Journal of Advances in Medicine and Medical Research

34(23): 35-43, 2022; Article no.JAMMR.92512
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Evaluation of the Effect of Low Level Laser Therapy in the Treatment of Stable Vitiligo

Hadeer M. Mostafa [a*], Esraa E. El Hawary [a], Shereen F. Gheida [a] and Elham M. Kassem [a]

[a] Dermatology and Venereology Department, Tanta University, Tanta, Egypt.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2022/v34i234837

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/92512

Original Research Article

Received 07 August 2022
Accepted 10 October 2022
Published 22 October 2022

ABSTRACT

Background: Vitiligo is a chronic cutaneous disease characterized by hypo- or depigmented patches that leave psychological impact on the patients. New treatment modalities have been developed to shorten the duration of treatment of vitiligo with fewer side effects.
Objective: To evaluate the effect of low-level laser therapy (LLLT) in the treatment of stable vitiligo.
Patients and Methods: The study included 20 stable vitiligo patients with overall symmetrical lesions. For each patient, one site was treated with LLLT & NB-UVB twice weekly for 3 month.
Results: There was statistically significant improvement in the re-pigmentation, 25% of patients showed excellent improvement, 40% of patients showed good improvement, 20% of patients showed moderate improvement, 10% of patients showed poor improvement and 5% of patients showed no improvement after 3 months therapy. Side effects were minimal and transient in both sides.
Conclusion: LLLT in combination with NB-UVB therapy could be considered as safe and tolerable technique for treatment of vitiligo. Longer follow up is needed.

Keywords: Low level laser therapy; NB-UVB therapy; vitiligo.

**Corresponding author;*

1. INTRODUCTION

Vitiligo is an acquired disorder of pigmentation, characterized by selective loss of melanocytes that can affect skin, mucous membranes, inner ear and leptomeninges [1]. The classical clinical presentation of vitiligo is hypo- or depigmented, discrete or coalescing, macules or patches that are surrounded by normal skin [2]. Vitiligo is the most common skin pigmentary disorder and affects approximately 0.5%-2% of the world's population [3].

Vitiligo can be classified into three major forms as 1) nonsegmental vitiligo including acrofacial, mucosal, generalized universal, mixed, 2) segmental vitiligo, and 3) unclassified/undetermined vitiligo [4].

The exact pathogenesis of vitiligo is not clear, many pathological factors are involved including genetic factors, autoimmunity, mutations and altered cellular environment [5]. The precipitating factors may include environmental factors, sunburn, pregnancy, stress, exposure to cytotoxic compounds, oxidative stress and trauma [6].

Many treatment options are available for vitiligo as topical, physical, systemic and surgical modalities [7]. Topical treatments include corticosteroids, calcineurin inhibitor and vitamin D analogues. Phototherapy includes psoralens with ultraviolet A (PUVA), narrow band ultraviolet B (NB-UVB) and excimer laser. Systemic treatments include oral corticosteroids, immunosuppressive agents as methotrexate, azathioprine and cyclosporine. Surgical treatments as epidermal grafting, punch grafting, cultured melanocyte grafting, and others may also be used [7-9].

"Narrow band ultraviolet B refers to a specific wavelength of ultraviolet radiation ranging from 311 to 312 nm. NB-UVB is used in the treatment of many skin diseases including psoriasis, atopic eczema, pruritus, lichen planus, polymorphous light eruption and early cutaneous T-cell lymphoma. There are two main steps by which NB-UVB exerts its effects in treatment of vitiligo. The first is stabilization of the depigmenting process and the second is stimulation of the residual follicular melanocytes" [10].

"Narrow band ultraviolet B is an office-based treatment that may require more than one year for its completion. Some patients may find this long duration of therapy inconvenient due to social and financial reasons" [11].

