

Topical Antioxidant and Narrowband versus Topical Combination of Calcipotriol plus Betamethathone Dipropionate and Narrowband in the Treatment of Vitiligo

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Abstract: Vitiligo is a specific, common, often heritable, acquired disorder characterized by well-circumscribed milky-white cutaneous macules devoid of identifiable functional melanocytes because of multifactorial and overlapping pathogenic mechanisms. The basic defect in vitiligo is loss of melanocytes. Narrowband ultraviolet B (NB-UVB) is an emerging, effective and safe therapy for vitiligo. Because of defective calcium homeostasis in depigmented skin, the vitamin D-3 analogs (calcipotriol and taclacitol) have been used topically in vitiligo, where modulation of the local immune response on specific T cell activation occurs. A new topical product containing a combination of vegetal catalase (CAT) and superoxide dismutase (SOD) has been used in vitiligo. *In vitro* studies demonstrated the capacity of this complex to dramatically reduce the production of free radicals in vitiligo cell and even to restore a normal level of melanin in melanocytes of vitiligo. Patients and Methods: The current study comprised a total of 40 patients with different clinical varieties of vitiligo. They were recruited from the Outpatient Clinic of Dermatology and Venereology Department, Tanta University Hospitals. *The studied patients were divided into:* G1: Included 20 patients subjected to topical combination of calcipotriol plus betamethazone dipropionate ointment with NB-UVB on the left side of the patient and NB-UVB alone on the right side of the same patient. G2: Included 20 patients subjected to topical SOD/CAT gel with NB-UVB on the left side of the patient and NB-UVB alone on the right side of the same patient. Results: Comparison in the response of the treatment in G1 and GII between right and left side revealed no statistically significant difference between the two sides. Comparison in the response in the left side in G I and G II showed no statistically significant difference in repigmentation between the two groups. There were no significant correlation between the results of the combination treatment plus NB-UVB in both groups and clinical criteria of vitiligo patients. There were statistically significant differences between distribution of sites of the lesions in vitiligo patients and treatment with topical applications plus NB-UVB regarding response of the treatment in the face and neck in G II. While in G I the face had excellent response but not statistically significant. Conclusions: The current study had shown that NB-UVB treatment alone is a moderately effective treatment for vitiligo. Betamethasone dipropionate / calcipotriol, when used in combination with NB-UVB were found to be superior in efficacy than NB-UVB alone, but the results were not statistically significant, while SOS/CAT gel does not appear to add any incremental benefit to NB-UVB alone. It could be recommended that further studies should be performed on this subject.

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1. Introduction

Vitiligo is an acquired depigmentary dermatosis characterized by sharply demarcated lesions heterogeneous in size and shape. The disease generally runs in a progressive course. The disease affects 1-2% of the world population, irrespective of age, gender, and skin color⁽¹⁾. From therapeutic and prognostic viewpoint, vitiligo is broadly classified into two major subtypes, segmental vitiligo (SV) including focal lesions confined to a segment of the body that does not progress towards generalized disease; and non-segmental (NSV) vitiligo which comprises all generalized usually symmetrical forms, including acrofacial vitiligo^(1,2). The etiopathogenesis of vitiligo is still not fully understood, and the major

theories include melanocyte destruction (autoimmune, neural and impaired redox status) and melanocyte inhibition or defective adhesion⁽³⁾. It proposes that vitiligo is a primary melanocytorrhagy disorder with altered melanocyte response to friction and possibly other types of stress, including their indolent attachment and subsequent transepidermal loss⁽⁴⁾. Calcipotriol is derived from 1-24-dihydroxy vitamin D₃ and has the same mechanisms of action as other vitamin D derivatives, and these mechanisms involve both genomic and non-genomic pathways⁽⁵⁾. In regards to vitiligo, the non-genomic mechanism is involved. Vitamin D increases intracellular calcium concentration through hydrolysis of phosphatidyl inositol phosphate,

leading to production of diacylglycerol and inositol triphosphate with subsequent release of intracellular calcium stores. The intracellular calcium concentration regulates a number of cellular functions including proliferation and differentiation of melanocytes. A combination of topical calcipotriol and corticosteroids demonstrated effectiveness in repigmenting vitiligo, even in patients who were previous topical corticosteroids failures.⁽⁶⁾ Abnormal antioxidant activity in peripheral blood mononuclear cells of vitiligo patients has also been observed, with increased SOD activity, and reduced CAT, glutathione and vitamin E levels. This variability in antioxidant levels was seen exclusively in subjects with active disease. These changes in antioxidants could be responsible for the generation of intracellular reactive oxygen species in vitiligo patients⁽⁷⁾. Topical applications of a combination of vegetal CAT and SOD has been used in vitiligo⁽⁸⁾. *In vitro* studies had previously demonstrated the capacity of a SOD + CAT complex to dramatically reduce the production of free radicals in vitiligo cell and even to restore a normal level of melanin in melanocytes of vitiligo.⁽⁹⁾ It is not only important to remove epidermal hydrogen peroxide (H₂O₂), but also for a successful treatment against vitiligo.⁽¹⁰⁾ The NB-UVB is an emerging, effective and safe therapy for vitiligo.⁽¹¹⁾ It is effective as PUVA, without side effects⁽¹²⁾. The road in the treatment for vitiligo looks promising as more and more knowledge about the disorder is being discovered, thus allowing doctors and pharmacists all around the world to develop future therapies⁽¹⁰⁾.

2. Patients and Methods

The current study comprised a total of 40 patients with different clinical varieties of NSV, diagnosed on the basis of the typical appearance of the skin lesions. The patients were recruited from the Outpatient Clinic of Dermatology and Venereology Department, Tanta University Hospitals, from March / 2010 to December / 2010 and follow up continued till March /2011. All patients were of Fitzpatrick skin type III– IV. The studied patients were treated as a part of an open - controlled right-left comparative study and divided into the following groups: G1, included 20 patients subjected to topical combination of calcipotriol (0.005%) plus betamethazone dipropionate (0.05%) ointment with NB-UVB and G2, included 20 patients subjected to topical SOD/CAT gel with NB-UVB.

Exclusion criteria:

Patients who had used any topical or systemic treatment or phototherapy during the 6 weeks prior to the incorporation in this study, pregnant or lactating

women, patients with any significant systemic, psychiatric or other dermatological conditions that may compromise the result of the study, any contraindication to phototherapy as: skin cancer or lupus erythematosus, special emphasis on patient's occupations and exclusion of those with inevitable sun exposure, patients who did not complete sessions or the follow up and who react to an application of the ointment/gel.

