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Could Phototherapy Reverse Visual Deficits in Patients with Relapsing-Remitting Multiple Sclerosis?

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Abstract

Background: *Multiple sclerosis is a neurodegenerative disease of the central nervous system, causing irreversible deficits of the visual pathway with unknown effective treatment.*
Purpose: *to investigate the efficacy of two original phototherapy programs on reversing the damage caused by multiple sclerosis to the neurophysiological functions of Optic nerves.*
Study Design*: Repeated measures randomized control trial.*
Materials and methods: *24 patients with relapsing-remitting multiple sclerosis, from both sexes completed the study, age 25-45 years; randomly assigned into four groups. 7 patients in the control group (1); received monthly Solu-Medrol. 6 Patients in group (2) received Solu-Medrol plus low intensity laser therapy LILT 850 nm. 6 patients in group (3) received Solu-Medrol plus broad band ultraviolet B radiation BB-UVBR (280-320 nm). 5 patients in group (4) received Solu-Medrol, scanner LILT and BB-UVBR; all three groups received sessions 3 days/week for 12 sessions. Visual evoked potentials (VEP) were assessed pre-treatment, post treatment, 3 months follow up.*
Results: *Highly significant improvement ($p=.009$) of the right Optic nerve was recorded in the BB-UVBR group, and was sustainable at follow up. Lesser improvements were recorded in the (LLLT+UVBR) group, VEP of the right eye showed significant improvement ($p=.022$). However; no statistically significant improvements were recorded between the four groups post treatment and at follow up ($p\geq0.05$).*
Conclusion: *BB-UVBR therapy solely has the potential to efficiently ameliorate the severity of disability status and reverse Optic neuritis, rather than LILT with a counterproductive role of the combination therapy.*
Key words: *Multiple Sclerosis, Phototherapy, Broad Band Ultraviolet B Radiation, Low Intensity Laser Therapy.*

Introduction

Multiple sclerosis (MS) affects 2.3 million people worldwide and is typically diagnosed with a peak onset between ages 20 and 40 [1, 2].MS is a chronic disease of central nervous system, characterized by dispersed foci of demyelination, and clinically multifocal symptoms, with a tendency to remitting and relapsing, which in the end, always leads to disability. The cause of the disease is unknown. Immunological mechanisms causing autoagression towards myelin sheaths in central nervous system are considered to be responsible for it [3-5].

Evoked potential tests measure the electrophysiologic responses of the nervous system to a variety of sensory stimuli, which is readily and non-invasively recorded[6, 7]. Of which the most clinically popular is the visual evoked potential (VEP) which can detect subclinical involvement of visual pathway in clinically definite MS with neither history of Optic neuritis or visual symptoms [8-9]. They are used primarily to measure the functional integrity of the visual pathways from retina via the optic nerves to the visual cortex of the brain [10, 11].

In MS, the pathological effect consists of axonal damage and loss in early stages of the disease; with no correspondence to the inflammatory autoimmune attack against myelin. Hence, axonal loss is directly related to permanent functional disability. These two consequences of the disease, even in its subclinical stages, are reflected in initial components of VEP, affecting its latency, amplitude, wave form or even affecting all of them [12, 13]. Affected Optic nerve with retrobulbar optic neuritis shows a delayed P100 component and over the years the VEP in patients with MS become progressively slower eventually attenuating in amplitude as demyelination increases [11].

Although the exact cause of multiple sclerosis (MS) is unknown, a number of genetic and environmental factors are thought to influence MS susceptibility. One potential environmental factor is sunlight and the subsequent production of vitamin D[14].Moreover, ultraviolet radiation, high levels of vitamin D_3 consumption and skin cancer were found to be inversely correlated with MS development and mortality risk[15-19].

Aside of stimulating vitamin D production, it is believed that UVR is likely suppressing disease independent of vitamin D production, and that vitamin D supplementation alone may not replace the ability of sunlight to reduce MS susceptibility [20].Whereas,local ultraviolet B (UVB) influences systemic immune reactions and attenuates systemic autoimmunity through induction of skin-derived tolerogenic dendritic cells and T regulatory cells [21].

