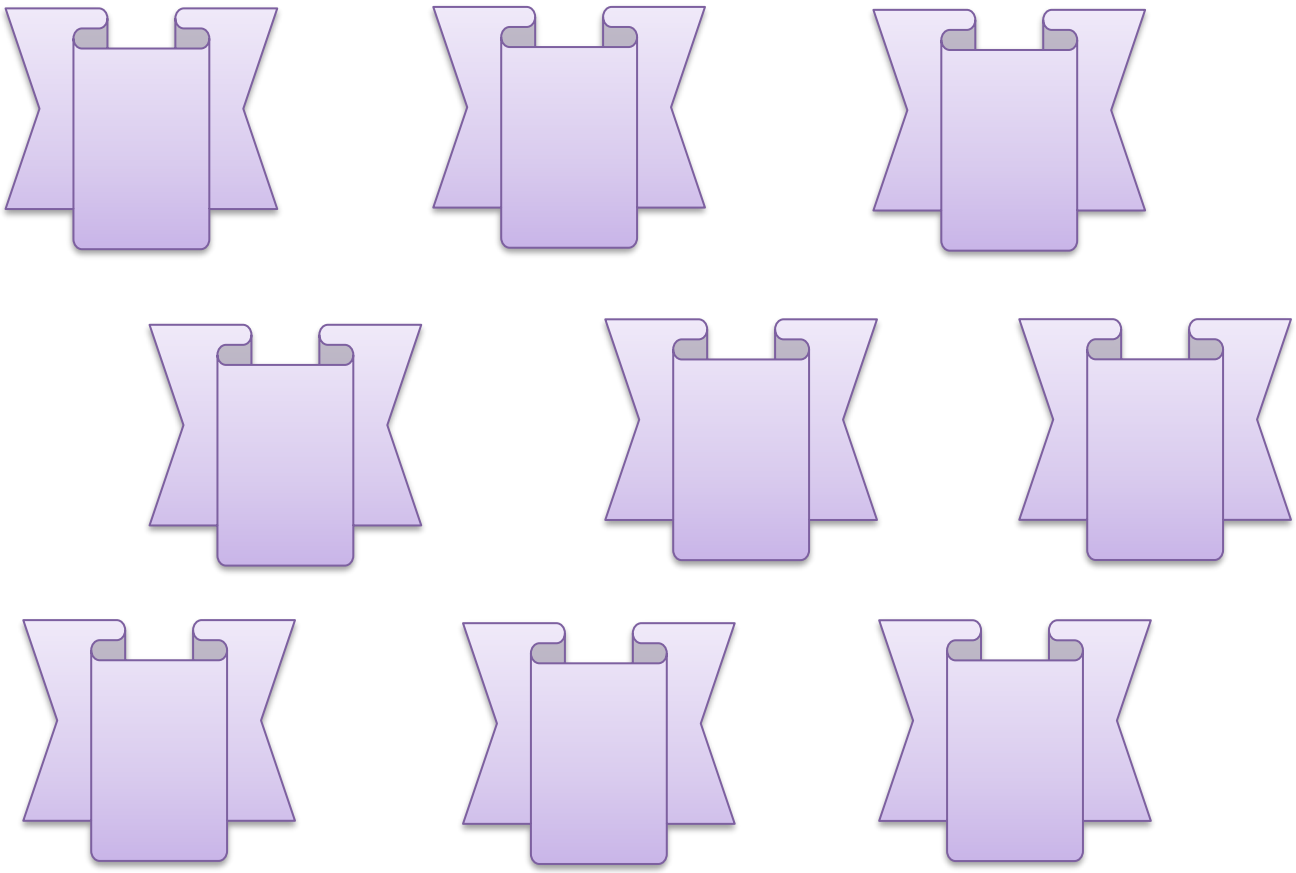
International Journal of Medical Arts

Volume 5, Issue 9, September 2023

https://ijma.journals.ekb.eg/



Print ISSN: 2636-4174

Online ISSN: 2682-3780

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main Subject [Dermatology]

Original Article

A Double-Blind Placebo Controlled Therapeutic Trial on Patients with Stable Non-Segmental Vitiligo Using a Specially Formulated Reducing Antioxidant Gel Enhanced by Excimer Light Exposure

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Article information

Received: 06-10-2023

Accepted: 30-10-2023

DOI: 10.21608/IJMA.2023.241003.1828.

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Citation: Hassan AAN, Ezzeddin SM, Elrewiny EM. A Double-Blind Placebo Controlled Therapeutic Trial on Patients with Stable Non-Segmental Vitiligo Using a Specially Formulated Reducing Anti-oxidant Gel Enhanced by Excimer Light Exposure. IJMA 2023 September; 5 [9]: 3654-3662. doi: 10.21608/IJMA.2023. 241003.1828.

