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Comparison of Photobiomodulation Therapy Types for Adults with Chronic Pain

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Abstract

Purpose : Our study aimed to compare the effectiveness of low-level laser therapy (LLLT) and light-emitting diode therapy (LEDT) for chronic pain intensity reduction and body temperature increase in older adults with chronic pain.

Methods : Overall, 144 of 332 participants' records were used in this retrospective chart review. The study was conducted at a private health center in Busan city and the integrative medical center of a tertiary care hospital in Daegu city, South Korea. Patients experiencing chronic pain for over 6 months were assigned to either the LLLT or LEDT group. Both groups underwent 16 sessions of phototherapy held twice a week for 8 weeks, with each session lasting 60 minutes. The primary outcomes for both groups were the mean visual analogue scale (VAS) scores and body temperatures in both groups. The secondary outcome was the correlation between changes in body temperature and pain intensity. Measurements were recorded at the baseline and at each follow-up session.

Results : A decrease in pain intensity and an increase in body temperature ($p<.001$) were observed in both groups. There was a significant difference in the VAS scores and temperature changes between the groups ($p<.001$). Odditionally, there were significant differences in the patterns of change in the VAS score and body temperature between the groups as the sessions progressed ($p<.01$), and a strong inverse correlation between body temperature and pain intensity changes were observed ($p<.01$).

Conclusion : The use of photobiomodulation therapy at a specific wavelength may improve pain severity and simultaneously increase the body temperature among elderly people with chronic pain.

Key Words : low-level laser therapy, pain, photobiomodulation, temperature

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Ⅰ. Introduction

1. Background

As the average life expectancy and middle aged and elderly population increase, the prevalence of chronic pain in the older population and the social cost both also gradually increase (Global burden of disease study Collaborators et al., 2015). Previous studies demonstrated that 13 %~50 % of adults in the United Kingdom experience chronic pain, and about 8 % are newly diagnosed with pain every year (Fayaz et al., 2016). In the United States, the prevalence of patients with chronic pain for over 6 months is 30.7 % (Johannes et al., 2010). The prevalence of mild to severe pain in South Korea was 29.8 % in 2017, and the incidence rate is increasing annually (Shin, 2017). As of 2013, the yearly medical cost of Korean pain treatment was $300 USD per year to prevent pain, $500 USD for mild pain, and $600 USD for severe pain (Shin, 2017). Addressing chronic pain among elderly people is a global public health priority, and health professionals require a more comprehensive understanding of chronic pain management (Goldberg & McGee, 2011). Many studies have reported the use of photobiomodulation therapy (PBMT) for pain relief, and it is a widely used non-drug therapy for musculoskeletal system disorders, such as low back pain (Vallone et al., 2014) and neck pain (Chow et al., 2009). PBMT involves the application of non-ionized light sources, such as lasers and light-emitting diodes (LEDs) (Anders et al., 2015). One type of PBMT is low-level laser therapy (LLLT) which requires the use of coherent laser light; another type, light-emitting diodes therapy (LEDT), has been proposed as an affordable alternative therapy. Body temperature may influence pain in chronic pain conditions, such as fibromyalgia (Larson et al., 2014). In Korea, PBMT is employed widely in wound care, pain reduction, and inflammation. Although there is abundant research on the use of PBMT, its mechanism of physical action is still unknown; additionally, their biochemical mechanisms are still not understood.

2. Purpose

Our study was conducted to compare the effectiveness of PBMT for chronic pain intensity reduction and body temperature increase among elderly patients with chronic pain.

Ⅱ. Methods

1. Study design and participants

Our study protocol was approved by the research ethics review committee of our institution(IRB No. YUMC 2020-02-019). After institutional review board approval, a retrospective chart audit was performed utilizing a 10 % random sample of all participants who visited a private health center at Busan, South Korea and the integrative medical center of a tertiary care hospital in Daegu city, South Korea from March 1, 2017 to August 31, 2017. The following patients were included in this study: (1) patients aged between 55~88 years; (2) patients who were experiencing generalized or psychosomatic pain for over 6 months; and (3) patients who did not take medications such as capsaicin, acetaminophen, aspirin, and ibuprofen or other pain control drugs; and thyroid-related drugs such as thyroxine, methimazole, and propranolol, 2 weeks prior to the first PBMT session. Patients with any kind of cancer or malignancy diagnosed at the hospital, significant psychiatric disorders, neurologic disorders such as dementia and Parkinson’s disease, a history of alcohol or drug dependency, cerebrovascular disorders, and thyroid disease were excluded.