All patients were subjected to the following:

- Complete history taking
- Thorough clinical and dermatological examination. The extent of the vitiligo was assessed and recorded.
- Colored digital photographs were taken for each patient before the first session as a baseline, before each visit at two weeks intervals, at the end of the treatment and monthly thereafter for the following 2 months during follow up period.
- All selected patients were instructed to avoid the use of any other vitiligo therapy (topical or systemic) during the whole duration of the study and follow up period. Informed written consent was obtained from all patients before starting treatment.

Pretreatment preparation of the patients:

- Application of the ointment or gel on the patient's anterior forearm as a thin layer over the entire affected site for 24 hours, to assess any reaction or sensitivity with the topical drug.
- The minimal erythema dose was calculated for all patients prior to the onset of the treatment. The treatment is initiated with 75 to 90% of this dose, varying according to the patient skin phototype (Table 1).

Table (1): Initial ultraviolet B radiation dose⁽¹³⁾.

Skin type	mj/cm ²	75% of dose(mj/cm ²)
I	20 – 30	19
II	25 - 35	23
III	30 -50	31
IV	45 – 60	37
V	60 – 100	50
VI	100 - 200	107

Treatment procedure:

G1: The patients instructed to apply topical

combination of calcipotriol/ betamethasone dipropionate ointment on the left side twice daily except on the day of NB-UVB session. GII: The patients instructed to apply topical SOD / CAT gel twice daily on the left side and from 2 hours before NB-UVB session.

-Each patient received NB-UVB (311-313 nm) session twice /week alone on the right side and with combination treatment on the left side.

-Post NB-UVB erythema usually appears 12 hours after the session. The dosage is gradually increased in order to minimize burn reactions to the UVR (Table 2).

Table (2): Ultraviolet B radiation according to degree of erythema⁽¹⁴⁾

Degree of erythema	Dose increment
0 (no erythema)	20%
1 (minimal erythema)	10%
2 (intense erythema)	Do not apply
3 (erythema and edema)	Do not apply
4 (erythema, edema and blisters)	Do not apply

Post treatment care:

After each session, the patients were instructed to avoid sun exposure as much as possible and to avoid skin rubbing or friction, a bland emollient like panthenol was prescribed to the patients if the irritation of the skin occurred and evaluation was done every 2 weeks for 48 sessions and for follow up period.

Assessment of the efficacy of the treatment:

-Physician's evaluation: clinical evaluations were done before treatment and two weeks after treatment sessions by three dermatologists.

-Patient's opinion: assessment of the over all vitiligo severity.

-Assessment of the mean value of the all evaluations.

-Digital image analysis of standardized colored

Table 3: The response of the treatment of the studied groups

		Response									
		No		Mild		Moderate		Excellent		Tot	
		N	%	N	%	N	%	N	%	N	%
Group I	Right	4	20	4	20	4	20	8	40	20	100
	Left	4	20	2	10	5	25	9	45	20	100
Group II	Right	5	25	5	25	1	5	9	45	20	100
	Left	4	20	4	20	4	20	8	40	20	100
Total		17	21.25	15	18.75	14	17.5	34	42.5	80	100

photographs taken of each visit was used to determine the percentage repigmentation of the vitiligo lesions.

Treatment efficacy was categorized as:

Excellent: which was designated if the patient showed great improvement >75% as compared to pretreatment condition and no noticeable lesions on the skin or any complication from the treatment procedure. Moderate: 50%-75%. Mild: 25%-50%. No response or treatment failure. : <25%

Statistical presentation and analysis of the present study was conducted, using the mean, standard error, unpaired student t-test, the Wilcoxon tests and chi-square by SPSS V12.

3. Results

Clinical results:

Comparison between studied groups revealed no significant differences as regard age, gender, family history (FH) and different sites of the vitiligo lesions, but there was significant difference between two groups as regard duration of the disease.

Treatment results:

-The response of treatment of the studied groups was illustrated in (Table 3).

-Comparison in the response of the treatment in G I and GII between right side and left side revealed no statistically significant difference between the two sides (Tables 4 &5).

-Comparison in the response in the left side showed no statistically significant difference in repigmentation between the two groups (Table 6)

-There were no any significant correlation between the combination treatment plus NB-UVB in both group and clinical criteria of vitiligo patients as age, gender, duration of the disease and patients with positive and negative FH. There were statistically significant differences between sites of vitiligo and treatment in the left side in the face, neck in G II [P = 0.005] while in G I the face had excellent response but not statistically significant (Table 7).

Table 4: Comparison in the response of the treatment between right side and left side in group I

Group I		Response					
		Right		Left		Total	
		N	%	N	%	N	%
No		4	20.00	4	20.00	8	20.00
Mild		4	20.00	2	10.00	6	15.00
Moderate		4	20.00	5	25.00	9	22.50
Excellent		8	40.00	9	45.00	17	42.50
Total		20	100.00	20	100.00	40	100.00
Chi-square	X ²	0.837					
	P-value	0.840					

Table 5: Comparison in the response of the treatment between right side and left side in group II

Group II		Response					
		Right		Left		Total	
		N	%	N	%	N	%
No		5	25.00	4	20.00	9	22.50
Mild		5	25.00	4	20.00	9	22.50
Moderate		1	5.00	4	20.00	5	12.50
Excellent		9	45.00	8	40.00	17	42.50
Total		20	100.00	20	100.00	40	100.00
Chi-square	X ²	6.400					
	P-value	0.093					

Table 6: Comparison in the response of the treatment in the left side between group I and group II

Left		Group					
		Group I		Group II		Total	
		N	%	N	%	N	%
No		4	20.00	4	20.00	8	20.00
Mild		2	10.00	4	20.00	6	15.00
Moderate		5	25.00	4	20.00	9	22.50
Excellent		9	45.00	8	40.00	17	42.50
Total		20	100.00	20	100.00	40	100.00
Chi-square	X ²	0.837					
	P-value	0.841					

Table 7: Relation between site of the lesions and response of the treatment in the left side in studied groups