ABSTRACT

Background: Vitiligo is a common skin condition that causes patches of lightening that affect 0.2 to 0.5 percent of the world's population. It is marked by chalky white macules because melanocytes are being selectively lost. Several ideas have been put forward about what causes the disease, such as an autoimmune, genetic, neural, biochemical, melanocyte cell self-destruction, or oxidative stress theory, which means that too much hydrogen peroxide [H2O2] builds up in the top layer of skin.

Aim of the Study: We want to find out how well a special gel called "pseudo catalase" with reducing ingredients fights the over-oxygenation of skin melanocytes and epidermal cells that is made worse by excimer light exposure in a person with stable non-segmental vitiligo compared to a gel that doesn't do anything different on the same person.

Patients and Methods: The study included 31 stable non-segmental vitiligo patients who attended the dermatological outpatients' clinic at Al-Hussein University Hospital in Cairo, Egypt, during the period between September 2021 and August 2022. The study was divided into 2 groups of lesions in the same patient: group A [test gel + excimer light, Narrow Band UVB exposure] and group B [placebo gel + excimer light, Narrow Band UVB exposure].

Results: The following results were recorded for our patients: The mean age was 25.7 ± 9.3 years. There were 18 males [58.1%] and 13 females [41.9%]. 22 patients [71%] were of skin type III and 9 cases [29%] were of skin type IV. The VASI score values detected showed a great difference before and after treatment, as group A was [0.42 ± 0.3] when compared with the VASI score in group B [1.12 ± 0.5].

Conclusion: Excimer-light-enhanced topical antioxidant pseudo-catalase gel is a highly efficient therapy in the treatment of stable non-segmental vitiligo.

Keywords: Pseudo-catalase gel; Antioxidant; Stable non-segmental vitiligo; Excimer light exposure.

INTRODUCTION

Vitiligo is defined by the selective loss of melanocytes and it is a skin condition that causes a loss of pigmentation. The non-scaly, chalky-white macule with clear borders is the characteristic lesion related to this condition. Vitiligo is a condition that is triggered by a number of different factors, and present research has made major progress in understanding the disease's etiology and how it developed. There have been several hypotheses put forth on the processes that lead to the loss of melanocytes [1].

Genetic and environmental variables, in addition to metabolic, oxidative stress, and cell detachment problems, have led to its current classification as an autoimmune illness [2].

The estimated worldwide incidence of the condition varies from 0.5 percent to 2 percent in both adults and children. About 5–16% of those with vitiligo have segmental vitiligo. Reports of SV's frequency vary widely from five percent to thirty percent [3].

Vitiligo has major impacts on patients' life quality, particularly for individuals with dark skin and/or living in countries with different cultures [4].

The epidermis, as the outermost component of skin, forms a barrier directly protecting against environmental stressors. This protection is assured by an intrinsic keratinocyte differentiation program, the pigmentary system, and local nervous, immune, endocrine, and microbiome elements. The neurohormonal mediators and cytokines used in these communications regulate physiological skin functions separately or in concert. Disturbances in the functions of these systems lead to cutaneous pathology that includes hypersensitivity reactions, pigmentary disorders [vitiligo, melasma, and hypo- or hyper-pigmentary responses], premature aging, and malignancies [melanoma and nonmelanoma skin cancers] [5].

Reactive oxygen species [ROS] are chemical compounds released from melanocytes and epidermal cells in response to different types of stress. They have destructive effects on the intracellular structure. They hinder normal physiological cell functions, leading to cell death [6].

Superoxide dismutase, malondialdehyde, and other oxidative stress indicators are high, whereas anti-oxidant molecules involving catalase, glutathione reductase, glutathione peroxidase, thioredoxin, or superoxide dismutase are significantly reduced in the skin and the blood in patients with vitiligo [6].

Pseudocatalase is a complex of bis-Mn^{II} $[EDTA]_2$ $[HCO3^{-}]2$, which mimics the effect of the natural catalase enzyme in the body, corrects errors in calcium homeostasis and restores normal catalase levels, both of which are deficient in vitiligo patients [7].

Excimer lasers and lamps are used to administer phototherapy in the form of broadband ultraviolet B [UVB], narrow-band [NB] UVB at 308 nanometers [PUVA], or targeted phototherapy. They stimulate the migration and proliferation of melanocytes, leading to repigmentation and also influencing the immune response [8].

The UVB reception in the skin not only activated central neuroendocrine pathways but also induced rapid systemic immunosuppressive effects, which showed an extended duration, as illustrated by inhibition of Th1 and Th2 activities in the spleen 30 and/or 90 minutes after UVB exposure that lasted for at least 24 hours. Moreover, UVB enhances skin and plasma levels of CRH, urocortin, b-endorphin, ACTH, and corticosterone levels, along with simultaneous stimulation of CRH gene and protein expression in the paraventricular nucleus of the hypothalamus and of MC2R, StAR [steroidogenic acute regulatory protein], and CYP11B1 genes in adrenals [9].

