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Evaluating the Efficacy of Topical Tetracycline in Enhancing the Effect of Excimer Light in the Treatment of Vitiligo

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Abstract

Background: Vitiligo is the leading cause of skin depigmentation. This disorder is characterized by persistent, acquired depigmentation due to a loss of melanocyte activity.

Aim of the study: The purpose of this study is to evaluate whether or not topical tetracycline can improve the efficacy of excimer light in the treatment of vitiligo.

Results: The most common affected sites were the face (7 patients, 23.3 %) and the knee (6 patients, 20 %), followed by the elbow (4 patients, 13.3 %), while the least affected sites were the abdomen, chest, and the neck (2 patients at each site, 6.7 %). Axilla, breast, foot, hand, leg, thigh, and wrist were affected in one patient (3.3 %) for each site. Also, there was a statistically significant difference (P -value = 0.002) between the right and left sides according to satisfaction rate, VASI score, and VETI score.

Conclusion: Our study confirmed that vitiligo can be effectively treated with a combination of topical tetracycline & excimer light. A combination of topical tetracycline and excimer light is statistically significant as regards response during sessions according to the Vitiligo Extent Tensity Index (VETI) score, patient satisfaction, and improvement in VASI score after 12 weeks of treatment for vitiligo.

Keywords: Tetracycline, Vitiligo extent tensity index, Vitiligo

1. Introduction

Vitiligo is a condition characterized by the loss of skin pigment cells (melanocytes) and the resulting white patchy skin.¹ Its clinical characteristics are well-defined milky white macules that are localized or in general distribution and often coalesce in large depigmented lesions. About 0.5–1% of people worldwide have vitiligo. Prevalence is most likely similar between sexes; however, it may be higher in people of color.^{1,2}

The tetracycline class of antibiotics (TCS) is widely used. The most common negative reactions to tetracycline antibiotics include skin discoloration and photosensitization. When the type of photosensitization mechanism is considered, it is possible to state that tetracycline antibiotics exhibit exclusively phototoxic activity.³

Both sexes are equally impacted. A family history of vitiligo exists in at least 30 % of cases.⁴

Typically, the onset of the illness occurs between the ages of 10 and 30 years.⁵

Vitiligo is a major dermatologic challenge, considering the many available therapeutic modalities.⁶ Monochromatic excimer light (mel, 308 nm) has been used in an increasing number of phototherapies recently.^{7,8}

2. Patients and methods

2.1. Patients

This intraindividual comparative research includes 30 patients with vitiligo. The patients were taken from the outpatient clinic of the Dermatology

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and Venerology Department in Al Hussein University Hospital.

2.1.1. Inclusion criteria

Case reports of 8–65-year-olds with stable vitiligo (no new lesions in the last 3 months), no topical therapies for at least 2 weeks, and no phototherapy for at least 8 weeks.

2.1.2. Exclusion criteria

Vitiligo patients who have tried various treatments within the past 3 months, patients with present or past history of photodermatoses or cutaneous malignancy, pregnant and lactating females, and patients who take immunosuppressive drugs.

2.1.3. All patients were subjected to the following

At the beginning, middle, and end of the 4th, 8th, and 12th weeks, patients underwent full history and general examination, a dermatological examination to check for lesions, and digital photography.

2.2. Method

Patients had their lesions divided into four quadrants, with side A being the left side, and received excimer light and topical Adco cyclizine treatment. When excimer light is used, it only be applied to the right side or side B.

All patients were told to rub ointments on side A (left side) for only half an hour before using the excimer light. Patients were also receiving eximer light phototherapy twice weekly.

After weeks 4, 8, and 12, we visited and assessed each case.

2.3. Evaluation of medical treatment

2.3.1. Clinical assessment

(1) Before each session, as well as at the beginning and end of the study, photographs were taken (mobile phone). (2) Three separate observers rated the degree of pigment loss using the Vitiligo Extent Tensity Index (VETI) score (Feily, 2014), and the mean of these scores was used to determine the severity of condition. (3) The patient satisfaction scale. (4) Safety assessment.

2.4. Statistical analysis

Statistical Package for the Social Sciences (SPSS), version 24 was used to analyze the data. When dealing with numerical information, mean and standard deviation were used. Percentages and frequencies were used to represent qualitative

data. The mean (or average) is the value at the mathematical center of a set of numbers, calculated by dividing the total of the numbers by their total number. The variability of a dataset is measured by its standard deviation (SD). When the SD is small, the values cluster close to the set's mean, but when it is large, the values are more dispersed.