Group	Site	Left(Topical application + NB-UVB)						Chi-square	
		No	Mild	Moderate	Excellent	Total	X ²	P-value	
Group I	Forearm	N	0	0	0	2	2	26.956	0.029
		%	0.00	0.00	0.00	10.00	10.00		
	Face	N	0	0	0	3	3		
		%	0.00	0.00	0.00	15.00	15.00		
	Leg	N	0	1	3	1	5		
		%	0.00	5.00	15.00	5.00	25.00		
	Trunk	N	0	0	0	2	2		
		%	0.00	0.00	0.00	10.00	10.00		
	Hand	N	2	0	2	0	4		
		%	10.00	0.00	10.00	0.00	20.00		
	Foot	N	2	1	0	1	4		
		%	10.00	5.00	0.00	5.00	20.00		
Group II	Forearm	N	2	1	1	1	5	32.750	0.005*
		%	10.00	5.00	5.00	5.00	25.00		
	Face	N	0	0	3	3	6		
		%	0.00	0.00	15.00	15.00	30.00		
	Leg	N	0	2	0	0	2		
		%	0.00	10.00	0.00	0.00	10.00		
	Neck	N	0	0	0	4	4		
		%	0.00	0.00	0.00	20.00	20.00		
	Trunk	N	2	0	0	0	2		
		%	10.00	0.00	0.00	0.00	10.00		
	Hand	N	0	1	0	0	1		
		%	0.00	5.00	0.00	0.00	5.00		

Digital photographs of treated patients included 4 photos:
1) Before treatment 2) After 3 months (24 session) 3) After 6 months (48 session) 4) During follow up
Digital photographs of patients treated in group I

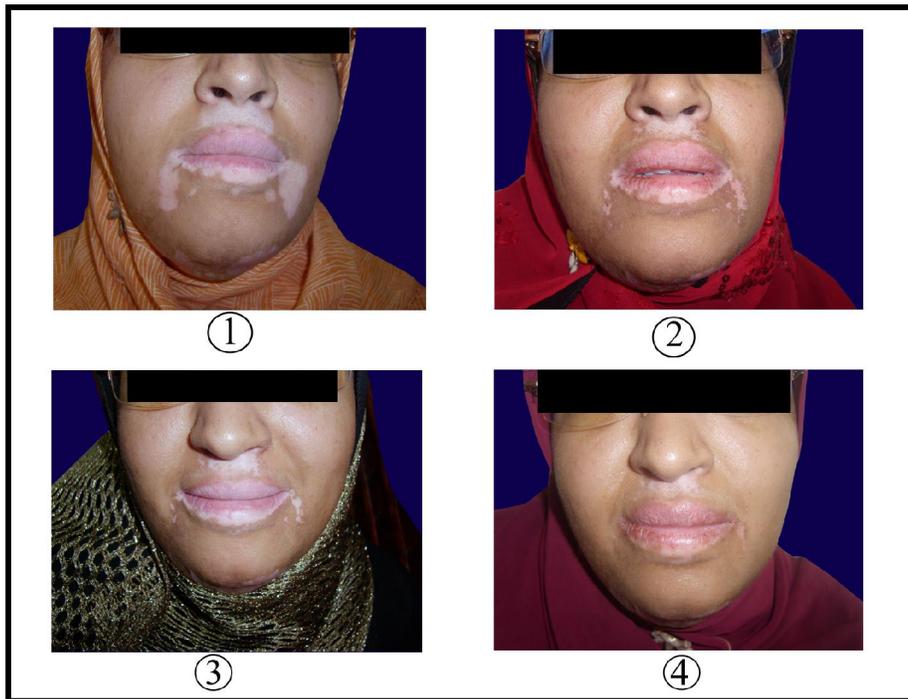


Photo1: Excellent response in both sides of the face (>75% repigmentation)

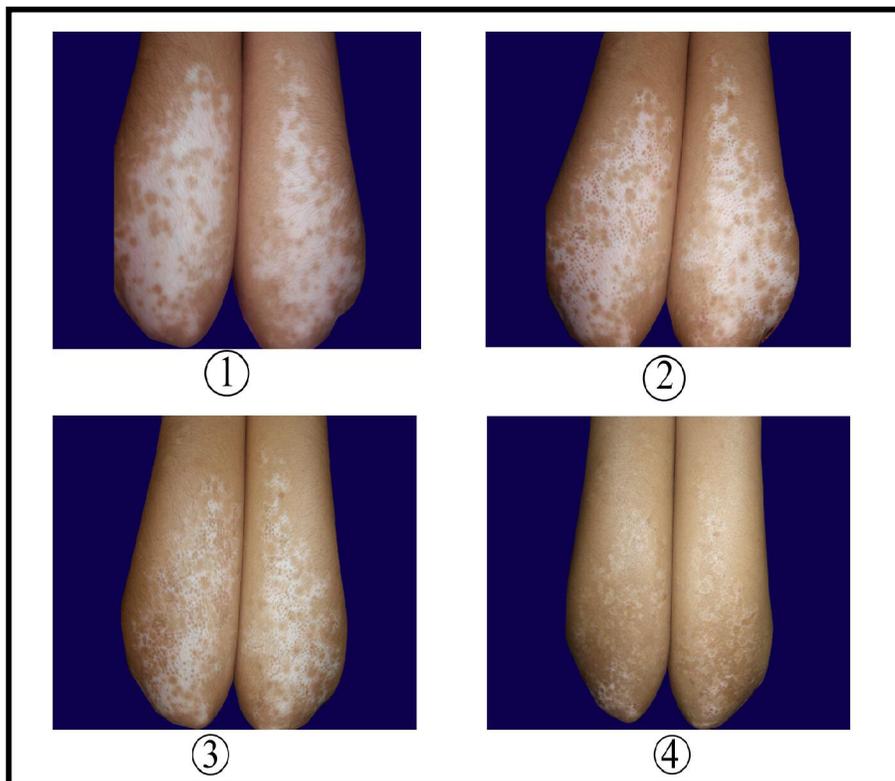


Photo2: Excellent response in both sides of the forearms (>75% repigmentation)