Compared with conventional phototherapies, it is superior in treating small, inaccessible skin folds [10].

The objective of this research was to determine the effectiveness of a pseudo-catalase gel enhanced by excimer light exposure in non-segmental vitiligo patients compared to a placebo gel on the same patient.

PATIENTS AND METHODS

This research involved 31 stable non-segmental vitiligo cases who attended the dermatological outpatient clinic at Al-Hussein University Hospital, Cairo, Egypt.

Inclusion criteria: age 18–45 years, both sexes, confirmed cases of stable non-segmental vitiligo, and not receiving any medication or phototherapy in the last 3 months.

Exclusion criteria: any other skin disease, any systemic morbid disease [HTN, DM, dyslipidemia, and thyroid disease], Any topical or systemic therapy within the last 3 months, such as steroids, NSAIDs, immunomodulation drugs like isoprinosine, echinosin, or similar drugs, Patients had unstable vitiligo, pregnant or breast-feeding females, and skin cancers.

After written informed consent was obtained, Local ethics committee approval at Al-Azhar University for the study was obtained.

Data collection

History-taking: full personal history, family history of vitiligo or alopecia areata, full medical history to exclude any other skin disease or any systemic morbid disease and full drug history of not taking any medication.

Clinical Examination: including estimation of the [VASI score] [Vitiligo Area Scoring Index [VASI]]. Daylight photography + photography under Wood's light for confirmation of the diagnosis

Lab work: CBC, liver profile, lipid profile, and thyroid hormone

Topical application of the testing gel nominated [gel A] in good amounts on the affected area and a large area of the skin around it, on the trunk, was applied on the front side of the body. The placebo gel nominated [gel B] was applied to the contralateral limb of the body and on the back. The gel and the placebo were provided in identical containers for each patient.

Excimer session exposure: Exposure to Excimer Sessions was done in a scheduled manner, starting with the smallest dose in a gradually increasing manner.

We started with a dosage of 200 mJ/cm2. The therapy was given twice weekly, on consecutive days**.**

Unless persistent erythema was observed, the dosage was raised by twenty percent from the first level. Only the afflicted areas were exposed during treatment, while UV-blocking goggles were utilized to protect the eyes.

RESULTS

The average age was 25.7 ±9.3 years, with a minimum of 18 years and a maximum of 45 years. Regarding gender, there were 18 males [58.1 %] and 13 females [41.9 %]. Regarding skin type, there were 22 cases [71%] of skin type III and 9 cases [29%] of skin type IV. As regards family history, there were 4 patients [12.9%] with a positive family history of vitiligo. 27 patients [87.1%] with a negative family history.

As regards group A lesions, the face was affected in 6 patients [19.4%] with a total number of 15 lesions, the neck was affected in 2 patients [6.5%] with a total number of 6 lesions, the breast was affected in 3 patients [9.7%] with a total number of 5 lesions, the abdomen was affected in 6 patients [19.4%] with a total number of 8 lesions, the upper limb was affected in 16 patients [51.6%] with a total number of 71 lesions, and the lower limb was affected in 12 patients [38.7%] with a total number of 46 lesions.

The total number of lesions in Group A was 151. As regards group B lesions, the upper limb was affected in 16 patients [51.6%] with a total number of 57 lesions, the lower limb was affected in 14 patients [45.2%] with a total number of 38 lesions, and the back was affected in 3 patients [9.7%] with a total number of 25 lesions. The total number of lesions in Group B was 120.

Highly significant [p-value < 0.001]. Decreased VASI in group A [0.42 ± 0.3] when compared with VASI in group B [1.12 ± 0.5] after treatment.

There was significant variation among group A and group B lesions as regards response. In group A lesions, there were 17 lesions [11.3%] with no response, 15 lesions [9.9%] with a mild response, 24 lesions [15.9%] with a moderate response, and 95 lesions [62.9%] with an excellent response. In group B lesions, there were 21 lesions [17.5%] with no response, 37 lesions [30.8%] with a mild response, 35 lesions [29.2%] with a moderate response, and 27 lesions [22.5%] with a marked response.

Table [1]: Demographic data for all examined individuals

		Studied patients [N = 31]	
Sex	Male	18	58.10%
	Female	13	41.90%
Age [years]	Mean ±SD	25.7 ± 9.3	
	Min – Max	18 – 45	
Skin type	Type III	22	71%
	Type IV	9	29%
Family history	Negative	27	87.10%
	Positive	4	12.90%

Table [2]: Lesions sites and total number in all studied patients

		No. of patients [n = 31]		Total no of lesions
Group A lesions	Face	6	19.40%	15
	Neck	2	6.50%	6
	Breast	3	9.70%	5
	Abdomen	6	19.40%	8
	Upper limb	16	51.60%	71
	Lower limb	12	38.70%	46
	Total	151 lesions		
Group B lesions	Upper limb	16	51.60%	57
	Lower limb	14	45.20%	38
	Back	3	9.70%	25
	Total	120 lesions		