On the other hand, low intensity laser therapy (LILT) has a wide range of medical applications, where protection from cell death, stimulation of healing and repair of injuries, reduction of pain, swelling and inflammation are needed [22]. Previous trials investigating the effect of light therapy in form of laser application to MS patients were conducted and showed objective clinical results obtained from patients suffering from multiple sclerosis as well as subjective improvement of their mental comfort and motive

power suggest that laser biostimulation is not only an alternative method of therapy of MS patients but also an effective method of rehabilitation in this so far incurable disease [23].

Phototherapy efficacy in reversing or ameliorating visual deficits suffered by patients with MS had never been challenged before in previous clinically applied research work. Therefore, our randomized controlled clinical trial is the first to test the efficacy of both low level laser therapy (LILT) and broad band ultraviolet B radiation (BB-UVBR) combined therapy in that arena.

Subjects and Methods:

Forty-Six patients with RRMS participated in this study. But only twenty-four patients completed the study. Patients were recruited from Neurology Department in Kasr Al-Ainy Hospital. Relapsing-Remitting Multiple Sclerosis diagnosed patients according to McDonald's Criteria [24]. Patients were selected while in remission state, and all signed written pre-treatment informed consent. The study was conducted in the Outpatient Clinic of the Faculty of Physical Therapy, Cairo University, through September 2013 to October 2014.

Patients were divided randomly into four groups (Control and three Study groups).

Group (1) Control group: 7 patients received monthly intravenous infusion of 1gm of Methylprednisolone (Solu-Medrol) as a drug therapy for MS. Group (2) Low Intensity Laser Therapy (LILT) group: 6 patients received Solu-Medrol in addition to scanner LILT 850 nm GaAlAs diode laser, on the cervical region for 10 minutes. Group (3) Ultraviolet B Radiation (UVBR) group: 6 patients received Solu-Medrol in addition to broad band BB-UVBR (280-320 nm), on the whole back region for 20 minutes. Group (4) (UVBR + LILT) group: 5 patients received Solu-Medrol in addition to scanner LILT on cervical region for 10 minutes, and then received BB-UVBR (280-320 nm) on the whole back for 20 minutes (using the same parameters of group 2 and 3), sessions in all study groups were 3 days/week (4 weeks) for 12 sessions.

The inclusion criteria were age range 25-45 years of both genders, in remission with ≤ 6 score on expanded disability status scale (EDSS), free from any systemic vascular, blood or neurological diseases, e.g. vasculitis, systemic lupus erythematosus, (SLE), diabetes, liver disease, kidney failure, heart failure, traumatic brain injury (TBI), cerebro-vascular accident (CVA), spinal cord injury, human immunosuppressive virus (HIV), hyperthyroidism, cancer or in risk of chemical or atomic radiation exposure. Skin types grade 3 or 4 that was free of any local or systemic comorbidity. Patients on antibiotics or photosensitizing drugs were weaned off for 21-30 days before joining the study. Pregnant patients and those allergic to phototherapy in addition to those who missed more than 3 successive sessions were excluded from the study.

Assessment Methods:

- EDSS according to Kurtzke[25].
- Evoked potentials and Electromyography (EMG) NIHON KOHDEN device (Model: JB 904 BK, 2007).

A-Testing procedures:

1. **Expanded disability scale (EDSS):**

The EDSS quantifies disability in eight Functional Systems (FS) and allows neurologists to assign a Functional System Score (FSS) in each of these FS; pyramidal, cerebellar, brain stem, sensory, bowel and bladder functions, visual, mental, and any other neurological findings due to MS[25]. Patients were referred to a neurologist for evaluation.