2. Data collection

The collected baseline data included demographics (age, sex, urban or rural residence, and economic status), body mass index (BMI), visual analog scale (VAS) score were recorded by making a mark on a 10 ㎝ line that differentiated between “no pain” and “worst pain”, and body temperature measured in armpit by digital thermometer. Data collection was performed by a single reviewer.

3. Laser therapy

Data of those who completed all 16 sessions were used in the final analysis. The patients in each group (LLLT and LEDT) underwent 16 sessions of PBMT therapy that were performed twice a week for a total of 8 weeks, with each session lasting 60 min. The sessions were performed in a quiet room after booking. In the LLLT group, participants used a thirty-diode cluster laser thermal mattress-type device with a wavelength of 650 ㎚ (VLP-9600, Vigen Medical Co., Ltd, South Korea), a red light and an energy density of 18 J/㎠; in the LEDT group, participants used a thirty-diode cluster LED thermal mattress-type device with a wavelength of 630 ㎚ (control type), a red light, and an energy density 3.6 J/㎠. Both devices had the same number light emission type, and mattress shape. As for how to use the equipment used in this test, the participants can lie on the mattress by himself according to the usage without any special operation. The medical devices used in this study was certified by the Korean Ministry of food and Drug Safety. The equipment characteristics and irradiation parameters are shown in Table 1.

Table 1. Parameters of the instruments used for photobiomodulation therapy

Parameters	LLLT device (VLP-9600®)[a]	LEDT device
Wave length (㎚)	650	630±20
Average optical output (㎽)	5	1
Time setting minute	60	60
Energy density (J/㎠)	18	3.6
Temperature setting (℃)	43	43
Spot size of cluster (㎠)	0.16	0.16
Number of spots	30	30
Light emission (each diode)	continuous	continuous

[a]LLLT thirty-diode cluster thermal mat device - and LED thermal mat device were manufactured by LEDT, light emitting diode therapy; LLLT, low-level laser therapy
[a]Korean FDA Approval No: A37020-01 (class 3)

4. Statistical analysis

The baseline characteristics between the 2 groups were compared using Pearson’s χ 2 test, an independent t-test, and Pearson’s correlation coefficient. The difference after 16 sessions between the two groups (LLLT vs LEDT) was analyzed with analysis of covariance while body temperature in baseline was adjusted. The repeated-measures analysis of variance was used to compare the VAS score and body temperature changes relative to baseline values between the 2 groups. A correlation analysis was conducted to determine the association between pain and body temperature. All statistics were analyzed using SPSS Ver 25.0 software (IBM Corp., Armonk, NY, USA), and p-values 0.05 were deemed statistically significant.

Ⅲ. Results

1. Participants

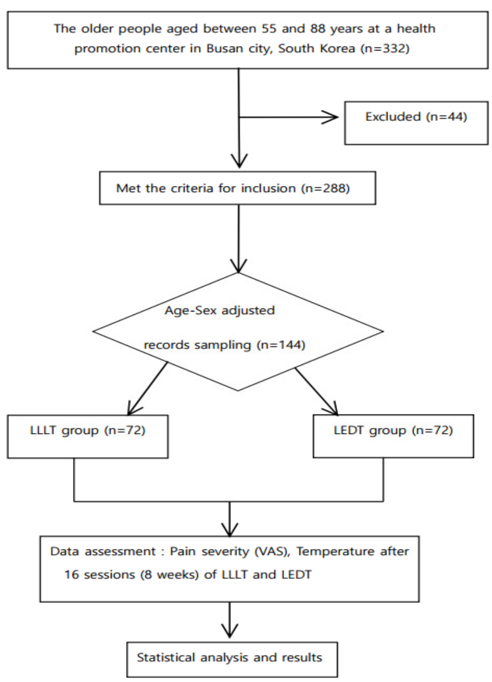
Altogether, the medical records of 332 participants were obtained from the attended health center and integrative medical center, and 288 met the criteria for inclusion. A 50 % random sample was selected, and a chart audit was performed. The final data analyses included 144 patients: 72 in the LLLT group and 72 in the LED group (Fig 1). The participants' demographics are summarized in Table 2. The mean age of each group was as follows; LLLT 72.33±8.90(55~87)years and LEDT 72.42±8.17 (57~88) years. There was no difference in mean ages between two groups. Although the overall number of men was lower than that of women, the difference was not statistically significant between the 2 groups in pain severity. economic status, and residence. However, the average baseline

