ORIGINAL ARTICLE

Efficacy of Low-Level Laser Therapy for the Treatment of Reproductive System Disorders: A Study of Sensitivity and Outcomes

Meerim Osmonova[1,2], Arystanbek Atykanov[1], Meerim Moldokanova[1], Kamilla Kerimkulova[1,2], Meerim Makambaeva[1], Altynai Zhumabekova[3]

[1]Department of Science, Salymbekov University, Bishkek, Kyrgyz Republic, [2]Department of Gynecology, DOC University Hospital, Bishkek, Kyrgyz Republic, [3]Honorary International Faculty, AJ Research Centre, AJ Institute of Medical Sciences and Research Centre, Mangaluru, Karnataka, India

Abstract

Introduction: Low-level laser therapy (LLLT) is a noninvasive treatment that stimulates cellular activity through photochemical processes. This study evaluated the efficacy of LLLT in the treatment of various reproductive system disorders, including tubo-ovarian abscesses (TOA), ovarian endometriomas, fallopian tubal patency, and tubo-peritoneal factor infertility. **Materials and Methods:** A total of 213 women of reproductive age were included in this study. Sensitivity (Se) to LLLT was assessed using refractometry and polarization photometry. Oxidative stress (OS) markers, such as lipid hydroperoxides (LHP), diene conjugates (DCs), overall antioxidant activity (AOA), and catalase activity (CAT), were measured. **Results:** The optical density and area of the optically active structures significantly increased after LLLT in all groups. Significant differences in OS markers were found among groups before LLLT. After LLLT, women with TOA showed a decrease in DC levels and an increase in CAT, whereas those with ovarian endometriomas exhibited a decrease in LHPs and DC levels, and an increase in AOA and CAT. Women with fallopian tubal patency had decreased DC levels and increased AOA. The Se and specificity (Sp) of ovarian reserve indicators for uterine appendage pathology were highest for DCs (Se = 84–95%, Sp = 80–92%). **Conclusion:** These findings suggest that LLLT is an effective treatment for various reproductive system disorders, and that individual Se to LLLT should be considered to enhance treatment efficacy.

Key words: Antioxidant activity, catalase activity, diene conjugates, fallopian tubal patency, lipid hydroperoxides, low-level laser therapy, ovarian endometriomas, tubo-ovarian abscesses, tubo-peritoneal infertility

INTRODUCTION

Low-level laser therapy (LLLT) uses low-intensity light to stimulate biochemical reactions in cells through photochemical processes rather than thermal processes.[1] This process involves photon absorption by cellular photoreceptors, triggering chemical changes similar to those in photosynthesis in plants. Unlike high-intensity laser therapy, LLLT is noninvasive and effectively treats various conditions, including pain, inflammation, and wound healing.[1]

LLLT is a complementary medical treatment that enhances wound healing through biostimulatory effects, based on the premise that specific light wavelengths can influence cellular activity.[2] This exposure increases metabolic and proliferative activities. LLLT is effective owing to its bactericidal properties and ability to stimulate cells and promote fibroblast and osteoblastic cell growth, differentiation, and calcification.[3] In addition, it boosts leukocyte chemotactic activity, aids blood clotting, and promotes new blood vessel formation, which improves the healing process.[4]

Selecting an appropriate laser therapy method and justifying its use based on the patient's sensitivity (Se) to infrared and red

Address for correspondence:
Meerim Osmonova, Department of Science, Salymbekov University, Bishkek, Kyrgyz Republic.
E-mail: meerimosmonova39@gmail.com

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laser light are crucial when employing LLLT. This approach hinges on the adaptive control of therapeutic management. The body's response to LLLT is mainly influenced by free radical lipid peroxidation (LPO) and antioxidant defense (AOD).[5] These processes are key players in the development of various clinical conditions, such as reproductive system disorders. When LPO and AOD are balanced by a complex regulatory system, optimal health is maintained. Disruption of this balance results in oxidative stress (OS).[6,7]