These tests were conducted:

Mann–Whitney U (MW): when matching between two means (for normally distributed data).

When comparing nonparametric data, the Chi-square test was used.

If the probability (*P*-value) was <0.05, it was deemed significant; if it was <0.001, it was considered very significant; and if it was >0.05, it was considered statistically insignificant.

3. Results

Table 1 shows that all cases included in the study are described here by their demographic information. The ages of the cases ranged from 8 to 60 years, with a mean age of 20.9 ± 15.04 years. Eight of the patients were males (26.7 % of the total), and 22 were females (73.3 % of the total). Four of the patients studied (or 13.3%) had a positive family history. The median age concerning duration was 1.97 years (range, 0.7–5 years), while the mean age at death was 1.97 ± 1.09 years across all patients investigated (**Table 2**).

Each patient's affected locations are included in this table. The most common affected sites were the face (7 patients, 23.3 %) and the knee (6 patients, 20 %), followed by the elbow (4 patients, 13.3 %), while the least affected sites were the abdomen, chest, and the neck (2 patients at each site, 6.7 %). Axilla, breast, foot, hand, leg, thigh, and wrist were affected in one patient (3.3 %) for each site (**Table 3**).

This table shows a statistically significant difference (*P*-value = 0.002) among the right and left sides according to the VETI score as follows: On the left side, there were 10 G4 patients (33.3 %), 5 G3 patients (16.7 %), 4 G2 patients (13.3 %), 10 G1 patients (33.3 %), and 1 G0 patient (3.3 %).

Table 1. Description of demographic data in all studied cases.

		Studied patients (N = 30)	
Age (years)	Mean \pm SD	20.9 \pm 15.04	
	Min - Max	8 - 60	
Sex	Male	8	26.7%
	Female	22	73.3%
Family history	No	26	86.7%
	Yes	4	13.3%
Duration (years)	Mean \pm SD	1.97 \pm 1.09	
	Min - Max	0.7 - 5	

Table 2. Description of affected sites in all studied patients.

Affected sites	Studied patients (N = 30)
Abdomen	2 (6.7 %)
Axilla	1 (3.3 %)
Breast	1 (3.3 %)
Chest	2 (6.7 %)
Elbow	4 (13.3 %)
Face	7 (23.3 %)
Foot	1 (3.3 %)
Hand	1 (3.3 %)
Knee	6 (20 %)
Leg	1 (3.3 %)
Neck	2 (6.7 %)
Thigh	1 (3.3 %)
Wrist	1 (3.3 %)

Table 3. Comparison of VETI score between right and left sides.

		Left side (N = 30)		Right side (N = 30)		Stat. test	P-value
VETI score	G0	1	3.3%	7	23.3%	X ² = 17.3	= 0.002 S
	G1	10	33.3%	18	60%		
	G2	4	13.3%	3	10%		
	G3	5	16.7%	0	0%		
	G4	10	33.3%	2	6.7%		

Table 4. Comparison of VASI scores between the right and left sides. MW, Mann–Whitney U test; S, P-value <0.05 is considered nonsignificant.

		Left side (N = 30)	Right side (N = 30)	Stat. test	P-value
VASI score	Mean	57.7	81.7	MW = 243	= 0.002 S
	±SD	32.6	20.8		

On the right side, there were 2 G4 patients (6.7 %), 0 G3 patients (0 %), 3 G2 patients (10 %), 18 G1 patients (60 %), and 7 G0 patients (23.3 %) (Table 4).

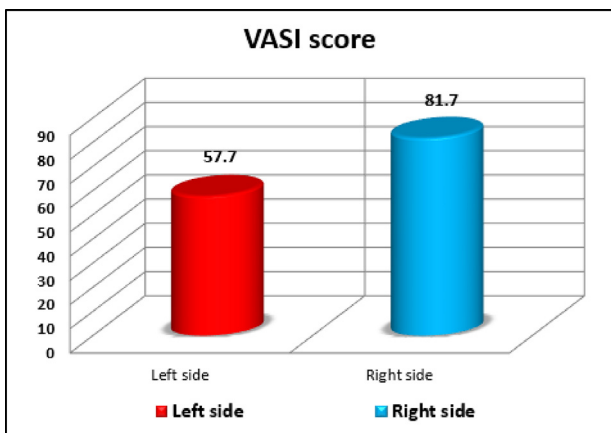


Fig. 1. Comparison of VASI score among right and left sides.