2. **Pattern reversal visual evoked potential**

- VEP examination was performed at the Clinical Neurophysiology Department, Kasr-Alainy Hospital. VEP was performed by NIHON KOHDEN device (Model: JB 904 BK, 2007)(fig.1).
- The recording electrode was placed 5cm mid occipital above the inion (Oz) and the reference electrode was placed over the mid-forehead (Fz) 11 cm above the nasion, and the ground one placed on the ear lobe according to the 10-20 international system of electrode application (fig.1). The stimulus used was an alternating checkerboard pattern. We stimulated each eye separately with a check size of 32^{o}with a stimulus rate at 1Hz. The patient was seated at a distance of 1 meter from the pattern stimulator and was asked to fix on a small spot placed in the center of the monitor.
- 100 stimuli were delivered then picked up by the recording electrodes then were summated and averaged.

B- Treatment procedures:

A. Low Intensity Laser Therapy (LILT):

Patients were positioned in a comfortable leaning forward sitting position, with foreheads rested on their hands to ensure straight cervical position. Then, the cervical region was rubbed by alcohol to minimize laser light reflection. LILT was applied using a calibrated ASA laser scanning device (He-Ne red laser 632.8 nm; 15 mW power as an aiming beam and GaAlAs diode laser, emitting near infrared wavelength (NIR) 850 nm, with total beam area (a) = 0.5 cm^2 (incident beam area = 0.01 cm^2 X 50 mm total width of the scanning beam). Pulsed wave (PW); pulse duration (PD) 50 ns (nanoseconds), frequency 2084 Hz, maximum power (Pmax) 10 W, calculated average power (AP) 0.00104 W. Radiant power 0.00208 W/cm^2, Radiant energy (Q) 2 J, Radiant exposure (E/a)act (4 J/cm^2).

The application site is determined by 3 points, one on C7 spinous process, and the two other points were situated 2.5 cm lateral to the C7 spinous process bilaterally. The LILT scanning started at the horizontal occipital line and ended at the C7 spinous process with a medium speed level. And 20±5 cm perpendicular distance from the laser aperture, while the patient is in a sitting position (fig.2).

B. Ultraviolet B Radiation (UVBR):

Using a calibrated Dr. Kern Quattro, Broad band (280-320 nm) UVB device, Patients were placed in a side lying position, with their back facing the UVBR device (fig.3). The back region was rubbed by alcohol to reduce UVR reflection. The BB-

UVBR (280-320 nm) was applied with a radiant power = 0.396 W/cm^2, and total sub-erythemal dose = 470 mJ/cm^2 on the whole back region from below the neck till the iliac crests from 100 cm distance perpendicularly from side lying, for 20 minutes (starting at 50% of the total dose (235 mJ/cm^2≈ 10 minutes for the first session), with an incremental increase of 10% of the total dose (47 mJ/cm^2≈ one minute increase/ session).

Follow Up:

All examinations were conducted once before the beginning of the s treatment programs, once at the end of the study time, and 3 months after the end of the study treatment program.

Primary outcome measure was VEP, secondary outcome was EDSS.

Statistical analysis:

Data was analyzed using IBM SPSS Advanced Statistics version 20.0 (SPSS Inc., Chicago, IL). Descriptive statistics were used for numerical data that were expressed as mean, standard deviation and range. The measured scales were tested for normality of distribution (Shapiro-Wilk test); all variables were found to be not normally distributed. Thus, nonparametric statistical tests were used to analyze the data. Kruskal Wallis Test was used for between groups analysis of variables, while Friedman Test was used for within group analysis.

Results:

Patients characteristics in the four groups were comparable at the baseline regarding Age (p=.482), BMI (p=.775), Duration of disease, and Sex (tab. 1).

1. Expanded disability status scale (EDSS)

For the Control Group (1); mean values of the disability status EDSS showed no significant difference (p=.135) from the baseline (3.4±1.6) to (3.4±1.6), (3.5±1.6) post treatment and at follow up; respectively. And also, for the LILT Group (2); mean values of the disability status EDSS showed no significant difference (p=.135) from the baseline (3±1.5) to (2.8±1.7), (2.8±1.7) post treatment or at follow up; respectively. While for the UVBR Group (3); mean values of the disability status EDSS showed significant decrease (p=.011) from the baseline (2.7±1.4) to (2±1.2), (1.8±1.1) post treatment and at follow up; respectively. Which was not the case for the LILT+ UVBR Group (4),where the mean values of the disability status EDSS showed non-significant improvement, though close, (p=.068) from the baseline (3±1.7) to (2.6±1.9) post treatment or (2.4±1.8) at follow up.