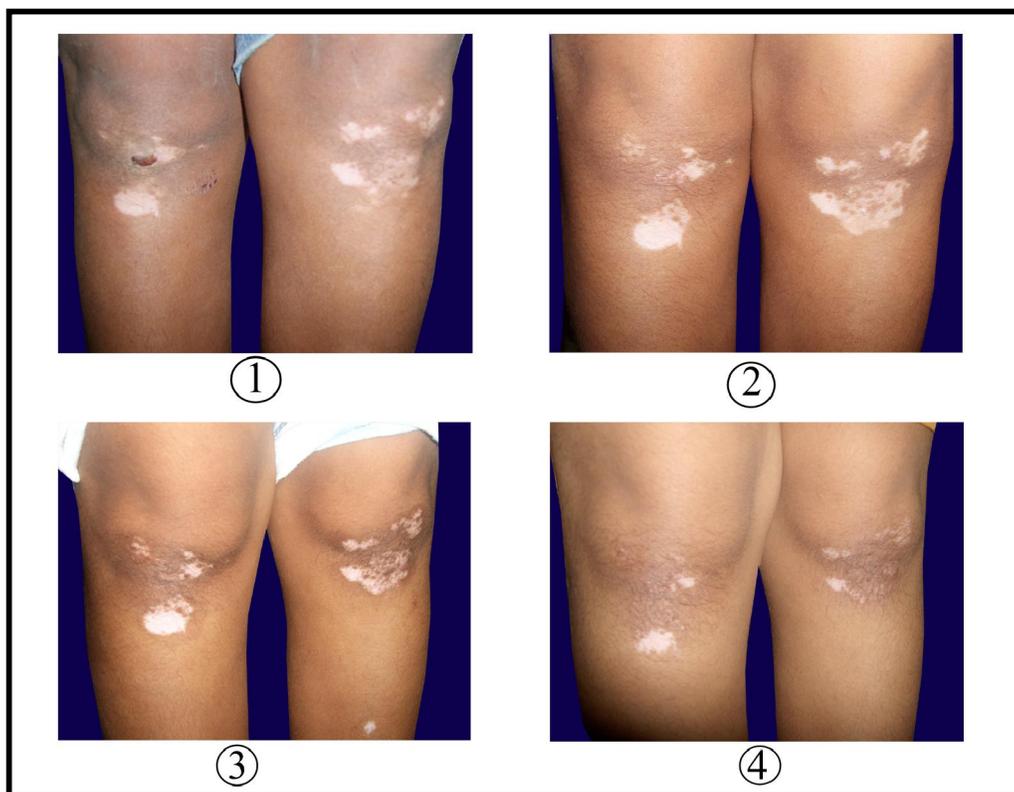


Photo 3: Moderate response in both sides of both knees (50%- 75% repigmentation)

Digital photographs of patients treated in group II

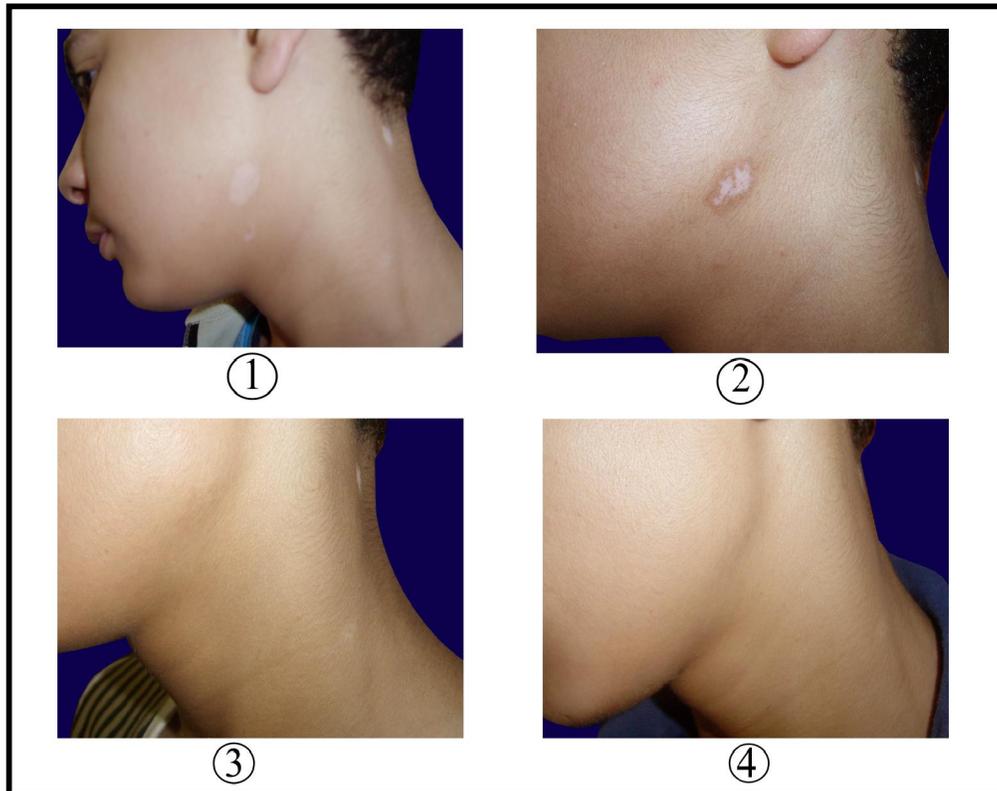


Photo 4 a: Excellent response of the left side of the face (>75% repigmentation)