Table [3]: Comparison between group A and group B with regard to VASI score

		Group A [N = 31]	Group B [N = 31]	Stat. test	P-value
VASI [before treatment]	Mean	1.58	1.5	MW = 404	0.819
	±SD	0.72	0.64		
VASI [after treatment]	Mean	0.42	1.12	**MW = 102**	**< 0.001**
	±SD	0.3	0.5		

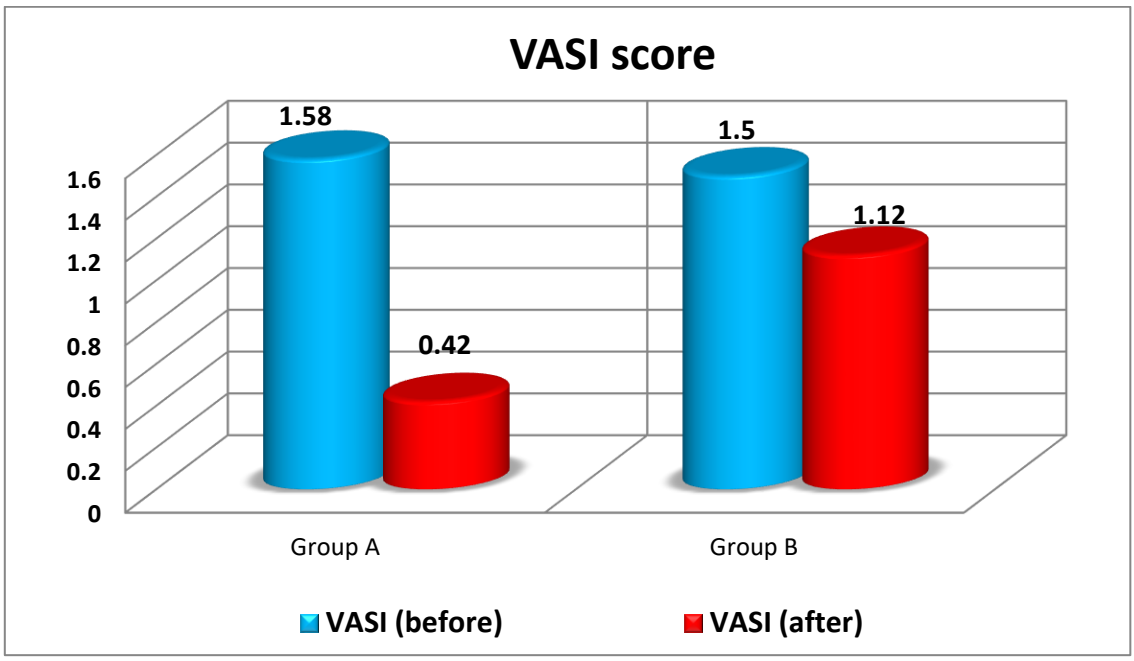

Figure [1]: Comparison between group A and group B as regards VASI score

Table [4]: Comparison of responses in all studied groups

		Group A [lesions = 151]		Group B [lesions = 120]		Stat. test	P-value
Response	No	17	11.30%	21	17.50%	$X^2 = 46.7$	< 0.001
	Mild	15	9.90%	37	30.80%		
	Moderate	24	15.90%	35	29.20%		
	Excellent	95	62.90%	27	22.50%		