Table 2. Demographic characteristics

	LLLT (n=72)		LEDT (n=72)		
	Mean±SD	*p*	Mean±SD	*p*	p^*
Mean age, years	72.33±8.90		72.42±8.17		.983 [a]
Men (%)	17 (23.6 %)		17 (23.6 %)	1.000	[b]
Women (%)	55 (76.4 %)		55 (76.4 %)	1.000	
Pain severity (Baseline)					
Sex					
Male	7.06±2.30	.499	7.06±1.44	.731	1.000
Female	7.49±2.15		7.24±1.96		.518
Age					
<65 years	6.67±2.00	.105	6.67±2.50	.273	1.000
>65 years	7.63±2.20		7.37±1.56		.481
BMI (kg/㎡)					
<24	7.30±1.91	.692	7.12±1.60	.704	.632
>25	7.54±2.63		7.29±2.15		.701
Economic status ($USD)					
>3,000	7.46±2.28	.243	7.05±2.04	.259	.548
>1,500~3,000	6.89±2.24		6.90±1.87		.979
<1,500	7.95±1.91		7.73±1.58		.675
Residence					
Urban	7.56±2.34	.426	7.30±1.66	.452	.547
Rural	7.14±1.92		6.81±2.40		.622
Temperature (Baseline)					
Sex					
Male	35.23±.53	.001	35.33±.29	.004	.500
Female	34.61±.80		35.00±.63		.005
Age					
<65 years	34.88±.67	.439	35.17±.48	.427	.139
>65 years	34.71±.83		35.04±.62		.019
BMI (kg/㎡)					
<24	34.74±.82	.822	35.04±.57	.537	.048
>25	34.78±.74		35.13±.61		.063
Economic status ($USD)					
>3,000	34.80±.67	.135	35.14±.48	.814	.073
>1,500~3,000	34.93±.81		35.08±.51		.396
<1,500	34.48±.83		35.02±.76		.032
Residence					
Urban	34.67±.89	.257	35.04±.61	.342	.022
Rural	34.87±.60		35.20±.49		.070

[a]Independent t-test, analysis of variance, [b]Pearson's chi-square test, BMI; body mass index, SD; standard deviation, LEDT; light-emitting diode therapy, LLLT; low-level laser therapy, p; p-value within group, p^*; p-value between group

temperature among the women, over 65 years of age (p=0.019), under 24 body mass index (p=0.048), economic status and residence were significantly different in the LLLT and LEDT groups (p<0.05).



LLLT, low-level laser therapy; LEDT, light emitting diode therapy; VAS, visual analog scale.

Fig 1. Flow chart of the study phases

2. Efficacy analysis and clinical outcomes

The primary outcome measures were the mean VAS scores and body temperatures in the LLLT and LEDT groups. There was no differences in the mean VAS scores and body temperatures of the LLLT and LEDT groups (7.39±2.18, and 7.19±1.84, and 34.75±0.79 ℃ and 35.08±0.59 ℃ at baseline). In the LLLT and the LEDT groups, the measurements for each group, such as pain severity and temperature were compared between session 0 and after session 16. There was a decrease in pain intensity and an increase in body temperature (p<0.001) in both groups when comparing the values obtained at the last treatment session with those at baseline effect was adjusted (Table 3). The LLLT group had a larger reduction in the VAS score and a more prominent increase in body temperature than the LEDT group (-5.19±1.69 and 1.33±0.62℃, respectively, p<0.05). The secondary outcome measure was the correlation between changes in the body temperature and pain intensity. The patterns of change in the VAS score and body temperature between the 2 groups varied significantly with session progression (Fig 2) (p<0.01). Over time, the intensity of pain (VAS score) decreased and body temperature increased in both groups.