Low level laser (LLL) is considered a low-energy laser; this means that when applied to the skin, not confer a thermal effect but acts by exerting biostimulatory effects [12]. "LLL has potential therapeutic applications in rheumatoid arthritis, wound healing, post herpetic neuralgia and recovery following nerve injury" [13]. In dermatology it has been applied in some skin disorders as androgenic alopecia [14], acne [15], psoriasis [16] and vitiligo [17]. "Regarding vitiligo, LLL induces locomotion of immature melanoblasts and promotes melanogenesis of differentiated melanoblasts *In vitro*" [17].

2. METHODOLOGY

The present study was carried on 20 patients with vitiligo of different age groups. diagnosis was based on clinical appearance of skin lesions and confirmed by Wood`s light examination. All patients were selected from the Outpatient Clinic of Dermatology and Venereology Department of Tanta University Hospital.

Inclusion criteria:

1. Patients diagnosed with stable vitiligo (VIDA=zero).
2. Patient who didn't receive any treatments for vitiligo at least one month before starting the treatment protocol.
3. Patients who will accept to be included in the study and sign written informed consent and ready for regular follow-ups and photographs.

Exclusion criteria:

1. Patients with other autoimmune diseases (such as thyroid disease, Addison's disease, pernicious anemia, insulin-dependent diabetes mellitus and alopecia areata).
2. Contraindications to phototherapy as photosensitivity skin disorders as xeroderma pigmentosa, lupus erythematosus and patients with personal or family history of skin cancer.
3. Contraindications to low level lasers as skin cancer, pregnancy and epilepsy.
4. Chronic systemic diseases (such as severe renal failure, severe respiratory insufficiency, severe anemia, congestive heart failure and chronic liver insufficiency).
5. Pregnant and lactating female.

- Patients seated comfortably and wore specific goggles (Endolaser- 422 Extra quality) to protect their eyes.
- The selected lesion was treated with low level pulsed diode 905 nm wavelength (ENDOLASER 422 – Enraf-Norius®, Netherland) for 2 minutes / cm2 of the affected patch with the dose 3 j/cm2, 5000HZ frequency.
- Laser probe was 100 mW, pulsed infrared diode with peak power of 100 W.
- The probe was in close contact with the skin and passed in a series of circles in close contact with each other toward the center till the total area was treated.
- Time of session was 20 minutes.
- Patients received LLLT session at the same day directly before receiving NB-UVB session.
- Phototherapy was received via eight NB fluorescent tubes (Philips TL 100 W/01; Philips BV, Eindhoven, the Netherlands) with a spectrum of 310–315 nm and a maximum wavelength of 311 nm were installed in a Waldmann UV-1000 unit (Waldmann GmbH, Schwenningen, Germany).
- Patients received NB-UVB therapy session twice weekly at the same day after receiving LLLT session until improvement occurs or for a maximum 3 months (24 sessions), starting with a dose of 0.21 J/cm2 independent of skin type and increased by 20% every session until we reached the MED. The patient's erythema was evaluated with every clinic visit. No NB-UVB exposure was allowed if erythema was still present before the session.
- During the NB-UVB sessions, the affected parts were exposed with the eyes protected by UV-blocking goggles. If the eyelids were the areas to be treated, patients were instructed to keep their eyes closed during exposure without wearing goggles.
- The patients were followed up for another 3 months after the last session.

2.1 Evaluation of the Treatment

It was done by

1- Evaluation of re-pigmentation

Photographs were taken at baseline and monthly before each session during the course of treatment using Canon camera 13 Mega Pixels and then monthly for 3 months after. Evaluation of re-pigmentation was done by 2 ways; three blinded dermatologists and visual analogue system score.