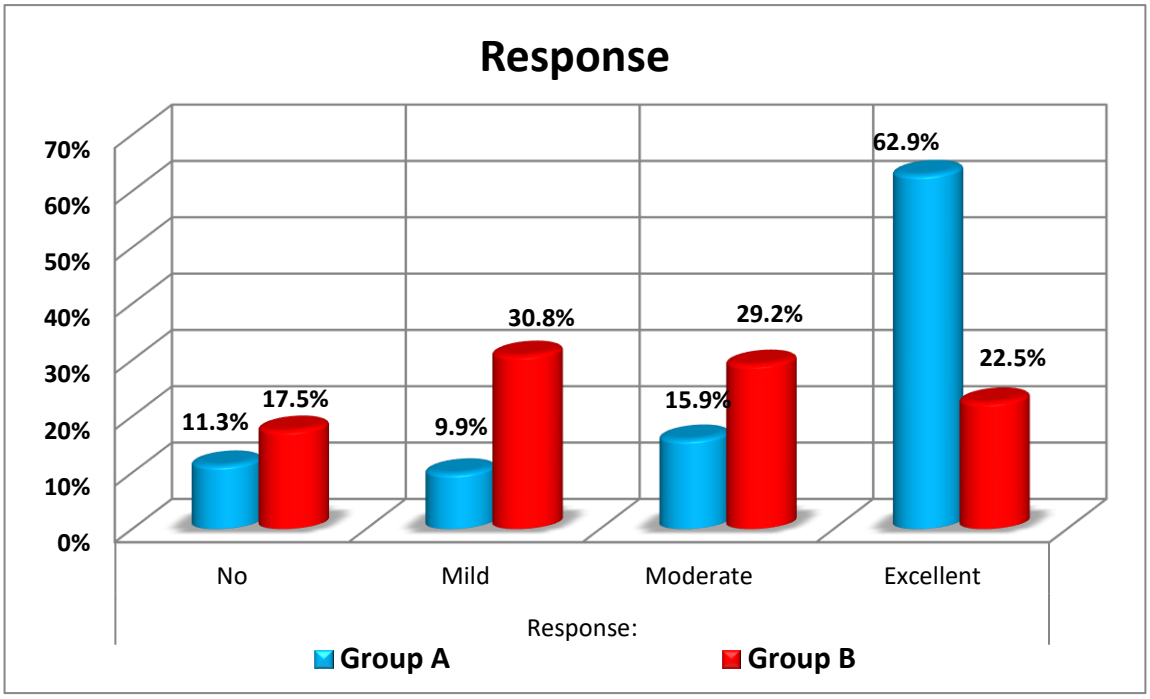

Figure [2]: Comparison of responses in all studied groups

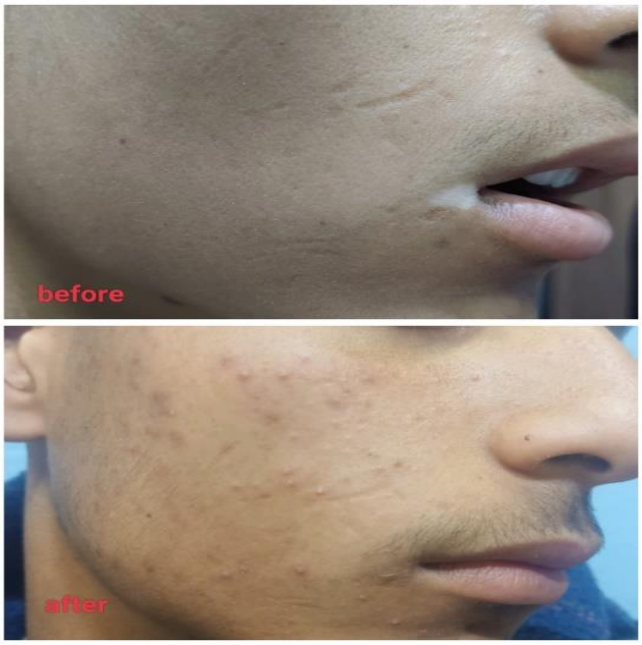

Figure [3]: A 19-year-old male with a face lesion for 2 years shows excellent improvement [test group] after 3 months [24 excimer sessions + antioxidant gel]

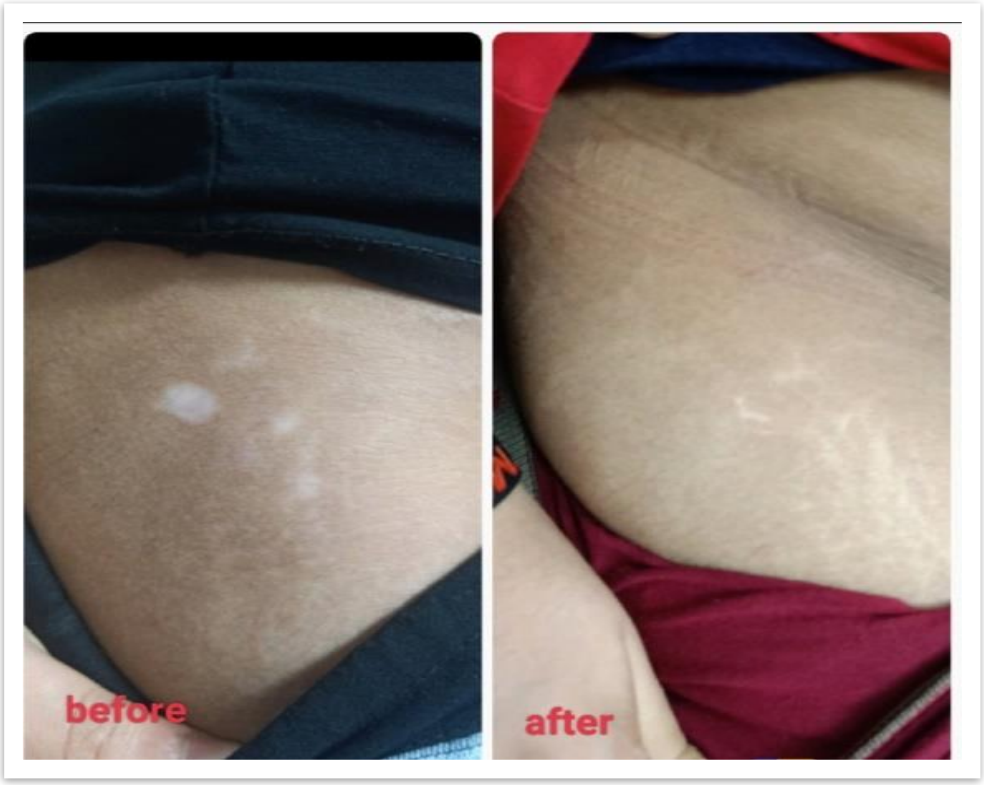

Figure [4]: 18-year-old male with an upper thigh lesion for 2 years

Shows excellent improvement [test group] after 6 months [42 excimer sessions + antioxidant gel]