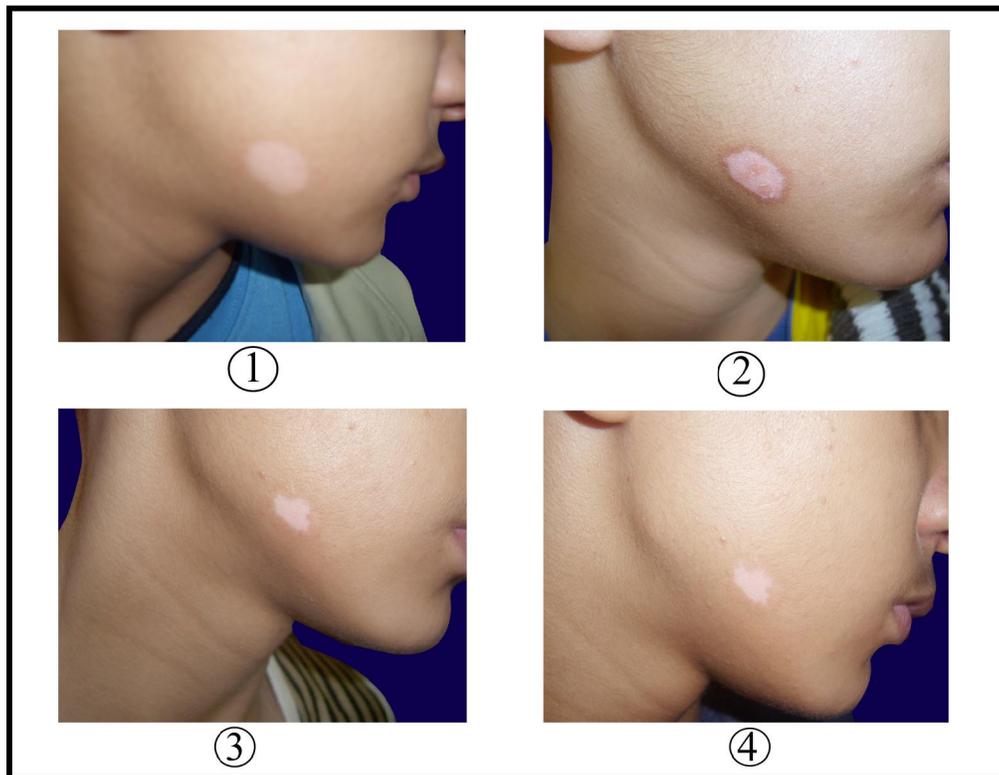


Photo 4 b : Mild response of right side of the face (25% 50% repigmentation)

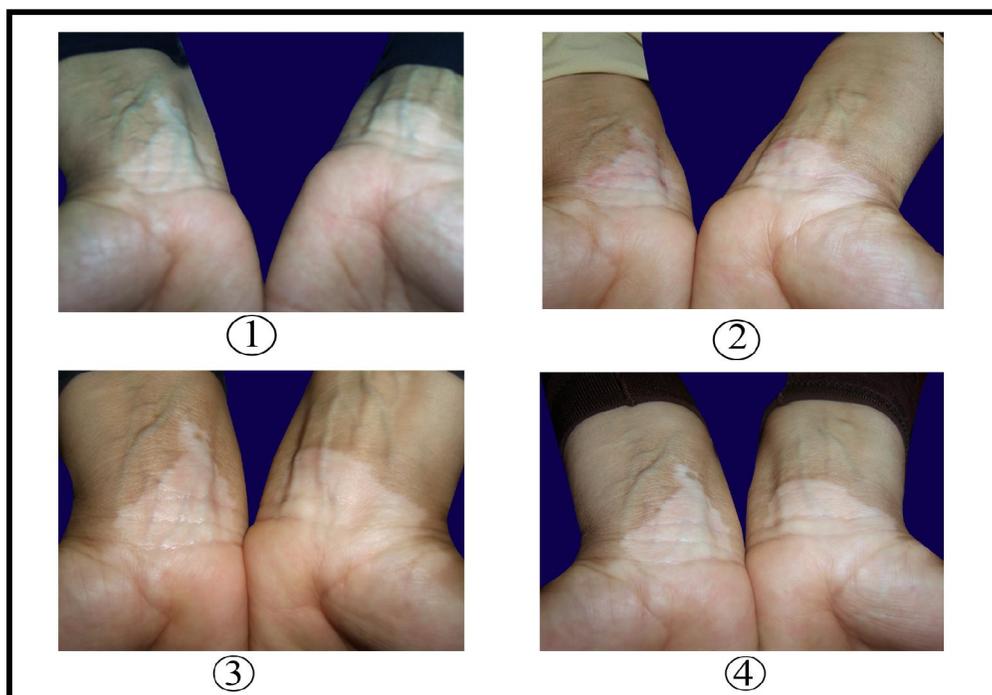


Photo 5: No response in both sides of the wrist and hands (<25% repigmentation)

4. Discussion

The treatment of vitiligo is a tough challenge to dermatologists. A variety of therapeutic agents have been tried on vitiligo but none is uniformly effective. Potent topical corticosteroids and phototherapy is the mainstay of treatment. Response rates of 56% and 63%, respectively, have been reported with the above modalities of treatment. But these modalities are often required for a longer duration of time and they carry a potential risk for various side-effects⁽¹⁵⁾. Vitiligo in the current study, affects both gender and can present at any age, this in agreement with the previous reports Kumaran *et al.*,⁽¹⁵⁾ Yuksel *et al.*,⁽¹⁶⁾. In clinical practice, parents with vitiligo very often wish to know the risk of their children developing vitiligo. In the current study, positive FH of vitiligo was seen in 15% in GI and 30% in GII. This agreed with the result of Kumaran *et al.*,⁽¹⁵⁾ in which the negative FH was more with his patients than those with positive FH.

NB-UVB therapy has also been reported to be safe in childhood vitiligo^(17,18). The mechanism of NB-UVB-induced repigmentation involves the stabilization of the depigmenting process and the stimulation of residual follicular melanocytes. In particular, NB-UVB is probably involved in the upregulation of the melanogenesis and melanocytes migration⁽¹⁹⁾. In the current study; number of the patients treated with NB-UVB alone were 40 patients received NB-UVB only in their right side; 42.5% achieved excellent repigmentation, 12.5 % achieved moderate repigmentation, 22.5 % achieved mild repigmentation and 22.5 % achieved no repigmentation. During post treatment follow up for 2 months 12.5% of the patients, the repigmentation faded after stopping the treatment. While in a study reported by Kishan Kumar *et al.*⁽²⁰⁾, only 2% patients developed depigmentation of repigmented sites during the follow-up period of 6 months after one year treatment with NB-UVB. Also in a study by Sitek *et al.*⁽²¹⁾, who assess the stability of NB-UVB-induced pigmentation on patients with generalized vitiligo, 16% experienced >75% stable repigmentation in 3 years after cessation of NB-UVB therapy. Chen *et al.*⁽²²⁾, performed a retrospective study on 72 patients to examine the efficacy of NB-UVB in the treatment of vitiligo and found that only one patient show mild repigmentation, 9 patients showed 75%-100% repigmentation, 24 patients showed 50%-75% repigmentation and 20 patients showed 25% -50% repigmentation. Also Anbar *et al.*,⁽²³⁾ performed a study on 150 patients. 90% NSV and 10% SV and found that; in NSV 48% of patients had marked pigmentation, 27% of patients had moderate repigmentation and in 25% of patients had mild

repigmentation, but patients with SV had only mild repigmentation.