2. Bilateral visual evoked potential (VEP)

Results of the Control Group (1)

Regarding the mean values of P100 of the right eye (Optic nerve), it showed highly significant (p=.001) deterioration. It was (132±15.5) pre-treatment, (135.4±16) post treatment, and (139.8±18) at follow up. Also the left eye showed highly significant (p=.002) deterioration, as it was (128±26) pre-treatment, (132.4±30) post treatment, and (140.2±29) at follow up (tab.2).

Results of the LILT Group (2)

Regarding the mean values of P100 of the right eye (Optic nerve), it showed improvement, though non-significant one (p=.223). Where, it was (133.5±15) pre-treatment, dropped to (125±17.3) post treatment, but rose again to (127.2±23.2) at follow up. Also the left eye showed non-significant (p=.115) improvement. As it was (139±25.6) pre-treatment, dropped to (130.3±25) post treatment, but rose again to (136.5±30.4) at follow up (tab.3).

Results of the UVBR Group (3)

Considering the mean values of P100 of the right eye (Optic nerve), it showed a highly significant improvement (p=.009). It was (131.2±29.3) pre-treatment, dropping to (121±30) post treatment, and (122.6±30) at follow up. However; the left eye showed non-significant (p=.115) improvement. It was (130±26.9) pre-treatment, dropping to (120±32.3) post treatment, but rose again to (135.3±35.3) at follow up (tab.4).

Results of the LILT+ UVBR Group (4)

Considering the mean values of P100 of the right eye (Optic nerve), it showed significant improvement (p=.022). It was (138±9.7) pre-treatment, then dropped to (130±9.6) post treatment, and (119.7±6) at follow up. However; the left eye showed non-significant (p=.165) improvement, It was (127±11.6) pre-treatment, rose to (132.3±8.7) post treatment, and dropped again to (123.5±14.6) at follow up, (tab.5).

Table (1): Demographic characteristics of patients

VARIABLES	GROUPS	N	X±SD	MIN-MAX	P-VALUE
Age (years)	Group (1)	7	31±5.7	25-43	.482
	Group (2)	6	31.3±7.2	25-45	
	Group (3)	6	30.8±3.6	25-34	
	Group (4)	5	35.4±6.9	26-44	
Duration (years)	Group (1)	7	7.5±4.5	2-15	---
	Group (2)	6	6.5±4.2	1-12	
	Group (3)	6	6.5±5.7	1-15	
	Group (4)	5	6.7±6.6	1-16	
BMI	Group (1)	7	25±3.3	20-31	.775
	Group (2)	6	25.2±4.7	19-32	
	Group (3)	6	26.3±5.6	19-33	
	Group (4)	5	23±2.8	20-26	
Sex No. (Male/Female)	Group (1)	7	4/3		---
	Group (2)	6	2/4		
	Group (3)	6	2/4		
	Group (4)	5	2/3		

Table (2): Mean values of P100 latencies of VEP for both eyes, pre-treatment, post-treatment, and at follow up for group (1).

VEP	Pre-treatment		Post-treatment		Follow up		P- Value
	X±SD	Min-Max	X±SD	Min-Max	X±SD	Min-Max	
Right Eye P100 (ms)	132±15.5	111.6-157	135.4±16	117.9-160	139.8±18	121-168	.001**
Left Eye P100 (ms)	128±26	78-154	132.4±30	71-158	140.2±29	82-161	.002**

X=Mean, SD=Standard deviation, Min= Minimum value, Max= Maximum value, ms= millisecond.
*= Significant difference (p< 0.05), **= highly significant difference (p< 0.000).