The use of LLLT for the treatment of reproductive system pathologies can be justified by considering the individual Se of biological fluids and OS indicators, which can enhance treatment efficacy and predict the restoration of reproductive function, including the restoration of the menstrual cycle, prevention of disease relapse, and improvement of fertility and quality of life. The necessity for these investigations arose because of a lack of understanding of the body's susceptibility to low-intensity laser therapy and the development of OS in women with reproductive system diseases. This study aimed to evaluate the efficacy of LLLT in the treatment of various reproductive system disorders, namely tubo-ovarian abscesses (TOA), ovarian endometriomas, fallopian tubal patency, and tubo-peritoneal infertility.

MATERIALS AND METHODS

This study included 213 women of reproductive age. Among them, 94 had TOA, 58 had ovarian endometrioma, and 61 had fallopian tubal patency along with tubo-peritoneal factor infertility. The women were examined between May 2023 and April 2024.

The diagnosis was confirmed through a combination of clinical presentation, pelvic organ ultrasound, hysterosalpingography, and diagnostic laparoscopy. The susceptibility of each individual to low-intensity laser irradiation was evaluated using refractometry and polarization photometry. A spectrophotometric approach was used to determine the presence of lipid hydroperoxides (LHPs) and diene conjugates (DCs) in blood plasma. The AOD system was assessed by measuring the catalase activity (CAT) and the overall antioxidant activity (AOA) of the blood plasma.

Statistical analyses were conducted using Statistica v8.0 software (StatSoft, Inc., Tulsa, OK, USA). Data are presented as the mean±standard deviation. Student's *t*-test was used to evaluate differences between groups. The margin of error was used to assess the range of variance within each group, considering the highest and lowest limitations. Confidence intervals were calculated as follows: $P = 95\%$ or $^{*}P < 0.05$, $P = 99\%$ or $^{**}P < 0.01$, and $P = 99.9\%$ or $^{***}P < 0.001$. In addition, Se and specificity (Sp) were determined.

Data confidentiality was maintained for the patients who provided informed consent. This study was approved by the Bioethics Committee of the International Higher School of Medicine in Kyrgyzstan (protocol no. 19, dated April 21, 2023) and was conducted in compliance with the criteria outlined in the Declaration of Helsinki.

RESULTS

The analysis of blood Se in the women groups [Table 1] showed that women with TOA had significantly higher optical density ($P < 0.01$) and area of optically active structures after irradiation compared with the initial values. The refractive index increased from 1.318 ± 0.004 to 1.349 ± 0.005, and the area of the optically active structures increased from 47 ± 5.5% to 79 ± 6.1%. Similar patterns were observed in women with ovarian endometrioma and fallopian tubal patency after LLLT ($P < 0.05$ and $P < 0.01$, respectively).

Laser treatment outcomes vary with the dosage, necessitating a thorough examination of each indication. An increase in optically active structures above 30% was considered a positive response, 15–29% adequate, and <15% unsatisfactory. Table 2 presents the responses to laser irradiation: 58.5% of women with TOA had a favorable response, 27.6% had a fair response, and 13.8% had a poor response. Among the women with ovarian endometrioma, the percentages of favorable, fair, and poor responses were 58.6%, 27.5%, and 13.8%, respectively. Among the women with fallopian tubal patency, the percentages of favorable, fair, and poor responses were 52.4%, 27.8%, and 19.6%, respectively. The Se and Sp of identifying individual blood samples for LLLT were 84% and 80%, respectively.

Analysis of the OS markers related to LPO and AOD parameters revealed significant differences in their initial states [Table 3]. Glycosylated protein concentrations were significantly higher in women with ovarian endometrioma than in those with TOA ($P < 0.001$) or fallopian tubal patency ($P < 0.01$), with concentrations being significantly higher in the latter than in the former ($P < 0.01$). Conversely, dehydrogenase levels in women with ovarian endometrioma or fallopian tubal patency were significantly higher than those in women with TOA ($P < 0.001$ and $P < 0.05$, respectively). In addition, women with ovarian endometrioma exhibited a contrasting pattern in the AOD system, notably in total AOA and CAT, showing a significant reduction compared with the other groups ($P < 0.05$).