❖ **Three blinded dermatologists:**

Evaluation of repigmentation according to the mean opinion of three blinded dermatologists was expressed qualitatively as the following [18]:

- No change (0%),
- Poor (1 –25%),
- Moderate (26–50%),
- Good (51 –75%),
- Excellent (76–99%),
- Complete regimentation (100%)

❖ **Visual analogue system score (VAS) [(180)]:**

Visual analogue system score was used as follows:

- 0-25% — Poor response (Grade I).
- 26-50% — Fair response (Grade II).
- 51-75% — Good response (Grade III).
- 76-100% — Excellent response (Grade IV)

2- Patient satisfaction

The degree of improvement according to the patient opinion; the patients were asked at the final visit about the overall satisfaction according to whether the patient not satisfied, slightly satisfied, satisfied or very satisfied.

3. RESULTS

❖ **Assessment of the efficacy of the therapeutic procedures**

1. **Regarding the three-dermatologist assessment:** The percentage of improvement ranged from 0 -100% with a mean of 68.2650 ±.41 and a median of 70.0%.

   This percentage was graded as follows one patient (5%) showed no improvement, 2 patients (10%) showed poor improvement, 4 patients (20%) showed moderate improvement, 8 patients (40%) showed good improvement and 5 patients (25%) showed excellent improvement.

2. **Regarding visual analogue system (VAS) score:** The grading ranged from 1-4 with mean 3.15 ± 0.88 and median 3.

3. **Regarding patient satisfaction:** One patient (5%) was not satisfied, 3 patients (15%) were

slightly satisfied, 7 patients (35%) were satisfied, and 9 patients (45%) were very satisfied.

4. **Regarding the pattern of re-pigmentation:** There were 10 patients (50%) with marginal pattern of re-pigmentation and 9 patients (45%) with follicular pattern of re-pigmentation.

5. **Evaluation of the safety and tolerability of the therapeutic procedure regarding the side effects:** 10% of patients showed marked erythema that lasted for more than 48 hours and required topical steroid treatment, 5% of patients showed burn like lesion at small site. Adjustment of dose of NB-UVB took place. No further side effects appeared through course of the disease, there was no recurrence reported during period of follow up.

6. **Relation between the degree of improvement and the clinical data of the patients:** There was no statistically significant relation between the degree of improvement and gender (p=0.290), age (p=0.630), family history (p=1.000), skin type (p=1.000), the duration of the disease (p=0.233), the type of vitiligo (p=0.165) or the site of the lesions (p=0.378).

7. **Relation between degree of improvement according to the assessment of three dermatologists committee with patient satisfaction and VAS score:** There was a significant relation between the degree of improvement assessed by three dermatologists committee and the patient satisfaction (p=0.032) and the visual analogue system (VAS) score (p=0.006).

8. **Correlation between the percentage of improvement according to the assessment of three dermatologists committee with the percentage of VAS score:** There was statistically positive correlation between the percentage of improvement and the percentage of VAS score (r =0.667, p =0.001).

9. **Correlation between degree of improvement with age and duration of vitiligo:** There was no correlation between the Degree of improvement with age (years) and duration of vitiligo (years).

Table 1. Three-dermatologist assessment

	LLLT/NB-UVB (n = 20)	
	No.	**%**
Degree of improvement		
No	1	5.0
Poor	2	10.0
Moderate	4	20.0
Good	8	40.0
Excellent	5	25.0
Percentage of improvement		
Min. – Max.	0.0 – 100.0	
Mean ± SD.	68. 2650 ±.41	
Median (IQR)	70.0 (50.0 – 90.0)	

MH: Marginal Homogeneity Test; Z: Wilcoxon signed ranks test

Table 2. Visual analogue system (VAS) score

VAS	LLLT/NB-UVB (n = 20)	
	No.	**%**
1	1	5.0
2	3	15.0
3	8	40.0
4	8	40.0
Min. – Max.	1.0 – 4.0	
Mean ± SD.	3.15 ± 0.88	
Median (IQR)	3.0 (3.0 – 4.0)	

IQR: Inter quartile range; SD: Standard deviation; MH: Marginal Homogeneity Test; Z: Wilcoxon signed ranks test