Table (3): Mean values of P100 latenciesof VEP for both eyes, pre-treatment, post-treatment, and at follow up for group (2).

VEP	Pre-treatment		Post-treatment		Follow up		P- Value
	X±SD	Min-Max	X±SD	Min-Max	X±SD	Min-Max	
Right Eye P100 (ms)	133.5±15	110-150	125±17.3	102-146	127.2±23.2	98.7-161	.223
Left Eye P100 (ms)	139±25.6	105-176.4	130.3±25	96.6-170	136.5±30.4	95-180	.115

X=Mean, SD=Standard deviation, Min= Minimum value, Max= Maximum value, ms= milliseconds.
*= Significant difference (p< 0.05), **= highly significant difference (p< 0.000).

Table (4): Mean values of P100 latencies of VEP for both eyes, pre-treatment, post-treatment, and at follow up for group (3).

VEP	Pre-treatment		Post-treatment		Follow up		P- Value
	X±SD	Min-Max	X±SD	Min-Max	X±SD	Min-Max	
Right Eye P100 (ms)	131.2±29.3	90.4-180	121±30	87.6-171	122.6±30	83.2-173	.009**
Left Eye P100 (ms)	130±26.9	85.2-165	120±32.3	80-174	135.3±35.3	67.6-188	.115

X=Mean, SD=Standard deviation, Min= Minimum value, Max= Maximum value, ms= milliseconds.
*= Significant difference (p< 0.05), **= highly significant difference (p< 0.000).

Table (5): Mean values of P100 latenciesof VEP for both eyes, Pre-treatment, post-treatment, and at follow up for group (4)

VEP	Pre-treatment		Post-treatment		Follow up		P- Value
	X±SD	Min-Max	X±SD	Min-Max	X±SD	Min-Max	
Right Eye P100 (ms)	138±9.7	116.5-143	130±9.6	118-138	119.7±6	111-126.9	.022*
Left Eye P100 (ms)	127±11.6	110-142.2	132.3±8.7	118-139	123.5±14.6	108-138.3	.165

X=Mean, SD=Standard deviation, Min= Minimum value, Max= Maximum value, ms= milliseconds.
*= Significant difference (p< 0.05), **= highly significant difference (p< 0.000).

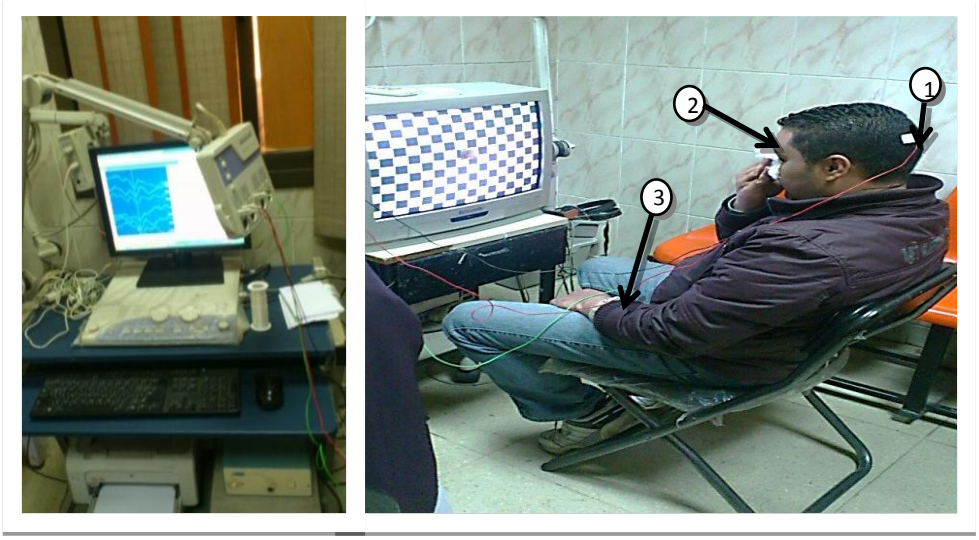

Figure1. Procedures ofthe Visual evoked potential (VEP) examination. Where, 1: The recording electrode was placed 5 cm mid-occipital above the inion (Oz), 2: The reference electrode was placed over the mid-forehead (Fz), 3: the ground electrode was placed on the wrist.