Table 5. Comparison of satisfaction rate between right and left sides.

		Left side (N = 30)		Right side (N = 30)		Stat. test	P-value
Satisfaction rate	Grade I	13	43.3%	25	83.3%	X ² = 14.3	= 0.002 S
	Grade II	2	6.7%	3	10%		
	Grade III	5	16.7%	0	0%		
	Grade IV	10	33.3%	2	6.7%		

This table showed that a statistically significant (P value = 0.002) amplified VASI score on the right side (81.7 ± 20.8) when compared with the left side (57.7 ± 32.6) (Fig. 1, Table 5).

This table showed a statistically significant difference (P-value = 0.002) among the right and left sides according to the satisfaction rate as follows: On the left side, there were 10 Grade IV patients (33.3 %), 5 Grade III patients (16.7 %), 2 Grade II patients (6.7 %), and 13 Grade I patients (43.3 %).

On the right side, there were 2 Grade IV patients (6.7 %), 0 Grade III patients (0 %), 3 Grade II patients (10 %), and 25 Grade I patients (83.3 %).

4. Case presentation

Figs. 2–4.

Before



After

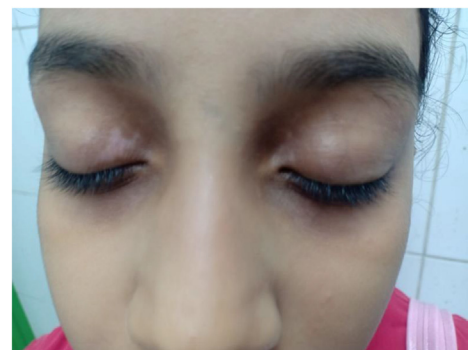


Fig. 2. A 12-year-old female with periorbital vitiligo. NB: Excimer light and tetracycline ointment on the left lesion and excimer light on the right lesion.



Fig. 3. A 36-year-old female. Vitiligo at the right breast. NB: Excimer light and tetracycline ointment on the left lesion, and excimer light on the right lesion.

5. Discussion

Depigmented patches of skin, hair, mucous membranes, and the retina are characteristic of vitiligo, an idiopathic skin condition characterized by the loss of melanocytes. For people of color and/or those who live in nations with vastly different cultural norms, it can have devastating repercussions on life satisfaction, self-image, marital happiness, and professional opportunities.⁹

Many medical therapies are currently available with the goal of slowing the disease's progression and prompting the skin to repigment. While there has been some disagreement about the efficacy and safety of both treatments for pigmentation, it is widely agreed that they are both viable options. However, there is currently no cure for vitiligo, and only a few treatments can help improve symptoms.¹⁰

Broadband UVB, narrowband UVB (NB-UVB), excimer light, excimer laser, and psoralen with UVA are all types of phototherapy used to treat vitiligo. Inducing T-cell apoptosis and stimulating the proliferation/migration of functional melanocytes in the perilesional skin and immature melanocytes in hair follicles are the main suggested mechanisms for inducing repigmentation in vitiligo by UV light.¹¹

One of the most successful treatments for localized vitiligo in both children and adults is focused