Topical corticosteroids have been used to treat vitiligo since 1970 with varying results⁽²⁴⁾. The mechanism of action on vitiligo is supposed to be the suppression of direct or antibody-dependent cytotoxicity⁽²⁵⁾. Glucocorticoids have also been implicated in the modulation of Th1/Th2 cytokine production, presumably by suppressing type 1 cells and/or by switching Th cells from Th1 to Th2 phenotype⁽²⁶⁾. Calcipotriol is derived from 1-24-dihydroxyvitamine D3. Vitamin D increases intracellular calcium concentration, which regulates a number of cellular functions including proliferation and differentiation of melanocytes⁽⁵⁾. Calcipotriol has recently been shown to be helpful in repigmentation of vitiliginous lesions when used as a monotherapy or in combination with PUVA. There have been several reports of hyperpigmentation after combined use of calcipotriol and phototherapy in psoriasis⁽¹⁵⁾. Combination treatment with topical calcipotriol and topical steroids has been shown to be efficacious in psoriasis and the side-effects related to steroids use were also decreased. Combination therapy reduced the irritation and hyperpigmentation seen with calcipotriol used alone. The anti-inflammatory activity of corticosteroids may be responsible for this beneficial effect⁽¹⁵⁾. Similar findings, reported by Lebwohl *et al.*,⁽²⁷⁾ Ruzicka and Lorenzl,⁽²⁸⁾ in patients with psoriasis. In the present study, in GI; left side of the patients had better repigmentation than right side but there was no statistically significant difference between both sides. In the left side about 45% of the patients achieved excellent pigmentation, 25% achieved moderate pigmentation, 10% mild pigmentation and 20% had no pigmentation, while in the right side about 40% of the patients achieved excellent pigmentation, 20% had moderate pigmentation, 20% had mild pigmentation and 20% had no pigmentation. In agreement with Kumaran *et al.*,⁽¹⁵⁾ who divided patients with localized vitiligo into three treatment groups. In GI, patients applied betamethasone dipropionate cream 0.05% twice daily; in GII, patients applied calcipotriol ointment 0.005% similarly; and in GIII, patients applied betamethasone dipropionate in the morning and calcipotriol ointment in the evening. When used individually, the betamethasone dipropionate and the calcipotriol were found to be equally effective but the combination of the two, appeared to give a significantly faster onset of repigmentation along with better stability of the achieved pigmentation and with lesser number of side-effects. Chiavérini *et al.*,⁽²⁹⁾ performed a prospective, right-left comparative, open study and examined the efficiency of topical

calcipotriol as a monotherapy for the treatment of vitiligo. They concluded that; it was not effective. In a clinical trial, the combination of NB-UVB and calcipotriol showed no increase in efficacy, probably due to the fact that calcipotriol is rapidly degraded (>90%) by UVR⁽³⁰⁾. In the current study during post-treatment follow-up, 3 patients in GI maintained their achieved pigmentation and the pigmentation continued to appear in their left side. In 3 patients the pigmentation started fading on stopping the therapy and one patient developed new lesions and the remaining 13 patients have stable pigmentation. In comparison to Kumaran *et al.*,⁽¹⁵⁾ they showed in their study that during post-treatment follow-up of 2 months, 26.6% in GI maintained their achieved pigmentation and in one of them the pigmentation continued to appear and complete repigmentation occurred in 20 weeks. In the remaining 55.6% patients the pigmentation started fading on stopping the therapy and 33.3% out of these 55.5% patients subsequently developed new lesions. In GII, 2 patients maintained their achieved pigmentation; in the remaining 66.7% it faded after stopping the treatment and 2 of these patients developed new lesions subsequently. In GIII, 90% of the patients who pigmented, maintained their achieved pigmentation. In only 9.1%, the pigmentation faded and multiple new lesions developed. In all the groups; the lesions with a diffuse type of repigmentation started to fade early. On comparing the patients in GIII to those in GI and II; the achieved pigmentation in vitiligo lesions of this group was much more stable.

Pseudocatalase is a bis-manganese III EDTA (HCO₃)₂ complex, capable of degradation of H₂O₂ to O₂ and H₂O after photo-activation with UVB or solar irradiation. After topical application of pseudocatalase preparation, a reduction of the H₂O₂ peak was detected *in vivo*. So, topical UVB-activated pseudocatalase can be successfully used for removing epidermal H₂O₂ in vitiligo.⁽³¹⁾ In the present study, topical SOD/CAT gel used with NB-UVB therapy. In GII: right side of the patients had better repigmentation than left side but there was no statistically significant difference between both sides. In the left side about 40% of patient achieved excellent pigmentation, 20% achieved moderate pigmentation, 20% achieved mild pigmentation and 20% had no pigmentation, while in the right side about 45% achieved excellent pigmentation, 5% achieved moderate pigmentation, 25% had mild pigmentation and 25% had no pigmentation. In agreement with Schallreuter and Rokos,⁽³²⁾ who studied the efficacy of this formulation SOD/CAT gel in the removal of reactive oxygen species they reported that the combination does not have the

capacity to reduce H₂O₂. In order to test the clinical efficacy of the combination they treated 6 patients with facial vitiligo over 4 months with the application of the formulation twice daily together with solar exposure for at least 30 minutes over 4 months and they did not notice any significant repigmentation. But low patient numbers and short treatment duration affected the efficacy of this study. Another study in which combination of SOD/CAT was used in the literature came from Kostovic *et al.*,⁽³³⁾. Their study included patients applied the gel containing SOD /CAT twice a day and received NB-UVB 3 times per week. 15.79% of the patients showed more than 75% repigmentation, 31.58% showed 26%-50% repigmentation and 5.26% showed 1%-25% repigmentation, where as no repigmentation was recorded in 5.26% of the patients. Sanclemente *et al.*,⁽³⁴⁾ compared the effect of topical 0.05% betamethasone valerate versus CAT/ SOD and concluded that; vitiligo repigmentation with topical CAT/SOD at 10 months is similar to repigmentation with topical 0.05% betamethasone valerate. Besides these, there is also another study which suggested that topical pseudocatalase was not effective in vitiligo. In this study, the efficacy of topical pseudocatalase mousse that contained pseudocatalase, calcium chloride, manganese chloride and sodium bicarbonate in a base enclosed in an aerosol canister pressurized by butane, applied twice daily to the hands and face of vitiligo patients in combination with twice-weekly NB-UVB phototherapy, was assessed and this treatment was not shown to be effective⁽³⁵⁾. However, the pseudocatalase formulation used in this study was different from that in other studies⁽³⁶⁾. Schallreuter *et al.*,⁽³⁷⁾ reported successful treatment of vitiligo with topical application of pseudocatalase and calcium followed by short term UVB light exposure. According to their study, repigmentation occurred in the majority of the cases after 2 to 4 months treatment. In all patients, active depigmentation was arrested. None of the patients developed new lesions or recurrence of the disease during 2 years follow up. During the follow up in GII, one patient maintained their achieved pigmentation; in 2 patients the pigmentation faded after stopping the treatment and 2 patients developed new lesions and the remaining 15 patients had stable pigmentation.