Table 3. Patient satisfaction

Patient satisfaction	LLLT/NB-UVB (n = 20)	
	No.	%
Not satisfied	1	5.0
Slight satisfied	3	15.0
Satisfied	7	35.0
Very satisfied	9	45.0

MH: Marginal Homogeneity Test

Table 4. Pattern of re-pigmentation

Pattern of regimentation	No.	%
No	1	5.0
Follicular	9	45.0
Marginal	10	50.0

Table 5. Safety and tolerability of the therapeutic procedure

Side effects	LLLT/NB-UVB (n = 20)	
	No.	%
Erythema lasting more than 48 hours	2	10
Burn like lesion	1	5

Table 6. Relation between the degree of improvement and the clinical data

	Degree of improvement (LLLT/NB-UVB)								Test of Sig	P
	No + poor (n = 3)		Moderate (n= 4)		Good (n = 8)		Excellent (n = 5)			
	No.	%	No.	%	No.	%	No.	%		
Gender										
Male	1	33.3	2	50.0	2	25.0	4	80.0	χ^2= 3.896	^{MC}p= 0.290
Female	2	66.7	2	50.0	6	75.0	1	20.0		
Age (years)										
<30	3	100.0	3	75.0	6	75.0	5	100.0	χ^2= 2.128	^{MC}p= 0.630
>30	0	0.0	1	25.0	2	25.0	0	0.0		
Min. – Max.	5.0 – 20.0		15.0 – 50.0		10.0 – 47.0		6.0 – 17.0		H= 7.183	0.066
Mean ± SD.	11.67 ± 7.64		27.0 ± 15.90		20.13 ± 13.01		10.20 ± 4.66			
Median	10.0		21.50		14.50		8.0			
Family history										
Negative	2	66.7	3	75.0	5	62.5	4	80.0	χ^2= 0.881	^{MC}p= 1.000
Positive	1	33.3	1	25.0	3	37.5	1	20.0		
Skin type										
III	1	33.3	2	50.0	4	50.0	2	40.0	χ^2= 0.667	^{MC}p= 1.000
IV	2	66.7	2	50.0	4	50.0	3	60.0		
Duration of vitiligo (years)										
Mean ± SD.	1.0 – 3.0		2.0 – 12.0		1.0 – 5.0		1.0 – 7.0		H=4.273	0.233
Mean ± SD.	2.33 ± 1.15		4.75 ± 4.86		3.88 ± 1.36		2.40 ± 2.61			
Median	3.0		2.50		4.0		1.0			
Type of vitiligo										
Generalized	2	66.7	3	75.0	8	100.0	5	100.0	χ^2= 4.056	^{MC}p= 0.165
Acral	1	33.3	1	25.0	0	0.0	0	0.0		
Site of vitiligo										
Extremities	0	0.0	2	50.0	5	62.5	2	40.0	χ^2= 9.416	^{MC}p= 0.378
Trunk	2	66.7	1	25.0	3	37.5	2	40.0		
Acral	1	33.3	1	25.0	0	0.0	0	0.0		
Face	0	0.0	0	0.0	0	0.0	1	20.0		

*χ^2: Chi square test; MC: Monte Carlo; H: H for Kruskal Wallis test; p: p value for comparing between different parameters; *: Statistically significant at p ≤ 0.05*

Table 7. Relation between degree of improvement according to the assessment of three dermatologists committee