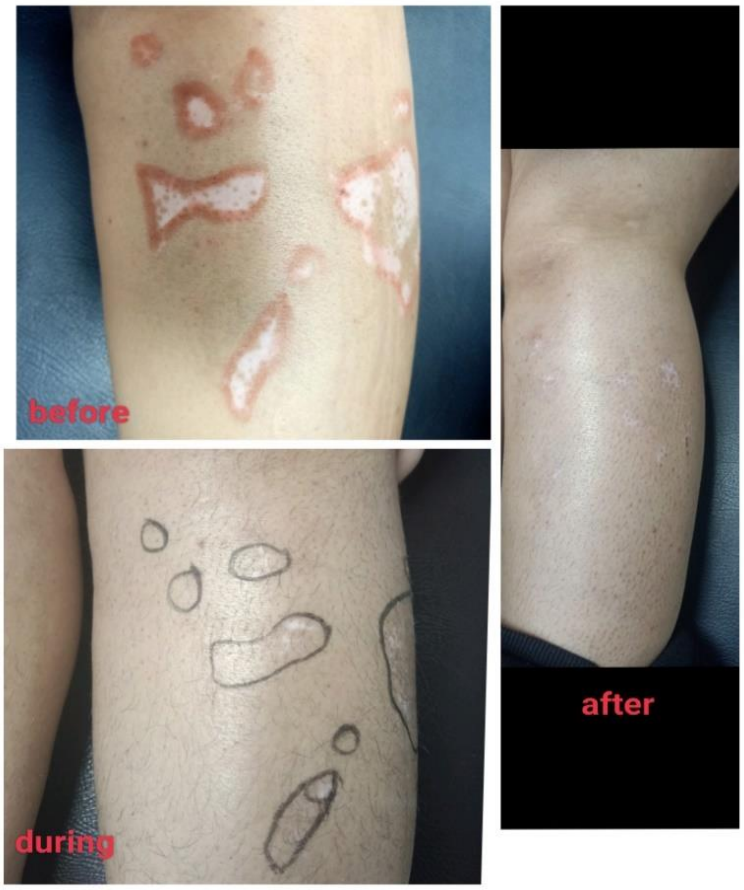

Figure [5]: A 25-year-old female with leg lesions for 5 years shows excellent improvement [test group] after 3 months [25 excimer sessions + antioxidant gel]

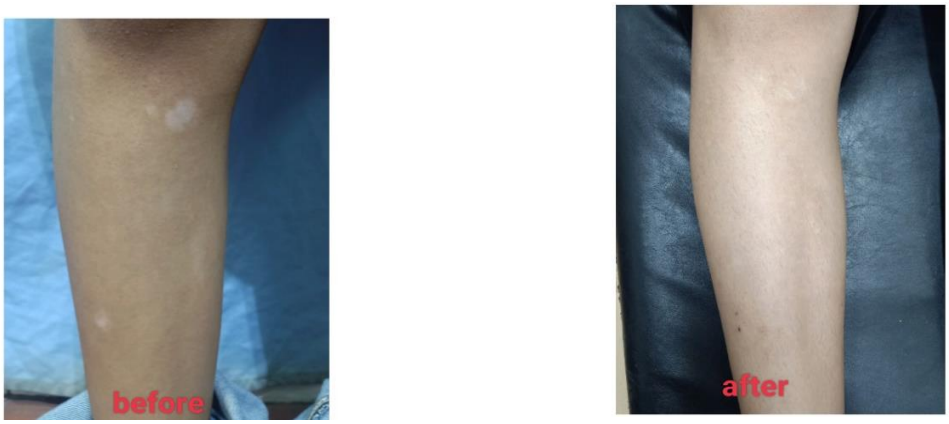

Figure [6]: An 18-year-old female with RT leg lesions for 4 years shows excellent improvement [test group] after 5 months [33 excimer sessions + antioxidant gel]

DISCUSSION

Vitiligo is a common autoimmune illness that causes the death of epidermal melanocyte cells, resulting in the appearance of white patches on the skin [11].

Although the precise pathogenesis is not fully understood, it is generally accepted that oxidative stress is the first stage in the death of melanocyte cells. Despite the fact that pathogenesis is complicated and depends on the interaction of a number of variables [12].

According to this hypothesis, the pseudo-catalase enzyme was used by many researchers in clinical trials on vitiligo disease, and some of them reported beneficial responses [13].