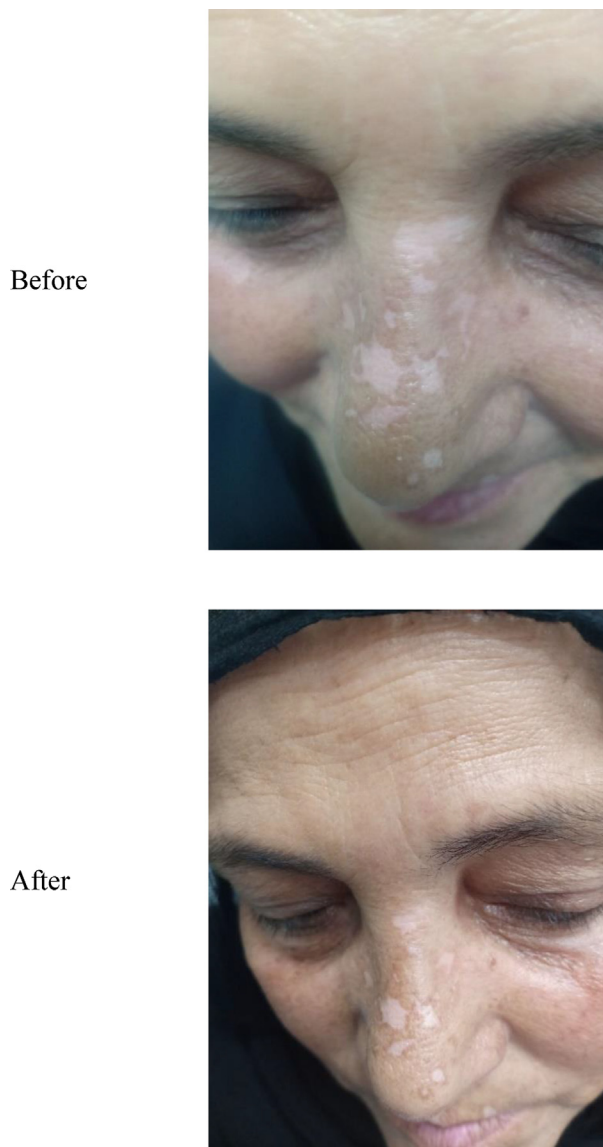


Fig. 4. A 60-year-old female with vitiligo on her face before and after treatment. NB: Excimer light and tetracycline ointment on the upper lesion, and excimer light on the lower lesion.

phototherapy with excimer light or targeted UVB devices. Single-method treatment rarely produces ideal results. There is a clear preference for and evidence of improved treatment outcomes with combination therapy.¹²

The use of tetracyclines is frequently linked to drug-induced pigmentation. The pathophysiology of drug-induced pigmentation has been defined in terms of four mechanisms: melanin accumulation, medicine accumulation, unique pigment production, and iron deposition.¹³

When administered systemically, tetracycline inhibits leukocyte chemotaxis and has antioxidative characteristics in addition to lowering the production of tumor necrosis factor-alpha and interleukin-

1. Tetracycline applied topically has the potential to be effective against vitiligo and has fewer side effects than systemic agents.¹⁴

However, if a combination of topical tetracycline and targeted phototherapy with excimer light can improve the efficacy of treatment for vitiligo, consequently, the purpose of this study was to assess whether or not topical tetracycline may improve the results of excimer laser therapy for vitiligo.

This randomized, controlled clinical trial included 30 patients with generalized, stable vitiligo. In each patient, using the vitiligo area severity index, we compared the pigmentation of two symmetrical lesions on the right and left sides. Both patches were treated by excimer light phototherapy twice a week for 12 weeks; each week, there was an increased energy dose of 0.05 J/cm.³

Tetracycline was applied to the assigned left patch half an hour before the application of the excimer light. After 4 weeks, 8 weeks, and 12 weeks, images of the lesions were taken, and pigmentations were compared with the beginning of the study using the aforementioned index. The Dermatology, Venereology, and Andrology Outpatient Clinic at Al-Azhar University Hospitals was used to recruit and screen patients for participation.

In this study, patches treated with tetracycline and excimer light phototherapy fared better than those treated with excimer light phototherapy alone. According to the Vitiligo Extent Tensity Index (VETI) score, the comparison between the left and right assigned vitiligo patches after treatment revealed a statistically significant increase in excellent repigmentation response (G4) (33.3 % vs. 6.7 %), good repigmentation (G3) (16.7 % vs. 0 %), moderate repigmentation (G2) (13.3 % vs. 10 %), and a statistically significant decrease in no repigmentation (G0) (3.3 % vs. 23.3 %) and fair repigmentation responses (G1) (33.3 % vs. 60 %) among left sides in comparison with the right side, respectively (P value = 0.002). Such improvement could result from the synergistic effect of the topical tetracycline and the excimer light.

Rok *et al.*¹⁴ showed the impact of tetracycline and UVA irradiation on cell viability and melanin production, to learn more about this cooperative effect (HEMn-DP), researchers studied the relationship between antioxidant defense mechanisms and cultivated normal human epidermal melanocytes. In cultivated melanocytes, tetracycline did not affect the melanization process, whereas exposure to UVA radiation induced melanogenesis, as evidenced by a steady rise in melanin concentration and tyrosinase activity.