	Degree of improvement (LLLT/NB-UVB)								Test of sig.	P
	Poor (n = 3)		Moderate (n= 4)		Good (n = 8)		Excellent (n = 5)			
	No.	%	No.	%	No.	%	No.	%		
Patient satisfaction										
Not satisfied	1	33.3	0	0.0	0	0.0	0	0.0	χ^2= 14.146*	MCp= 0.032*
Slight satisfied	2	66.7	1	25.0	0	0.0	0	0.0		
Satisfied	0	0.0	1	25.0	5	62.5	1	20.0		
Very satisfied	0	0.0	2	50.0	3	37.5	4	80.0		
VAS										
1	1	33.3	0	0.0	0	0.0	0	0.0	χ^2= 16.085*	MCp= 0.006*
2	2	66.7	1	25.0	0	0.0	0	0.0		
3	0	0.0	3	75.0	4	50.0	1	20.0		
4	0	0.0	0	0.0	4	50.0	4	80.0		
Min. – Max.	1.0 – 2.0		2.0 – 3.0		3.0 – 4.0		3.0 – 4.0		H= 12.288*	0.006*
Mean ± SD.	1.67 ± 0.58		2.75 ± 0.50		3.50 ± 0.53		3.80 ± 0.45			
Median	2.0		3.0		3.50		4.0			

*χ^2: Chi square test; MC: Monte Carlo; H: H for Kruskal Wallis test; p: p value for comparing between different parameters; *: Statistically significant at p ≤ 0.05*

Table 8. Correlation between the percentage of improvement according to the assessment of three dermatologists committee

VAS	Percentage of improvement	
	r_s	P
LLLT/NB-UVB	0.667	0.001*

*r_s: Spearman coefficient; *: Statistically significant at p ≤ 0.05*

Table 9. Correlation between degree of improvement with age and duration of vitiligo

	Degree of improvement	
	r_s	P
Age (years)	-0.314	0.178
Duration of vitiligo (years)	-0.098	0.681

4. DISCUSSION

"Vitiligo, a common depigmenting skin disorder, has an estimated prevalence of 0.5–2% of the population worldwide and up to 1.2% in Egypt" [19]. "The disease is characterized by the selective loss of melanocytes which results in typical non-scaly, milky-white macules" [19]. The exact pathogenesis of vitiligo is not clear, many pathological factors are involved including genetic factors, autoimmunity, mutations and altered cellular environment [20].

Several treatment modalities are available: each having certain indications and limitations [21,22]. "The treatment can be broadly classified under medical and surgical modalities. A combination of traditional and newer treatments may work synergistically to provide additional improvement in patients' disease state, quality of life and reduce the potential side effects" [23].

"Low level laser treatment has been shown to be a safe and effective treatment modality for patients with vitiligo" [24].

This study included 20 patients with stable vitiligo. One site received LLLT & NB-UVB. The procedure was repeated twice weekly for every patient until improvement occurred or for a maximum 3 months (24 sessions).

To our knowledge, this is the first study that uses LLLT followed by NB-UVB in treatment of vitiligo at different body sites.

The present study showed better results than that the study of Mandel et al. [25] that involved "18 vitiligo patients, in which the LLLT exposure was administered five times per week without NB-UVB sessions for 10 minutes for 6–8 months. In their study, repigmentation was seen in 63.9% of patients and some follicular repigmentation

was seen in 34.4% of patients versus current study in which repigmentation was seen in 95% of patients and follicular repigmentation was seen in 45% of patients. This difference can be explained by the synergistic effect of NB-UVB when added to LLLT sessions in the current study".

On the other hand, Wu et al. [26], work included "forty patients with stable stage segmental vitiligo on the head and/or neck where they used LLLT locally at 3.0J/cm2 with point stimulation once or twice weekly. The majority exhibited initial repigmentation at the edges (perilesional repigmentation) after receiving an average of 17±10 treatments". They had much higher number of total sessions reaching 190 sessions to achieve their results.

AlGhamdi et al. [27] studied the "invitro effects of LLLT using different lasers (red/blue) and ultraviolet light on human melanocyte viability, proliferation and migration. Their study showed that LLLT significantly enhanced the viability, proliferation and migration of normal cultured human melanocytes".