Additionally, a strong inverse correlation was observed between body temperature and pain intensity changes (p<0.01). The intensity of pain reduced with increasing body temperature (Table 4).

Table 3. Clinical outcomes at baseline and after 16 sessions

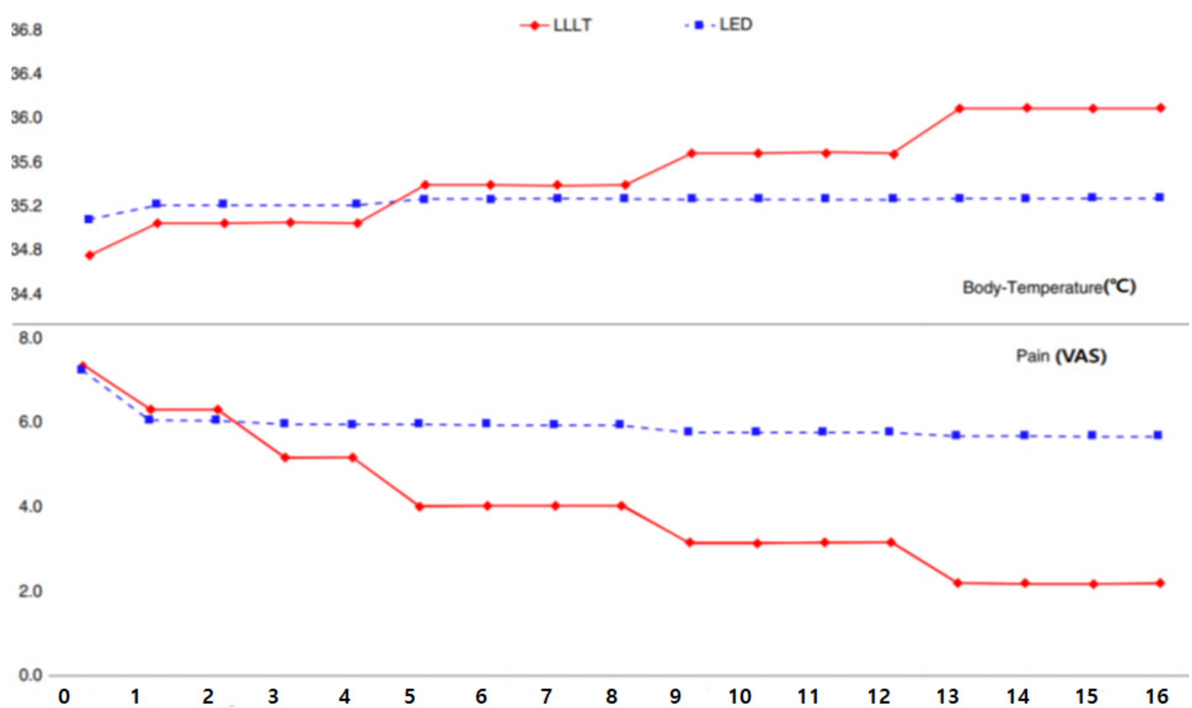
	LLLT (n=72)	LEDT (n=72)		
	Mean±SD	Mean±SD	p^a	p^b
	Pain severity (VAS)			
Baseline	7.39±2.18	7.19±1.84	.564	
After 16 sessions	2.19±1.26	5.61±1.84	<.001	<.001
Difference within group	-5.19±1.69	-1.58±1.32	<.001	<.001
	Body temperature, ℃			
Baseline	34.75±.79	35.08±.59	.508	
After 16 sessions	36.08±.38	35.28±.61	<.001	<.001
Difference within group	1.33±.62	.20±.21	<.001	<.001

[a]Independent *t*-test, [b]p value by analysis of covariance adjusted by baseline, LEDT; light emitting diode therapy, LLLT; low-level laser therapy, SD; standard deviation, VAS; visual analog scale

Table 4. Correlation between pain severity and body temperature

Body Temperature \ Pain Severity	LLLT	LEDT	Total
LLLT	-.965**	-.760**	-.952**
LEDT	-.885**	-.943**	-.921**
Total	-.974**	-.794**	-.967**

**Correlation coefficient; p<.01; LEDT, light emitting diode therapy; LLLT, low-level laser therapy



LLLT: low-level laser therapy, LED: light-emmiting diode, VAS: visual analog score
Repeated measure analysis of variance, p<0.01

Fig 2. Changes in pain severity and body temperature according to sessions.