Our research, based on the findings of others, confirms the value of combining topical with 308 nm excimer light for the treatment of vitiligo.

Schallreuter [14] demonstrates that topical application of a readily penetrating pseudo-catalase/calcium complex in combination with a short-term narrow-band UVB exposure can successfully prevent epidermal oxidative stress, leading to successful regimentation.

Also, in a study performed in a pediatric population by **Schallreuter *et al.*** [15], patients were treated with a twice-daily application of pseudocatalase PC-KUS activated with low-dose narrow-band UVB [nb-UVB].

The total number of lesions in Group A was 151. The total number of lesions in Group B was 120. Highly significant decreased VASI in group A [0.42 ± 0.3] when compared with VASI in group B [1.12 ± 0.5] after treatment.

There was significant variation among group A and group B lesions as regards response. In group A lesions, there were 17 lesions [11.3%] with no response, 15 lesions [9.9%] with a mild response, 24 lesions [15.9%] with a moderate response, and 95 lesions [62.9%] with an excellent response. In group B lesions, there were 21 lesions [17.5%] with no response, 37 lesions [30.8%] with a mild response, 35 lesions [29.2%] with a moderate response, and 27 lesions [22.5%] with an excellent response.

In a study done by **Soliman *et al.*** [16] at Cairo University Hospitals, thirty patients were investigated; half of them [Group A] were given vitiskin® [a pseudo-catalase hydrogel] in addition to excimer light, while the other half [Group B] were given excimer light alone. Within three months, both groups showed some repigmentation in their vitiliginous lesions, in accordance with the research. The two groups did not have the same level of repigmentation, and the variation was significant.

Because of this, it may be concluded that combination therapy is preferable to curing localized vitiligo, even though both methods alone were successful.

In a study done by **Leone *et al.*** [17], it was observed that treatment of vitiligo using an excimer laser and a topical antioxidant cream was superior to a placebo cream. Based on the findings, the regimentation of the lesions treated

with the active cream occurred sooner than those treated with the placebo. Individuals with vitiligo who utilize topical antioxidants may have better responses to excimer laser therapy.

A study done by **Kostovic *et al.*** [18] consisted of 22 individuals, 19 of whom remained in the trial for the full 6 months. In addition to three weekly sessions of excimer light phototherapy, patients applied a gel containing the enzymes pseudo-catalase and superoxide dismutase twice daily. Overall repigmentation in excess of 50% was seen in 11 of 19 patients [57.9%] by the study's completion. Three [15.79%] of the patients had repigmentation of more than 75%, six [31.58%] demonstrated repigmentation of 26%–50%, one [5.26%] revealed repigmentation of 1%–25%, and one [5.26%] indicated no repigmentation at all. Patients responded best to treatment on their face and neck, as 11 out of 14 [78.6%] saw at least 50% repigmentation. In accordance with the results of the study, a treatment strategy for vitiligo that combines phototherapy with a gel containing pseudo-catalase and dismutase is feasible.

Our consequences were in agreement with those of **Soliman *et al.*** [16] who found that, within three months, both groups experienced some repigmentation of their vitiliginous lesions. That was because the combination therapy was more effective and superior in achieving good effects.

Our results were in agreement with the results of **Leone *et al.*** [17] who demonstrated that the regimentation of the lesions administered the active cream occurred sooner than those administered the placebo.

On the other hand, **Naini *et al.*** [19], in a pilot study on 30 patients with non-segmental vitiligo, used pseudo-catalase plus superoxide dismutase creams against a placebo cream plus UVB. The results showed no significant distinction between the control and test lesions in any patient.

Also, double-blind, randomized, placebo-controlled research done by **Bakis-Petsoglou *et al.*** [20] on individuals with non-segmental vitiligo indicated that topical pseudo-catalase cream did not appear to give any extra benefit to NB-UVB alone.

Conclusion: Based on our findings, we concluded that the antioxidant pseudo-catalase gel paired with excimer light exposure was a successful therapy for vitiligo. In the therapy group, there are very statistically significant variations in VASI values before and after treatment.

Financial and non-financial relations and activities of interest: None

REFERENCES

1. Picardo M, Dell'Anna ML, Ezzedine K, Hamzavi I, Harris JE, Parsad D, Taieb A. Vitiligo. Nat Rev Dis Primers. 2015 Jun 4;1:15011. doi: 10.1038/nrdp.2015.11.

2. Bergqvist C, Ezzedine K. Vitiligo: A Review. Dermatology. 2020;236[6]:571-592. doi: 10.1159/000506103.

3. Kota RS, Vora RV, Varma JR, Kota SK, Patel TM, Ganjiwale J. Study on Assessment of Quality of Life and Depression in Patients of Vitiligo. Indian Dermatol Online J. 2019 Mar-Apr;10[2]:153-157. doi: 10.4103/idoj.IDOJ_14_18.