The mechanism by which LLLT induces the repigmentation of vitiligo include improving mitochondrial function, and increasing ATP synthesis and oxygen consumption, which leads to cellular regenerative pathways [28]. "LLLT induces the activation and proliferation of the melanocyte precursors, followed by their upward migration onto the nearby epidermis to form perifollicular pigment islands" [29].

"In addition, LLLT causes a significant increase in bFGF release from both keratinocytes and fibroblasts. It also produces a significant increase in NGF release from keratinocytes. BFGF is a putative melanocyte growth factor, whereas NGF is a paracrine which plays an important role in melanocyte survival in the skin" [24].

One of the findings in the current study was that no marked adverse effects were reported in the sites treated with LLLT when combined with NB-UVB. Erythema was reported in 2 patients (10%) and burn like lesion in one patient (5%) on both treatment sites. As those side effects were reported in both treatment sites of the patients they could be attributed to NB-UVB not to LLLT. Zheng et al. [30] reported that; "unlike therapy with ultraviolet light, LLLT did not result in erythema, bullous formation or hyperpigmentation. In addition, long-term LLLT treatment of periocular vitiligo lesions did not lead to any impairment in visual acuity, even if no eye protection equipment was worn during therapy" [30].

In the present study, there was no significant relation between degree of improvement and duration of vitiligo and this agreed with Tallab et al. [31], Hamzavi et al. [32]. However, in other studies as those reported by Kapoor et al. [33], Anbar et al. [18], they found that the duration of the disease was inversely correlated with the repigmentation percentage. This may be explained by the exhaustion of the melanocyte storage present in the outer root sheath of the hair follicle with time elapsed [34].

Like our study, Wu et al. [26] concluded that there was no significant difference between the early-onset (≤ 12 years old) and late-onset (> 12 years old) groups in terms of treatment response.

Acral vitiligo is considered a comparatively treatment resistant form of vitiligo. It showed a lower response to medical therapies; hence surgical options have more commonly been used for in this variant of vitiligo [35]. However, the present study showed that there was insignificant relation between type of vitiligo and degree of improvement. This can be attributed to small number of cases of acral vitiligo only 2 patients (10%) of the current study.

Various laser types were investigated for their efficacy in treatment of vitiligo eighter alone or in combination with other modalities. Doghaim et al. [36] confirmed the superior results of fractional CO2 laser when combined with NB-UVB. While Shin et al. [37] proved that "combined treatment of NB-UVB and excimer laser in vitiligo may enhance the treatment response without remarkable side effects, therefore might also increase the compliance of the patients to the treatment". In addition; Yan et al. [38] combined "Er: YAG (2940 nm) with topical betamethasone and NB-UVB for resistant NSV and reported that Er: YAG resurfacing has many obstacles as difficulty in regulation of the resurfacing depth and wound care, and possibility of scars due to excessive skin injury despite the successful results".

5. CONCLUSION

In conclusion, this study demonstrated that LLLT seems to be safe and effective in different body sites, cheapand does not require costly devices and well-equipped rooms.

ETHICAL APPROVAL

This work got the agreement of ethical committee of scientific research at Faculty of Medicine, Tanta University (34304/12/20).