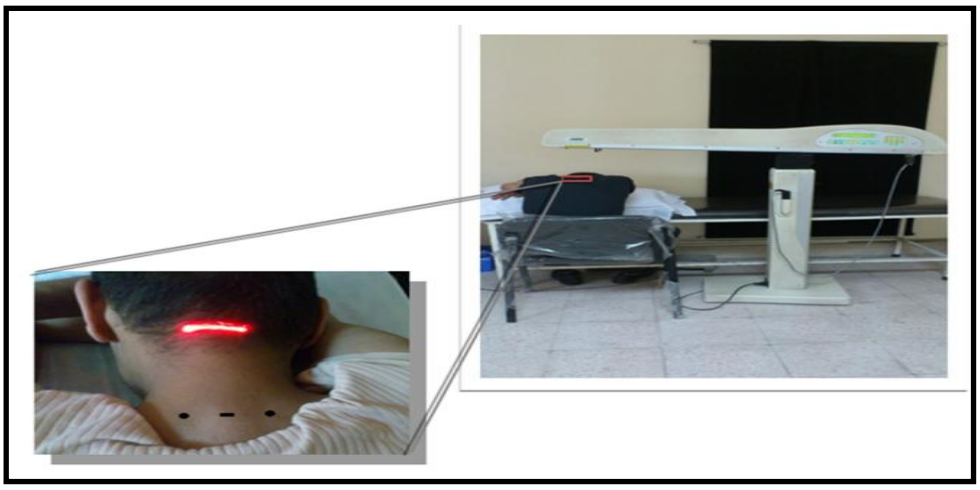

Figure2. LILT application using the ASA laser scanning device. The application site is determined by 3 points, one on C7 spinous process, and the two other points were situated 2.5 cm lateral to the C7 spinous process bilaterally. The scanning started at the horizontal occipital line and ended at the C7 spinous process.

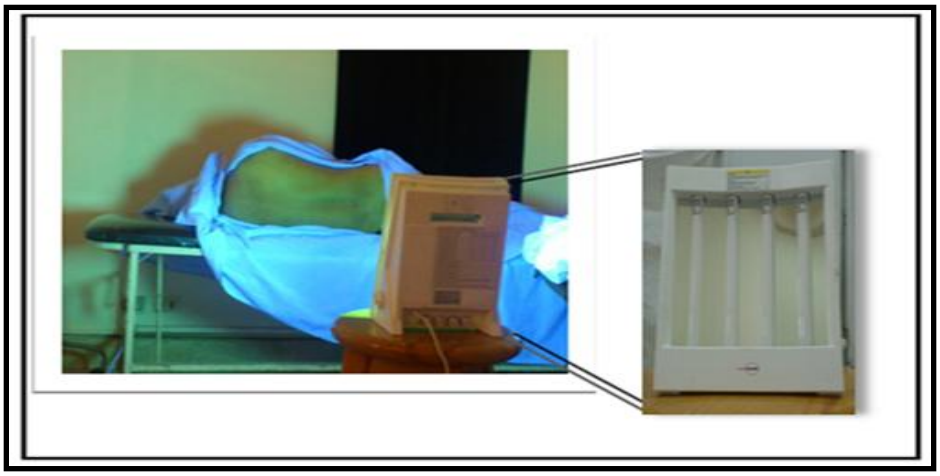

Figure3. BB-UVB radiation for the patient's back from below the neck to the iliac crest, while in side lying position with all other body parts covered and eyes protected by the UVB goggles.

Discussion

This study was conducted to investigate the efficacy of using the combined therapy of low intensity laser therapy (LILT) and ultraviolet B radiation (UVBR) of novel, and premeditated energy doses to achieve the targeted depth and photochemical responses required to tackle the underlying etiologies (Autoimmunity triggered by vitamin D_3 deficiency, and vascular deficits that cause decreased total cerebral blood volume) of relapsing-remitting multiple sclerosis.