4. Rodrigues M, Ezzedine K, Hamzavi I, Pandya AG, Harris JE; Vitiligo Working Group. New discoveries in the pathogenesis and classification of vitiligo. J Am Acad Dermatol. 2017 Jul;77[1]:1-13. doi: 10.1016/j.jaad.2016.10.048.

5. Slominski AT, Slominski RM, Raman C, Chen JY, Athar M, Elmets C. Neuroendocrine signaling in the skin with a special focus on the epidermal neuropeptides. Am J Physiol Cell Physiol. 2022 Dec 1;323[6]:C1757-C1776. doi: 10.1152/ajpcell.00147.2022.

6. Bergqvist C, Ezzedine K. Vitiligo: A focus on pathogenesis and its therapeutic implications. J Dermatol. 2021 Mar;48[3]:252-270. doi: 10.1111/1346-8138.15743.

7. Yildirim M, Korkmaz S, Erturan İ. Role of antioxidants in vitiligo. Comprehensive Textbook on Vitiligo. 2020 Sep 16;1452020.

8. Pacifico A, Leone G. Photo[chemo]therapy for vitiligo. Photodermatol Photoimmunol Photomed. 2011 Oct;27[5]:261-77. doi: 10.1111/j.1600-0781.2011.00606.x.

9. Slominski AT, Zmijewski MA, Plonka PM, Szaflarski JP, Paus R. How UV Light Touches the Brain and Endocrine System Through Skin, and Why. Endocrinology. 2018

May 1;159[5]:1992-2007. doi: 10.1210/en. 2017-03230.

10. Deng Y, Li J, Yang G. 308-nm Excimer Laser Plus Platelet-Rich Plasma for Treatment of Stable Vitiligo: A Prospective, Randomized Case-Control Study. Clin Cosmet Investig Dermatol. 2020 Jul 23;13:461-467. doi: 10.2147/CCID.S260434.

11. Taneja N, Sreenivas V, Sahni K, Gupta V, Ramam M. Disease Stability in Segmental and Non-Segmental Vitiligo. Indian Dermatol Online J. 2021 Aug 2;13[1]:60-63. doi: 10.4103/idoj.IDOJ_154_21.

12. Mohammed GF, Gomaa AH, Al-Dhubaibi MS. Highlights in pathogenesis of vitiligo. World J Clin Cases. 2015 Mar 16;3[3]:221-30. doi: 10.12998/wjcc.v3.i3.221.

13. Kemp EH, Gavalas NG, Gawkrodger DJ, Weetman AP. Autoantibody responses to melanocytes in the depigmenting skin disease vitiligo. Autoimmun Rev. 2007 Jan;6[3]:138-42. doi: 10.1016/j.autrev.2006.09.010.

14. Schallreuter KU. Successful treatment of oxidative stress in vitiligo. Skin Pharmacol Appl Skin Physiol. 1999 May-Jun;12[3]:132-8. doi: 10.1159/000029867.

15. Schallreuter KU, Krüger C, Würfel BA, Panske A, Wood JM. From basic research to the bedside: efficacy of topical treatment with pseudocatalase PC-KUS in 71 children with vitiligo. Int J Dermatol. 2008 Jul;47[7]:743-53. doi: 10.1111/j.1365-4632.2008.03660.x.

16. Soliman M, Samy NA, Abo Eittah M, Hegazy M. Comparative study between excimer light and topical antioxidant versus excimer light alone for treatment of vitiligo. J Cosmet Laser Ther. 2016;18[1]:7-11. doi: 10.3109/14764172.2015.1052510.

17. Leone G, Paro Vidolin A. Effect of an antioxydant cream versus placebo in patients with vitiligo in association with excimer laser. A pilot randomized, investigator-blinded, and half-side comparison trial. G Ital Dermatol Venereol. 2015 Aug;150[4]:461-6. PMID: 26224232.

18. Kostović K, Pastar Z, Pasić A, Ceović R. Treatment of vitiligo with narrow-band UVB and topical gel containing catalase and superoxide dismutase. Acta Dermatovenerol Croat. 2007;15[1]:10-4. PMID: 17433173.

19. Naini FF, Shooshtari AV, Ebrahimi B, Molaei R. The effect of pseudocatalase/ superoxide dismutase in the treatment of vitiligo: A pilot study. J Res Pharm Pract. 2012 Oct;1[2]:77-80. doi: 10.4103/2279-042X.108375.

20. Bakis-Petsoglou S, Le Guay JL, Wittal R. A randomized, double-blinded, placebo-controlled trial of pseudocatalase cream and narrowband ultraviolet B in the treatment of vitiligo. Br J Dermatol. 2009 Oct;161[4]:910-7. doi: 10. 1111/j.1365-2133.2009.09252.x.

International Journal of Medical Arts

https://ijma.journals.ekb.eg/
Print ISSN: 2636-4174
Online ISSN: 2682-3780