From a photobiological perspective, Odorici *et al.*¹⁵ showed that photosensitivity reactions occur

when a photosensitizing compound, like tetracycline, which has been identified as a phototoxic but not photoallergic medication, absorbs light energy.

Lesions' elevated epidermal levels of tumor necrosis factor-alpha and interleukin-1 may contribute to the loss of melanocytes and the subsequent death of keratinocytes by inhibiting the synthesis of melanogenic cytokines. Tetracycline, according to research by Monk *et al.*,¹⁶ can inhibit IL-1 and TNF-alpha production.

The effectiveness of tacrolimus and 308-nm excimer light in treating vitiligo was compared by Nistic *et al.*¹⁷ with that of 308-nm excimer light monotherapy. Fifty-three vitiligo sufferers joined the study. There were three categories of patients: Twenty patients in Group I were given oral vitamin E and excimer light 308 nm twice weekly; 20 patients in Group II were given oral vitamin E and excimer light 308 nm twice weekly in addition to 0.1 % tacrolimus once a day; and 13 patients in Group III were given only oral vitamin E. Moderate repigmentation was seen in 35 % of patients in Group I, good repigmentation in 30 %, excellent repigmentation in 25 %, and poor repigmentation in 10 % in Group II, and moderate repigmentation was seen in 25 % of patients in Group II, good repigmentation in 40 %, excellent repigmentation in 30 %, and poor repigmentation in 5 % in Group III.

After intravenous infliximab (a tumor necrosis factor-alpha inhibitor), vitiligo lesions in a patient were absent, as described by Lv *et al.*¹⁸ The scientists suggested that tumor necrosis factor-alpha (TNF-alpha) stops the development of melanocyte stem cells, suggesting that TNF-alpha inhibitors could be a useful treatment for vitiligo. Combining 308-nm monochromatic excimer light with 0.1 % tacrolimus ointment is effective and safe for the treatment of segmental vitiligo, according to a study by Shah *et al.*¹⁹ Repigmentation of at least 75 % was seen in 77.8 % of patients. In detail, 35.6 % of patients demonstrated full repigmentation (Grade 5), while 42.2 % showed repigmentation of at least 75 %. (Grade 4).

Bae *et al.*²⁰ conducted a meta-analysis of eight RCTs with a total of 425 patches/patients and found that a combination of excimer light and topical calcineurin inhibitors was more effective than excimer lamp monotherapy for vitiligo.

The comparison between the left and right assigned vitiligo patches after treatment according to the Vitiligo Area Scoring Index (VASI) score revealed a statistically significant improvement in patches treated with tetracycline plus excimer light phototherapy in comparison with the treatment with excimer light phototherapy only (81.7 ± 20.8 vs. 57.7 ± 32.6 , respectively) (P value = 0.002).

Five of thirty cases (16.6 %) showed improvement in pigmentation when treatment was compared with placebo in a study by Kalafi and Jowkar²¹ assessing the efficacy of topical tetracycline and phototherapy on individuals with generalized stable vitiligo. Similarly, 16.6 % of cases showed better repigmentation on the placebo side compared with the medication side. The mean pigmentation, based on VASI, changed significantly from 90.1667 to 86.6667 in the tetracycline + narrow band UVB group and on the placebo side (Vaseline + narrow-band UVB) from 89.6667 to 86.8333 with no statistically significant differences between both treated sides, which is in contradiction with the present findings. Such differences could be attributed to the different study protocols, as in that study, tetracycline was applied only at night and then the phototherapy was received in the morning; moreover, a different form of phototherapy was used (NB-UVB phototherapy).

5.1. Conclusion

This study shows that vitiligo can be effectively treated with a combination of topical tetracycline and excimer light. A combination of topical tetracycline and excimer light is statistically significant as regards response during sessions according to the Vitiligo Extent Tensity Index (VETI) score, Vitiligo Area Scoring Index (VASI) score, and patient satisfaction after 12 weeks of treatment.

Authorship

All authors have a substantial contribution to the article.

Disclosure

The authors have no financial interest to declare concerning the content of this article.

Conflicts of interest

The authors declared that there were no conflicts of interest.