For these purposes, electrophysiological studies (visual evoked potentials (VEP) for Optic nerves, expanded disability scale (EDSS) were used.

Photobiomodulation using light in the near-infrared (NIR) range (630-1100 nm) with low-energy lasers has shown a therapeutic effect in various clinical conditions, with a penetration depth up to 50 mm [26,27]. Its mechanism of action is believed to be through activation of cellular photoacceptors (cytochrome C oxidase; localized in the mitochondrial respiratory chain which is a key molecule in the electron transport chain leading to production of ATP) and subsequent activation of transcription factors leading to improved energy metabolism and mitochondrial function [28-31].

LILT of 670 nm, 5 J/cm^2 for 3 min, at a power intensity of 28 mW/cm^2, showed more sustained effectiveness in ameliorating disease severity of EAE in C57BL/6 Mice through the down-regulation of pro-inflammatory cytokines (interferon-c, tumor necrosis factor-a) and up-regulation of anti-inflammatory cytokines (IL-4, IL-10) in vitro and in vivo [32]. This was also confirmed in-vitro by Song et al [33].

Moreover, LILT exerts both local and systemic circulatory, and neuroprotective effects, as it increases blood flow locally and remotely from the application site through manipulating the autonomic nervous system; maintaining homeostasis of the internal environment [34, 35].Which could benefit patients with MS, as cerebral blood perfusion was reported to be reduced [36].

In the current study we used a longer wave length NIR (850 nm), in pulsed wave (PW), Radiant energy (Q) 2 J, Radiant exposure $(E/a)_{act}$4 J/cm^2 to ensure deeper penetration with minimum attenuated energy level [27]and reach the vertebral arteries in the cervical region to induce the targeted photochemical reaction of LILT; improving cerebral blood flow and supplying more energy ATP to neural tissues to promote its recovery [37,38]. Also, benefit from the possibility of the bioresonance occurring between the frequency of the light pulses and the neuronal electromagnetic frequency which in some way may explain a number of the beneficial results with LILT using true pulsed light [39].

Another type of phototherapy commonly used in dermatology is Broad Band Ultraviolet B Radiation (BB-UVBR) with wavelengths of 290-320 nm. BB-UVBR with a peak at 298 nm can supply 90-95% of body requirements of vitamin D, other than diet supplements [40,41]. Also it has beneficial potentials in reducing the morbidity associated with systemic immune disorders including multiple sclerosis. It is not dependent on circulating levels of 25(OH)D; which support that vitamin D_3 synthesis is not essential for mediating the immunosuppressive effects of UVBR[42,43].

Within the limitations of this study, no significant differences of VEP and EDSS were recorded between groups; pre-treatment, post treatment, and at follow up. However; important and significant changes were recorded within groups regarding these measures.

Clinically, the severity of disability scale EDSS for group (1) showed insignificant (p=.135) differences from the baseline to post treatment and follow up. Also, in group (2) there were no significant improvement (p=.135) of the disability scale EDSS from the baseline to post treatment and follow up. That may be attributed to inefficient dosage of the LILT program or the sample size was not enough to show significance as the one reported in Peszyñski-Drews et al. (2003)study, as they reported a significant 1 point decrease in EDSS after LILT for patients with primary and secondary progressive MS [23].

In contrast, in group (3) the disability scale EDSS showed significant improvement (p=.011) from the baseline to post treatment and follow up, which may be due to UVBR immune-modulatory and anti-inflammatory effects [44, 45).

Group (4) also showed improvement of the disability scale EDSS, though non-significant (p=.068) from the baseline to post treatment and follow up. That may indicate the possible counterproductive role of combining LILT to UVBR program.