Changes in the analyzed indicators were identified at the end of LLLT [Table 4]. In women with TOA, the concentration of DCs in the blood decreased ($P < 0.05$) and that of CAT increased ($P < 0.05$) relative to their values before LLLT. In women with ovarian endometrioma, the concentrations of LHPs ($P < 0.05$) and DCs ($P < 0.01$) decreased and total AOA and CAT increased ($P < 0.05$). In women with

Table 1: Optical indicators of blood sensitivity to low-level laser therapy in women with different reproductive system disorders

S. No.	Groups of women and study periods	Optical density, units	Area of optically active structures, %
1	Tubo-ovarian abscess (*n*=94)		
	Period before exposure	1.318±0.004	47.0±5.5
	Period after exposure	1.349±0.005	79.0±6.1
		<0.01**	<0.01**
2	Ovarian endometrioma (*n*=58)		
	Period before exposure	1.322±0.004	50±6.3
	Period after exposure	1.347±0.001	84.4±7.1
		<0.05*	<0.05*
3	Fallopian tubal patency (*n*=61)		
	Period before exposure	1.326±0.006	51±5.9
	Period after exposure	1.351±0.005	83.4±7.5
		<0.01**	<0.01**

Values are expressed as the mean±standard deviation. *P<0.05; **P<0.01, ***P<0.001

Table 2: Comparison of the response of blood to laser irradiation in the examined women with different reproductive system disorders

S. No.	Groups of women examined	Response of blood to low-level laser therapy, %		
		Good (%)	Satisfactory (%)	Bad (%)
1	Tubo-ovarian abscess (*n*=94)	55 (58.5)	26 (27.6)	13 (13.8)
2	Ovarian endometrioma (*n*=58)	34 (58.6)	16 (27.5)	8 (13.8)
3	Fallopian tubal patency (*n*=61)	38 (52.4)	17 (27.8)	12 (19.6)

Values are presented as n (%)

Table 3: Oxidative stress indicators in the blood of the examined women during the period before low-level laser therapy

S. No.	Groups of women examined	Analyzed OS indicators			
		LHPs, pmoL/mL	DCs, pmoL/mL	AOA, %	CAT, mcat/L
1	Tubo-ovarian abscess (*n*=94)	0.944±0.065	0.386±0.021	18.2±1.11	17.46±0.87
2	Ovarian endometrioma (*n*=58) P2-1	3.41±0.291	0.723±0.145	14.5±0.67	14.2±0.87
		<0.001***	<0.001***	<0.05*	<0.05*
3	Fallopian tubal patency (*n*=61)				
	P3-1	1.891±0.183	0.578±0.077	16.9±0.95	18.94±1.05
	P3-2	<0.01**	<0.05*	>0.05	>0.05
		<0.01**	>0.05	<0.05*	<0.05*

Values are expressed as the mean±standard deviation. *P<0.05; **P<0.01, ***P<0.001. LHPs: Lipid hydroperoxides, DCs: Diene conjugates, AOA: Antioxidant activity, CAT: Catalase activity

fallopian tubal patency, DC levels decreased and AOA increased ($P < 0.05$) during this period.

The analysis of the Se and Sp of the indicators of ovarian reserve for the pathology of uterine appendages in women showed that the highest significance corresponded to the values of DCs (Se = 84–95%, Sp = 80–92%) and AOA (Se = 75–83%, Sp = 75–84%).