References

- Ezzedine K, Sheth V, Rodrigues M, et al. Vitiligo is not a cosmetic disease. *J Am Acad Dermatol*. 2015;73:883–885.
- Mohammed GF, Gomaa AH, Al-Dhubaibi MS. Highlights in pathogenesis of vitiligo. *World J Clin Cases*. 2015;3:221.
- Dubakienė R, Kuprienė M. Scientific problems of photosensitivity. *Medicina*. 2006;42:619–624.
- Mahajan VK, Vashist S, Chauhan PS, Mehta KI, Sharma V, Sharma A. Clinico-epidemiological profile of patients with vitiligo: a retrospective study from a tertiary care center of North India. *Indian Dermatol Online J*. 2019;10:38.
- James W, Berger T, Elston D. *Disease of the Skin*. eleventh ed. Beijing, China: Saunders; 2011.
- Bacigalupi RM, Postolova A, Davis RS. Evidence-based, non-surgical treatments for vitiligo: a review. *Am J Clin Dermatol*. 2012;13:217–237.
- Park KK, Liao W, Murase JE. A review of monochromatic excimer light in vitiligo. *Br J Dermatol*. 2012;167:468–478.
- Li R, Qiao M, Wang X, Zhao X, Sun Q. Effect of narrow band ultraviolet B phototherapy as monotherapy or combination therapy for vitiligo: a meta-analysis. *Photodermatol Photoimmunol Photomed*. 2017;33:22–31.
- Elsherif R, Mahmoud WA, Mohamed RR. Melanocytes and keratinocytes morphological changes in vitiligo patients. A histological, immunohistochemical and ultrastructural analysis. *Ultrastruct Pathol*. 2022;46:217–235.
- Kubelis-López DE, Zapata-Salazar NA, Said-Fernández SL, et al. Updates and new medical treatments for vitiligo. *Exp Ther Med*. 2021;22:1, 1.
- Esmat S, Hegazy RA, Shalaby S, Hu SC, Lan CC. Phototherapy and combination therapies for vitiligo. *Dermatol Clin*. 2017;35:171–192.
- Majid I, Imran S. Excimer light therapy in childhood segmental vitiligo: early treatment gives better results. *Dermatol Ther*. 2020;33:e13408.
- Afrin A, Cohen R. Doxycycline-associated hyperpigmentation: a case report and literature review. *Cureus*. 2022;14:1–10.
- Rok J, Buszman E, Delijewski M, Otręba M, Beberok A, Wrześniok D. Effect of tetracycline and UV radiation on melanization and antioxidant status of melanocytes. *J Photochem Photobiol B Biol*. 2015;148:168–173.
- Odorici G, Monfrecola G, Bettoli V. Tetracyclines and photosensitive skin reactions: a narrative review. *Dermatol Ther*. 2021;34:e14978.
- Monk E, Shalita A, Siegel DM. Clinical applications of non-antimicrobial tetracyclines in dermatology. *Pharmacol Res*. 2011;63:130–145.
- Nistico S, Chiricozzi A, Saraceno R, Schipani C, Chimenti S. Vitiligo treatment with monochromatic excimer light and tacrolimus: results of an open randomized controlled study. *Photomed Laser Surg*. 2012;30:26–30.
- Lv Y, Li Q, Wang L, Gao T. Use of anti-tumor necrosis factor agents: a possible therapy for vitiligo. *Med Hypotheses*. 2009;72:546–547.
- Shah S, Sakhiya J, Deshpande P, Sakhiya D, Inamadar AC. Safety and efficacy of the combination of 308-nm monochromatic excimer light and topical 0.1% tacrolimus ointment in segmental vitiligo: an open-label study. *J Clin Aesthet Dermatol*. 2020;13:E69.
- Bae JM, Hong BY, Lee JH, Lee JH, Kim GM. The efficacy of 308-nm excimer laser/light (EL) and topical agent combination therapy versus EL monotherapy for vitiligo: a systematic review and meta-analysis of randomized controlled trials (RCTs). *J Am Acad Dermatol*. 2016;74:907–915.
- Kalafi A, Jowkar F. Evaluation of the efficacy of topical tetracycline in enhancing the effect of narrow band UVB against vitiligo: a double-blind, randomized, placebo-controlled clinical trial. *Int Sch Res Notices*. 2014;2014:1–12.