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Abdel-Malek ZA, Jordan C, Ho T, Upadhyay PR, Fleischer A, Hamzavi I. The enigma and challenges of vitiligo pathophysiology and treatment. Pigment Cell Melanoma Res. 2020;33(6):778-87.
2. Kyriakis KP, Palamaras I, Tsele E, Michailides C, Terzoudi S. Case detection rates of vitiligo by gender and age. Int J Dermatol. 2009;48(3):328-9.
3. Passeron T, Ortonne JP. Physiopathology and genetics of vitiligo. J Autoimmun. 2005;25:63-8.
4. Xu X, Jiang M, Zhang C, Qiao Z, Liu W, Le Y et al. new insights into segmental vitiligo: A clinical and immunological comparison with nonsegmental vitiligo. Pigment Cell Melanoma Res. 2022;35(2):220-8.
5. Van Den Boorn JG, Konijnenberg D, Dellemijn TA, Van Der Veen JW, Bos JD, Melief CJ et al. Autoimmune destruction of skin melanocytes by perilesional T cells from vitiligo patients. J Invest Dermatol. 2009;129(9):2220-32.
6. Rashighi M, Harris JE. Vitiligo pathogenesis and emerging treatments. Dermatol Clin. 2017;35(2):257-65.
7. Rodrigues M, Ezzedine K, Hamzavi I, Pandya AG, Harris JE. Vitiligo working group. Current and emerging treatments for vitiligo. J Am Acad Dermatol. 2017; 77(1):17-29.
8. Birlea SA, Costin GE, Norris DA. Cellular and molecular mechanisms involved in the action of vitamin D analogs targeting vitiligo depigmentation. Curr Drug Targets. 2008;9(4):345-59.
9. Malakar S, Lahiri K. Spontaneous repigmentation in vitiligo: Why it is important. Int J Dermatol. 2006;45(4): 478-9.
10. Arora AK, Dogra S. Narrowband ultraviolet B and beyond: Evolving role of phototherapy in vitiligo. Pigment Int. 2015; 2(1):9-20.
11. Nicolaidou E, Antoniou C, Stratigos AJ, Stefanaki C, Katsambas AD. Efficacy, predictors of response and long-term follow-up in patients with vitiligo treated with narrowband UVB phototherapy. J Am Acad Dermatol. 2007;56(2):274-8.
12. Madhumathi D, Santhosh Kuma MP. Low-level laser therapy in oral and maxillofacial surgery - A review. Drug Invention Today. 2018;10(5):685-91.
13. Mohammed IF, Kaka LN. Promotion of regenerative processes in injured peripheral nerve induced by low-level laser therapy. Photomed Laser Surg. 2007;25 (2):107-11.
14. Dodd EM, Winter MA, Hordinsky MK, Sadick NS, Farah RS. Photobiomodulation therapy for androgenetic alopecia: A clinician's guide to home-use devices cleared by the Federal Drug Administration. J Cosmet Laser Ther. 2018;20(3):159-67.
15. Aziz-Jalali MH, Tabaie SM, Djavid GE. Comparison of red and infrared low-level laser therapy in the treatment of acne vulgaris. Int J Dermatol. 2012;57(2): 128-30.
16. Zhang P, Wu MX. A clinical review of phototherapy for psoriasis. Lasers Med Sci. 2018;33(1):173-80.
17. Lan CC, Wu CS, Chiou MH, Hsieh PC, Yu HS. Low-energy helium-neon laser induces locomotion of the immature melanoblasts and promotes melanogenesis of the more differentiated melanoblasts: Recapitulation of vitiligo repigmentation *In vitro*. J Invest Dermatol. 2006;126(9):2119-26.
18. Anbar TS, El-Ammawi TS, Abdel-Rahman AT, Hanna MR. The effect of latanoprost on vitiligo: A preliminary comparative study. Int J Dermatol. 2015;54:587-93.
19. Bergqvist C, Ezzedine K. Vitiligo: A review. Dermatology. 2020;236(6):571-92.
20. Mohammed GF, Gomaa AH, Al-Dhubaibi MS. Highlights in pathogenesis of vitiligo. WJCC. 2015;3(3):221.
21. Kawalek AZ, Spencer JM, Phelps RG. Combined excimer laser and topical tacrolimus for the treatment of vitiligo: A