No association was found in this study between response to treatment and age gender of patients, FH and duration of disease. This has been confirmed by several other studies⁽³⁸⁻⁴⁰⁾. Although some studies report such an association with the age of the patient that reported that children respond faster to NB-UVB with lesser number of exposures and cumulative dose of NB-UVB.⁽²⁰⁾ Although AL Mokadem *et al.*,⁽⁴¹⁾

found a significant negative correlation between duration of the disease and clinical response. In addition; Anbar *et al.*,⁽²³⁾ and De Francesco *et al.*,⁽⁴²⁾ reported that short duration of the disease was associated with better results.

The current study found in GI; the best results obtained with the face in the left side than the foot and acral parts, also in GII; the face in the left side had the best results than other parts of the body. In agreement with Gamil *et al.*,⁽¹⁹⁾ the best results were found for facial lesions, with the trunk and proximal limbs having good to moderate repigmentation, but the hands and feet were resistant to the combination treatment. Also Schallreuter *et al.*,⁽⁴³⁾ in a retrospective study of 71 children with vitiligo found that more than 75% repigmentation was achieved in 66 of the 71 children on the face/neck, 48 of 61 children on the trunk, and 40 of 55 children on the extremities after NB-UVB activated pseudocatalase daily treatment for 8-12 months. The therapy had no side-effects. The favorable results obtained on the face may be due to stimulation of the melanocytic reservoirs in the hair sheaths by NB-UVB, as repigmentation occurred in a perifollicular pattern and was not seen in lesions with white a melanotic hair.⁽¹⁸⁾ In addition, the face in particular is a body site with a great number of pilosebaceous units, which are activated by NB-UVB. The lower repigmentation rates in the acral regions may be attributed to lack of hair follicles. The darker skin phototype, as seen in Egyptian patients with higher initial and total cumulative NB-UVB doses and more frequent exposure, are predisposing factors to good response to NB-UVB in vitiligo⁽⁴⁴⁾. Treatment responses of vitiligo lesions could be different due to the disease duration, gender, age of the patients, their skin phenotype and location of the lesion. Therefore, we suggest that it is necessary to plan other further studies with properly matched-patients on disease duration and gender ratio, and to further study the relationship between clinical parameters of the patients and response to treatment. The adverse effects in the present study were minimal like erythema burning, irritation and none of the patients required discontinuation of therapy. The adverse effect profile observed in the current study was similar to that reported in the other literatures. All these studies, including this one, clearly establish the safety profile of NB-UVB therapy.

Conclusions

The treatment of vitiligo is a tough challenge to dermatologists. A variety of therapeutic agents have been tried on vitiligo but none is uniformly effective. Recent advances in the pathogenesis of vitiligo have

contributed to find better treatments; however progression of the disease and partial or lack of complete repigmentation still occurs in a good number of patients. The current study had shown that NB-UVB treatment alone was a moderately effective treatment for vitiligo. Betamethasone dipropionate / calcipotriol, when used in combination with NB-UVB were found to be superior in efficacy and safe than NB-UVB alone, but the results were not statistically significant. SOD/ CAT gel does not appear to add any incremental benefit to NB-UVB alone. So, further evaluation of the combination in large scale should be undertaken. Many studies should be performed to determine which treatment is the best for vitiligo. Since there is no consensus on the pathogenesis of vitiligo, a treatment to completely cure vitiligo does not exist. More randomized controlled trials on the treatment of vitiligo are necessary.

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References

1. Bleehen SS, Anstey AV (2010): Disorders of skin colour. In: Burns T, Breathnach S, Cox N, Griffiths C, eds. Rook's Textbook of Dermatology, 8th edn. Oxford: Blackwell Science. p: 58:46-9.
2. Gauthier Y, Cario AM, Taieb A (2004): A critical appraisal of vitiligo etiologic theories. Is melanocyte loss a melanocytorrhagy? *Pigment Cell Res.*; 16: 322-32.
3. Hameed A, Rani Z, Hasnain A (2005): Vitiligo : new etiology- based treatments. *J Pak Ass Dermatol.*; 15: 252-60.
4. Gauthier Y, Cairo AM, Lepreux S (2003): Melanocyte detachment after skin friction in non lesional skin of patients with generalized vitiligo. *Br J Dermatol.*; 148:95 -101.
5. Guilhou JI (2001): Calcipotriol. *Ann Dermatol.*; 128: 229-37.
6. Travis LB, Silverberg NB(2004): Calcipotriene and corticosteroid combination therapy for vitiligo. *Pediatr Dermatol.*; 21: 495-8.
7. Dell'Anna ML, Maresca V, Briganti S, et al. (2001): Mitochondrial impairment in peripheral blood mononuclear cells during the active phase of vitiligo. *J Invest Dermatol.* ; 117:908-13.
8. Zhang Y, Wang JZ, Wu YJ, et al. (2002): Anti-inflammatory effect of recombinant human superoxide dismutase in rats and mice and its mechanism. *Acta Pharmacol Sin.*; 23: 439-44.