Ⅳ. Discussion

In this study, we observed that the application of PBMT at a specific wavelength reduced the pain severity and simultaneously increased the body temperature among the older adult patients with chronic pain. A previous study suggested that there are sex-related differences in body temperature regulation, such as sudomotor activity, the rate of metabolic heat production during exercise, and neuronal modulation of temperature control (Gagnon & Kenny, 2012). Similar to those reported in previous studies, we observed sex differences in core body temperature. Additionally, in this study, the baseline pain score was higher among women than in men, but the difference was not significant. Recent reviews indicate an association between the regulation of pain and temperature that may contribute to widespread fibromyalgia-related pain. Multiple pain and thermoregulatory pathways exist that can influence each other (Gupta et al., 2017).

In our study, the higher the patient's core temperature, the lower the VAS score. Many previous studies have shown that low-power lasers or LED lights with a wavelength spectrum of 660 ㎚~905 ㎚ have a beneficial effect on pain, inflammation, and tissue repair (Hamblin, 2017). In some experimental studies, laser irradiation in the visual infra-red range was demonstrated to affect the ion channels of the transient receptor potential (TRP) cation channels family. The TRP channels are ion channels with a family of 6 proteins, mainly located in the plasma cell membrane of human and animal cells (Samanta et al., 2018). TRP channels display transient elevations of potential in response to light stimuli. In particular, laser irradiation in the visual and infrared as well as ultraviolet ranges can modulate the function and expression of TRP ion channels. This may form the basis for the effect of LLLT (Wang et al., 2014). LLLT has an effective anti-inflammatory and wound-healing activity on the dermis or mast cells (MC). Whether the level of extracellular adenosine-5′ -triphosphate (ATP) or purine acts on the purinergic signaling of mast cells and neurons, it can be modulated by laser irradiation, but the exact mechanism is not yet known. One animal study revealed that laser irradiation attenuates the extracellular ATP contents of neurons through the modulation of ecto-ATPase activity, and laser irradiation enhances extracellular ATP synthesis and increases MCs ATP activity by promoting ATP synthesis. The opposite response to these 2 cells suggests a complex mechanism for the effect of LLLT (Wang et al., 2015). TRPV3 is a temperature-sensitive TRP ion channel that is stimulated by warm temperatures. In addition, this channel is regulated by various physiological factors such as extracellular cation, acidic environment, intracellular ATP, membrane potential, and arachidonic acid. One recent study suggested that TRPV3 may play an important role in pain sensation, itching, and inflammatory diseases of the skin (Luo & Hu, 2014). Temperature-sensitive TRP ion channels that act as drug targets for neuropathic pain are currently being investigated. A previous study indicated that by, heating and cooling the body, the threshold of pain caused by temperature stimulation moved in the opposite direction (Alfonsi et al., 2016). There are a variety of animal and clinical studies that indicate the interaction between the pain regulation system and thermoregulation system, considered part of homeostasis of the human body. While the relationship between pain and body temperature is not well understood, it appears to be driven by various factors.

A major limitation of this study is that it is a retrospective chart review. Having depended on the subjective memory of the participants, it is possible that the data in the medical records were not correct. In addition, there may be variations in the participant's subjective pain score recording and axillary temperature measurements. In particular, for the elderly, pain or related symptoms could be expressed atypically and communication might be difficult due to presence of cognitive disorders or participants may minimize their symptoms (Schwan et al., 2019). In this study, there were no record of any unusual side effects that the subjects complained except that some sparticipants felt a little hot. It is necessary to overcome these limitations through well-designed prospective studies in the future.

Ⅴ. Conclusions

In conclusion, our findings suggest that the PBMT at a wavelength 630~ 650 ㎚ may reduce pain severity and simultaneously increase the body temperature of the older adults with chronic pain. This is the first observational study to suggest an interaction between body temperature and pain relief by PBMT in elderly patients with chronic pain.

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