pilot study. Dermatol Surg. 2004;30(2): 130-5.
22. Kanwar AJ, Kumaran MS. Childhood vitiligo: Treatment paradigms. Indian J Dermatol. 2012;57(6):466-74.
23. Dillon AB, Sideris A, Hadi A, Elbuluk N. Advances in vitiligo: An update on medical and surgical treatments. J Clin Aesthet Dermatol. 2017;10(1):15-28.
24. Yu HS, Wu CS, Yu CL, Kao YH, Chiou MH. Helium-neon laser irradiation stimulates migration and proliferation in melanocytes and induces repigmentation in segmental-type vitiligo. J Invest Dermatol. 2003;120(1):56-64.
25. Mandel AS, Haberman HF, Pawlowski D, Goldstein E. Non PUVA nonsurgical therapies for vitiligo. Clin Dermatol. 1997; 15(6):907-19.
26. Wu CS, Hu SC, Lan CC, Chen GS, Chuo WH, Yu HS. Low-energy helium-neon laser therapy induces repigmentation and improves the abnormalities of cutaneous microcirculation in segmental-type vitiligo lesions. The Kaohsiung J Med Sci. 2008; 24(4):180-9.
27. AlGhamdi KM, Kumar A, Ashour AE, AlGhamdi AA. A comparative study of the effects of different low-level lasers on the proliferation, viability, and migration of human melanocytes *In vitro*. Lasers Med Sci. 2015;30(5):1541-51.
28. Avci P, Gupta A, Sadasivam M, Vecchio D, Pam Z, Pam N et al. Low-level laser (light) therapy (LLLT) in skin: stimulating, healing, restoring. InSeminars in cutaneous medicine and surgery. NIH Public Access. 2013;32(1):41.
29. Lan CC, Wu SB, Wu CS, Shen YC, Chiang TY, Wei YH et al. Induction of primitive pigment cell differentiation by visible light (helium-neon laser): A photoacceptor-specific response not replicable by UVB irradiation. J Mol Med (Berl). 2012; 90(3):321-30.
30. Mezghani S, Hammami A, Amri M. Low-level laser therapy: Effects on human face aged skin and cell viability of hela cells exposed to UV radiation. Arch Biosci. 2015;67(1):25-9.
31. Tallab T, Joharji H, Bahamdan K, Karkashan E, Mourad M, Ibrahim K. Response of vitiligo to PUVA therapy in Saudi patients. Int J Dermatol. 2005; 44(7):556-8.
32. Hamzavi I, Jain H, McLean D, Shapiro J, Zeng H, Lui H. Parametric modeling of narrowband UV-B phototherapy for vitiligo using a novel quantitative tool: The vitiligo area scoring index. Arch Dermatol. 2004; 140(6):677-83.
33. Kapoor R, Phiske MM, Jerajani HR. Evaluation of safety and efficacy of topical prostaglandin E2 in treatment of vitiligo. Br J Dermatol. 2009;160(4):861-3.
34. Dalla A, Parsad D, Vinay K, Thakur V, Sendhil Kumaran M. A prospective study to assess the efficacy of various surgical modalities in treatment of stable vitiligo patches over resistant sites. Int J Dermatol. 2020;59(7):837-42.
35. Yazdani Abyaneh M, Griffith RD, Falto-Aizpurua L, Nouri K. Narrowband ultraviolet B phototherapy in combination with other therapies for vitiligo: Mechanisms and efficacies. J Eur Acad Dermatol Venereol. 2014;28(12):1610-22.
36. Doghaim NN, Gheida SF, El-Tatawy RA, Mohammed Ali DA. Combination of fractional carbon dioxide laser with narrow band ultraviolet B to induce repigmentation in stable vitiligo: A comparative study. J. Cos. Dermatol. 2019;18(1):142-9.
37. Shin S, Hann SK, Oh SH. Combination treatment with excimer laser and narrowband UVB light in vitiligo patients. Photodermatol Photoimmunol Photomed. 2016;32(1):28-33.
38. Yan R, Yuan J, Chen H, Li YH, Wu Y, Gao XH, et al. Fractional Er: YAG laser assisting topical betamethasone solution in combination with NB-UVB for resistant non-segmental vitiligo. Lasers Med Sci. 2017;32(7):1571-7.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/92512