Moving to the electrophysiological results, where P100 prolonged latency was used to quantify visual pathway defects as it's the most reliable

and consistent measure of the optic nerve response; being least affected by technical factors and degree of patient cooperation [46]. In control group (1); VEP of the right and left eyes showed significant deterioration (p=.001, .002; respectively) and the same percentages of patients with affected Optic nerves P100≥ 100 ms were 100%, and 85.7% of the right and left eyes; respectively unchanged post treatment or at follow up. That is mostly attributed to the inflammatory autoimmune attack against myelin and axons posed by MS [10,12, 13].

For the LILT group (2), VEP of the right and left eyes showed improved (P100 latency less than 100ms) response, though non-significant (p=.223, .115; respectively). While the percentages of patients with evident Optic neuritis of the right and left eye were the same 100% pre-treatment, and post treatment, but dropped to 83.3% at follow up. What indicates that the light intensity used in this study reached the threshold value I_0 to produce biostimulatory effects on the CNS [47], stimulating healing of deeper nerves [48] reducing inflammation [49],and sustaining its effect on a relatively long-term level.

Regarding the results of the UVBR group (3) VEP of the right eye (Optic nerve), it showed a highly significant improvement (p=.009). The mean latency of P100 decreased post treatment, which was sustainable at follow up. That may be attributed to immunomodulatory and neurotrophic effects of UVBR and its induced vitamin D_3[50,44, 45, 51].However; the left eye showed non-significant (p=.115) improvement, which might need a longer follow up period and larger size study to show significance.

While, percentages of patients with evident Optic neuritis of the right and left eyes were 83.3% pre-treatment, dropped to 66.7% post treatment, but rose again to 83.3% at follow up which indicate fast and efficient potentials of UVBR in repairing chronic deficits of visual acuity, which is not offered by the standard treatment by intravenous corticosteroids, not to mention its systemic side effects [52, 53].

Surprisingly, lesser improvements were recorded in the (LILT+UVBR) group (4), where the VEP of the right eye showed significant improvement (p=.022); the mean latency of P100 decreased post treatment and kept decreasing throughout the follow up period. Also, as in group (3), non-significant (p=.165) improvement of the left eye as in group (3) was recorded. But the percentages of patients with evident Optic neuritis of the right and left eyes were 100% pre-treatment, that stayed the same post treatment, and at follow up; indicating an undermining effect of combining LILT to UVBR .

The body of evidence lack and require clinical randomized control studies to propose save and efficient doses of UVB for chronic use in clinical practice to induce systemic immunosuppression for patients with RRMS; to avoid the unsubstantiated carcinogenicity risk of using skin application of both narrow and broad band UVB on the long term [20, 43, 54, 55]. As no melanoma cancer was correlated to long term of either type of UVB radiation so far [56].

Hereby, our study offered two novel supplemental phototherapy programs that give fast and relatively long-term relief of MS symptoms; and hopefully better work endurance with better visual acuity that eventually could improve quality of life for patients with RRRM, where no pharmacological intervention (immune-suppressant, immunomodulating drugs, or Amantadine) is solely efficient enough for that task without conjoint rehabilitation (exercise, energy or fatigue self-management education) [57, 58].

Conclusion

Our preliminary findings suggest that BB-UVBR therapy solely has the potential to efficiently ameliorate the severity of disability status and reverse Optic neuritis, rather than LILT with a counterproductive role of the combination therapy. Also, larger randomized controlled studies using the same doses of UVBR and LILT or other modified doses for different skin types are needed for more conclusive results and clinical implementation.

Implementations

1) The findings of the current study suggest that UVBR or LILT proposed treatment programs should be included in the treatment of individuals with relapsing-remitting multiple sclerosis as supple-mental immunomodulatory therapies.
2) The findings of the current study suggest that UVBR has a potent and relatively fast ameliorating effect on severity of disability that consequently improving the activities of daily life and physical work capacity.
3) The findings of the current study suggest that UVBR can efficiently reverse the chronically damaged Optic nerves in a short period of time and sustain changes for a relatively long term; providing a new hope for better visual acuity for patients with MS.

Conflicts of Interest

Authors state no conflicts of interest.

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