the thyroid hormone secretion.[36]

The thyroid gland is sensitive to the oxidative process. Studies indicated that high levels of reactive oxygen species are produced in the thyroid gland in physiological conditions. It was shown that LLLT could have a major impact on the reduction of reactive oxygen species levels in the thyroid gland.[37] LLLT inhibited thyroid gland damage and helped tissue recovery. It was also shown that LLLT accelerated thyroid recovery and function during 14 days after ionizing radiation in an animal model for radiation-induced thyroid damage. The activity of the super-oxide dismutase enzyme downregulated significantly during the first week of LLLT. This reduction would help the thyroid tissue to detoxify free radicals and recover its function by decreasing oxidative stress. Moreover, the serum levels of alanine transaminase and aspartate aminotransferase reduced after LLLT.[38] Several studies indicated that LLLT stimulated blood circulation into the thyroid gland, improved its function and affected thyroid hormones. LLLT upregulated the levels of T3 and T4 thyroid hormones.[39]

A randomized, placebo-controlled clinical trial was done on 23 patients to assess the LLLT effects on chronic autoimmune thyroiditis (CAT) hypothyroidism and thyroid function. The patients received a continuous-wave diode laser device using the punctual method in continuous emission mode at an output power of 50 mW twice a week for 5 weeks. Patients were followed up for 9 months after LLLT sessions. The results showed that the levels of T3, T4, TSH, and fT4, which indicated the thyroid function, increased significantly, and the need for LT4 decreased for 22 patients during the 9 months of follow-up. On the other hand, the volume of the thyroid gland normalized in 25% of LLLT-treated patients, and the levels of serum thyroid peroxidase antibodies TPOAb decreased significantly.[40]

As mentioned before inflammatory cytokines such as TNF-α and IFN-γ play a crucial role in the pathogenesis of the AIT. Therefore, increasing the levels of anti-inflammatory cytokines such as transforming growth factor β (TGF-β) modulates the inflammatory microenvironment and plays a major role in self-tolerance maintenance.[41] Studies indicated that increasing serum concentration of TGF-β could inhibit autoimmune diseases including CAT.[42] It was shown that LLLT stimulated TGF-β production in AIT along with decreasing the levels of pathogenic TPOAb.[40] LLLT also

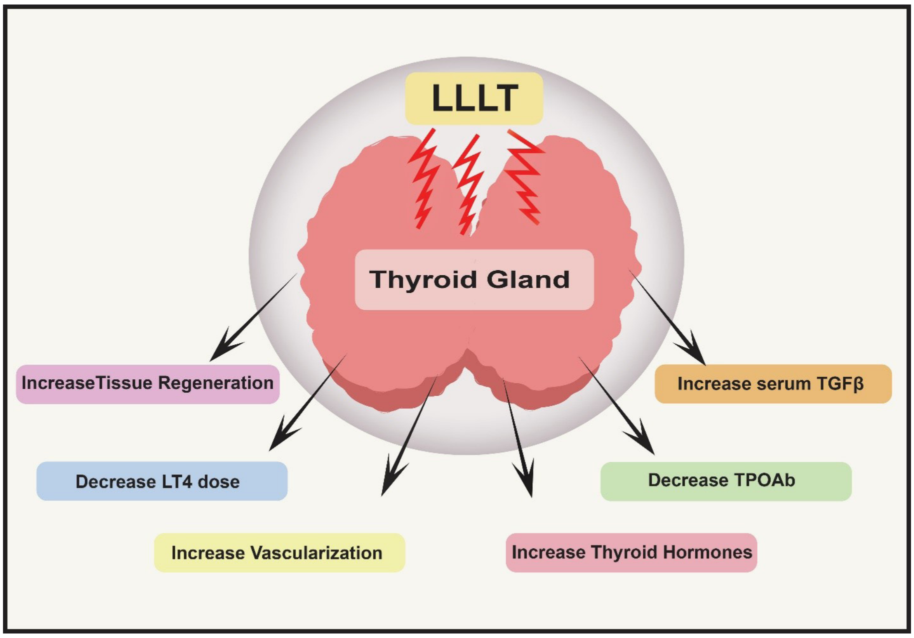

Figure 1. Represent the Effects of Low-Level Laser Therapy on Thyroid Gland .

improved vascularization and helped the regeneration of thyroid gland follicular cells.[43,44] A randomized, placebo-controlled trial investigating the effects of LLLT (830 nm, 50 mW output power) on 43 CAT patients showed that LLLT significantly induced the secretion of TGF-β cytokine compared to the control group 30 days after the treatment. It was also shown that thyroid function improved after LLLT intervention.[45]

An interesting study conducted by Mikhailov et al on 42 AIT patients indicated that LLLT could have major beneficial effects on autoimmune responses and might modulate them. It was shown that LLLT inhibited the function of T cells and hampered B cell proliferation and activation. It was also demonstrated that autoimmune responses in 78% of patients were normalized after 4 months of LLLT therapy. Moreover, Patients felt better and the size of the thyroid gland decreased (Figure 1).[46]

Interestingly, the long-term follow-up of 43 patients for 6 years showed that LLLT was a safe intervention for the treatment of CAT. Moreover, the LT4 dose (μg/d) need for obtaining normal thyroid function significantly decreased in the group treated with LLLT. The level of anti-TPO autoantibody decreased, and a significant improvement in thyroid function, volume and vascularization was observed. Due to the non-ionizing properties of LLLT (830 nm), there is no risk of the growth of malignant nodules or the worsening of autoimmune responses.[47]

Discussion

As recent studies have shown, LLLT has a great impact on modulating the immune responses and inflammation by decreasing the levels of inflammatory cytokine, *reactive oxygen species*, and nitric oxide.[48] LLLT also induces the production of antioxidant molecules and growth factors which help regeneration of injured tissue. In AIT, it was shown that LLLT was a noninvasive, quick and safe intervention, which increased thyroid hormones and improved thyroid function. Moreover, there was no risk of developing malignant nodules.[49]

However, more studies are needed to clarify the exact mechanism of action of LLLT on inhibiting immune responses. Also, more long-term follow-up studies need an exact evaluation of the persistence of the effects of LLLT.[50]

In spite of the beneficial effects of LLLT, there is a variety of issues that should be addressed. Besides social and ethical issues, there are some major professional factors influencing the effects of LLLT; for example, the power and radiation time of LLLT should be carefully adjusted due to the inhibitory and inflammatory effects. It seems that more advanced studies are required to address LLLT issues.[49]

Conclusion

LLLT could be a safe and useful therapeutic approach for the treatment of AIT. This intervention leads to a decrease in the patient's LT4 dose and an improvement in thyroid function.

Ethical Considerations

Not applicable.

Conflict of Interests

The authors declare that they have no conflict of interest.

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