9. Lange RW, Germolic DR, Foley JF, et al. (1998): Antioxidants attenuate anthralin-induced skin inflammation in BALB/c mice: role of specific pro inflammatory cytokines. *J Leukoc Biol.*; 64: 170-6.
10. Schallreuter KU, Moore J, Behrens WS, et al.(2002): Rapid initiation of repigmentation in vitiligo with Dead Sea climatotherapy in combination with pseudocatalase (PC-KUS). *Int J Dermatol.* ; 41:482-7.
11. Kanwar AJ, Dorga S, Prasad D, et al.(2005): Narrow-band UVB for the treatment of vitiligo: An emerging effective and well tolerated therapy. *Int J Dermatol.*; 44:57-60.
12. El Mofty M, Mostafa W, Esmat S, et al.(2006): Narrow-band ultraviolet B 311 nm in the treatment of vitiligo: Two right-left comparison studies. *Photodermatol Photoimmunol Photomed.*; 22:6-11.
13. Morison WL (1993): PUVA photochemotherapy. In: Lim HW, Soter NA. New York: Marcel Dekker; pp: 327-45.
14. Zanolli MD, Felmam SR, Clark AR, et al.(2004): Phototherapy treatment protocols for psoriasis and other phototherapy responsive dermatoses. Parthenon Publishing Group Inc, New York; 13-16:18-20.
15. Kumaran MS, Kaur I, Kumar B (2006): Effect of topical calcipotriol, betamethasone dipropionate and their combination in the treatment of localized vitiligo. *J Eur Acad Dermatol Venereol.*; 20:269-73.
16. Yuksel E, Aydin F, CantyrkT, et al.(2009): Comparison of the efficacy of narrow band ultraviolet B and narrow band ultraviolet B plus topical catalase-superoxide dismutase treatment in vitiligo patients. *Eur J Dermatol.* ; 19: 341-4
17. Hercogova J, Buggiani G, Prignano F, et al. (2007): A rational approach to the treatment of vitiligo and other hypomelanoses: pigmentary disorders. *Dermatol Clin.*; 25:383-92.
18. Njoo MD, Bos JD, Westerhof W(2000):Treatment of generalized vitiligo in children with narrow-band (TL-01) UVB radiation therapy. *J Am Acad Dermatol.*; 42:245-53.
19. Gamil H, Attwa E, Ghonemy S (2010): Narrowband ultraviolet B as monotherapy and in combination with topical calcipotriol in the treatment of generalized vitiligo . *Clin Exp Dermatol.*; 35: 914–26.
20. Kishan Kumar Y, Rao G, Gopal, K, et al.(2009): Evaluation of narrow-band UVB phototherapy in 150 patients with vitiligo. *Indian J Dermatol Venereol Leprol.* ; 75:162-6.
21. Sitek JC, Loeb M, Ronnevig JR (2007): Narrowband UVB therapy for vitiligo: does the repigmentation last?. *J Eur Acad Dermatol Venereol.*; 21:891-6
22. Chen G, Hsu M, Tai H, et al.(2005): Narrow-band UVB treatment of vitiligo in Chinese. *J Dermatol.* ; 32: 793–800.
23. Anbar TS, Westerhof W, Abdel-Rahman AT, et al. (2006): Evaluation of the effects of NB-UVB in both segmental and non-segmental vitiligo affecting different body sites. *Photodermatol Photoimmunol Photomed.*; 22:157-63.
24. Hartmann A, Bröcker E, Becker J (2004): Hypopigmentary skin disorders: Current treatment options and future directions. *Drugs*; 64: 89.
25. Hann SK, Kim H, Im S (1993): The change of melanocyte cytotoxicity after systemic steroid treatment in vitiligo patients. *J Dermatol Sci.*; 6: 201-5.
26. Miyaura H, Iwata M(2002): Direct and indirect inhibition of Th1 development by progesterone and glucocorticoids. *J Immunol.*; 168: 1087.
27. Lebwohl M, Siskin SB, Epinette W.(1996): A multicentre trial of calcipotriene ointment and halobetasol ointment compared with either agent alone for the treatment of psoriasis. *J Am Acad Dermatol.* ; 35: 268–9.
28. Ruzicka T, Lorenz B (1997): Calcipotriol with or without betamethasone for psoriasis. *Br J Dermatol.* , 138: 254–8.
29. Chiaverini C, Passeron T, Ortonne JP (2002): Treatment of vitiligo by topical calcipotriol. *J Eur Acad Dermatol.*; 16: 137-8.
30. Lebwohl M, Quijije J, Gilliard J, et al.(2003): Topical calcipotriol is degraded by ultraviolet light. *J Invest Dermatol.* ; 121:594-5.
31. Yildirim M, Baysal V, Inaloz HS, et al. (2003): The role of oxidants and antioxidants in generalized vitiligo. *J Dermatol.* ;30:104-8.
32. Schallreuter KU, Rokos H(2005): Vitix-a new treatment for vitiligo? *Int J Dermatol*; 44: 969-70
33. Kostovic K, Pastar Z, Pasic A, et al.(2007): Treatment of vitiligo with narrow-band UVB and topical gel containing catalase and superoxide dismutase. *Acta Dermatol Venereol Croat.*; 15: 10-4.
34. Sanclemente G, Garcia J, Zuleta J, et al. (2008): A double-blind, randomized trial of 0.05% betamethasone vs. topical catalase/dismutase superoxide in vitiligo. *J Eur Acad Dermatol Venereol.*; 22:1359- 64.
35. Patel DC, Evans AV, Hawk J (2002): Topical pseudocatalase mousse and narrowband UVB phototherapy is not effective for vitiligo: an open, single-centre study.*Clin Exp Dermatol.*; 27: 641-4.

36. Schallreuter KU (2003): Effectiveness of pseudocatalase formulation in vitiligo. *Clin Exp Dermatol.*; 28: 562-3.
37. Schallreuter KU, Wood JM, Lemke KR, et al. (1995): Treatment of vitiligo with a topical application of pseudocatalase and calcium in combination with short term, UVB-exposure: a case study on 33 patients. *Dermatology*; 190: 223-9.
38. Hamzavi I, Shapiro J (2004): Parametric modeling of narrow band UV-B phototherapy for vitiligo using a novel quantitative tool. *Arch Dermatol.* ; 140:677-83.
39. Nicolaidou E, Antoniou C, Stratigos AJ, et al (2007): Efficacy, predictors of response, and long-term follow-up in patients with vitiligo treated with narrowband UVB phototherapy. *J Am Acad Dermatol.*; 56: 274-8.
40. Kanwar AJ, Dogra S (2005): Narrow-band UVB for the treatment of generalized vitiligo in children. *Clin Exp Dermatol.*, 30:332-6.
41. AL Mokadem S, El Sheikh A (2008): The role of pimecrolimus in vitiligo. *Egy J Dermatol Online*; 4:230-6
42. De Francesco V, Stinco G, Laspina S, et al.(2008): Immunohistochemical study before and after narrow band (311 nm) UVB treatment in vitiligo. *Eur J Dermatol.*; 18: 292-6.
43. Schallreuter KU, Krüger C, Würfel BA, et al. (2008): From basic research to the bedside: efficacy of topical treatment with pseudocatalase PC-KUS in 71 children with vitiligo. *Int J Dermatol.*; 47:743-53
44. Brazzelli V, Antoninetti M, Palazzini S et al. (2007): Critical evaluation of the variants influencing the clinical response of vitiligo: study of 60 cases treated with NB-UVB phototherapy. *J Eur Acad Dermatol Venereol*; 21: 1369-74.

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