DISCUSSION

LLLT is a specialized treatment for women with reproductive system diseases, including chronic illnesses of the appendages, endometriosis, and pelvic adhesions, which can result in tubal factor infertility. Extensive evidence supports the efficacy of this method.[8,9]

Table 4: Oxidative stress markers in the blood of examined women during the period after low-level laser therapy

S. No.	Groups of women examined	Analyzed OS indicators			
		LHPs, pmoL/mL	DCs, pmoL/mL	AOA, %	CAT, mcat/L
1	Tubo-ovarian abscess (*n*=94)				
	Period before exposure	0.944±0.065	0.386±0.021	18.2±1.11	17.46±0.88
	Period after exposure	0.891±0.059	0.296±0.03	19.5±1.08	20.1±0.83
		>0.05	<0.05*	>0.05	<0.05*
2	Ovarian endometrioma (*n*=58)				
	Period before exposure	3.41±0.291	0.723±0.145	14.5±0.67	14.2±0.87
	Period after exposure	2.72±0.21	0.424±0.092	19.7±0.95	17.4±0.67
		<0.05*	<0.01*	<0.05*	<0.05*
3	Fallopian tubal patency (*n*=61)				
	Period before exposure	1.891±0.183	0.578±0.077	16.9±0.95	18.94±1.05
	Period after exposure	1.625±0.98	0.39±0.064	20.4±1.22	19.6±1.05
		>0.05	<0.05*	<0.05*	>0.05

Values are expressed as the mean±standard deviation. *P<0.05; **P<0.01, ***P<0.001. LHPs: Lipid hydroperoxides, DCs: Diene conjugates, AOA: Antioxidant activity, CAT: Catalase activity

LLLT effectively treats painful conditions by stimulating β-endorphin release, modulating A-alpha nerve fiber conduction, improving blood and lymphatic circulation, and facilitating waste metabolite removal. Furthermore, it controls primary dysmenorrhea by decreasing the production of prostaglandins E and F via superoxide dismutase acceleration.[10,11]

Consequently, LLLT blood irradiation in the studied groups of women led, to some extent, to the inhibition of free radical LPO owing to the activation of AOD processes, mainly its enzymatic component, which resulted in a decrease in OS in these pathologies of the female reproductive system. Numerous studies have demonstrated that LLLT affects cell growth, metabolism, blood vessel formation, cell death, and inflammation. Unlike pharmaceutical drugs, the varying laser characteristics and dosages of LLLT are crucial.[12] Insufficient doses may produce a weak cellular response, whereas excessive doses can inhibit growth or induce cell death; these responses vary by tissue type. Furthermore, Hamblin *et al*. found that similar biological reactions occur in some tumor cells exposed to radiation, possibly stimulating tumor growth.[13]

From the data obtained, it can be inferred that with a good and satisfactory response of the body to infrared laser radiation, LLLT has pathophysiologically determined mechanisms of compensatory and adaptive reactions, limiting the cellular aspects of OS, which are most clearly demonstrated in women with ovarian endometrioma. Laser biostimulation within the therapy accelerates tissue healing, improves microcirculation, and stimulates fibroblast, collagen, and nerve fiber growth.[14] In addition, LLLT alleviates pain and reduces inflammation. For example, far-infrared LLLT is used to treat endometriosis by promoting endometrial growth and functionality at the cellular level, significantly restoring and repair tissue function as well.[14,15]

LLLT is essential for the treatment of various clinical conditions; however, its cellular effects remain unclear despite extensive research. The main limitation of this study was its small sample size. Although the data suggest that LLLT is safe, concerns remain regarding its potential to stimulate tumor cell growth post-treatment. Elucidating the molecular mechanisms triggered by laser exposure may lead to novel medical applications of LLLT, contingent on addressing safety concerns.

CONCLUSION

The response of women with uterine appendage pathology to LLLT in the infrared spectrum is typically characterized by a favorable and satisfactory outcome in >80% of cases. Blood irradiation with LLLT led to a limited occurrence of OS. This suggests a targeted therapeutic effect of LLLT in the treatment of uterine appendage diseases.

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