

Efficacy of topical 5% fluorouracil (5%- FU) needling in vitiligo

Mai Abdulkhaliq Ibrahiem

Mohammed Adel Ismaiel

Medicine College || Tishreen University || Syria

Abstract: Objective: The aim of this study is to assess the efficacy of topical 5- fluorouracil (5%- FU) with micro needling in treating stable vitiligo. In addition to, assessment the side effects of the treatment.

Patients and Methods: A Prospective study (Before & After) conducted for the period one year (April 2019- April 2020) at Tishreen University Hospital in Lattakia- Syria, 31 patients with stable vitiligo who received treatment with micro needling and topical 5- fluorouracil (5%- FU) were included in this study.

Results : The median age was 36 years, 67.70% of patients were female. Focal type was found in 61.3%, and most common sites of vitiligo involvement were hand and feet (33.7%), followed by trunk (24.8%) and extremities (24.8%). After 6 months of treatment, improvement was excellent in 63.4%, and very good in 23.8%. The lesions of neck and trunk were responded better to treatment than those in other parts of the body. Regarding of side effects, pain, erythema, and itching were reported in 100% followed by ulceration in (16.1%).

Conclusion: Topical 5%- fluorouracil (5%- FU) with needling appears to be an effective and safe method in treating stable vitiligo. Except of pain, erythema, and itching after procedure, significant complications not occurred in most patients.

Keywords: vitiligo, 5- fluorouracil, micro needling, repigmentation

فعالية الحقن الموضعي بالإبر الدقيقة لـ 5% fluorouracil في علاج الهق

مي عبد الخالق إبراهيم

محمد عادل اسماعيل

كلية الطب البشري || جامعة تشرين اللاذقية || سوريا

المستخلص: هدفت الدراسة إلى تقييم فعالية العلاج بالحقن الموضعي بالإبر الدقيقة لـ (5%- FU) 5% fluorouracil لدى مرضى الهق المستقر، بالإضافة لتحديد الآثار الجانبية الناتجة عن هذا العلاج.

طريقة البحث: كانت هذه دراسة مستقبلية (قبل، بعد) أجريت في مشفى تشرين الجامعي في اللاذقية- سوريا خلال الفترة الممتدة ما بين نيسان 2019- نيسان 2020، شملت الدراسة 31 مريضاً مصاباً بالهق المستقر تلقوا العلاج بالحقن الموضعي بالإبر الدقيقة لـ (5%- FU) النتائج: بلغ معدل العمر 36 سنة، 67.7% من المرضى هم من الإناث. مثل الهق البؤري النمط السريري الأكثر مشاهدة (61.3%)، وإن إصابة اليدين والقدمين هي الأكثر تواتراً (33.7%) تلاها الجذع (24.8%) والأطراف (24.8%). حدث تحسن ممتاز لدى 63.4% من المرضى وجيد جداً لدى 23.8% بعد 6 أشهر من العلاج، وتم الحصول على النتائج العلاجية الأفضل في العنق والجذع مقارنة مع أجزاء الجسم الأخرى. بدراسة الآثار الجانبية للعلاج فإن الألم، الحمى والحكة حدثت في 100% من الحالات تلاها التقرح في 16.1%.

الاستنتاج: يعتبر العلاج بالحقن الموضعي بالإبر الدقيقة لـ (5%- FU) علاجاً فعالاً وأمناً عند مرضى الهق المستقر. باستثناء الألم، الحمى والحكة التي حدثت بعد هذا الإجراء لم يلاحظ وجود اختلاطات هامة في معظم المرضى.

الكلمات المفتاحية: الهق، 5- fluorouracil، الإبر الدقيقة، عودة التصبغ.

Introduction.

Vitiligo is a relatively common acquired disorder of pigmentation characterized by the development of well- defined white macules on the skin. It is the most frequent cause of depigmentation with estimated prevalence rates range from 0.1 to 2 percent in both adults and children [1, 2]. Vitiligo affects equally males and females, and may appear at any age with peak incidences in the second and third decade of life [3].

The etiology of vitiligo is unknown, and multiple theories have been proposed for melanocyte destruction in vitiligo. These include genetic, autoimmune, neural, biochemical, oxidative stress, viral infection, and melanocyte detachment mechanisms. Vitiligo is classified in two broad categories: nonsegmental vitiligo (NSV) and segmental vitiligo (SV) [4, 5].

The treatment of vitiligo is still one of the most difficult dermatological challenges. These include topical, systemic, light- based therapies and surgical techniques which together may help in halting the disease, stabilizing depigmented lesions and stimulating repigmentation [6, 7]. Although several interventions are available to treat patients with vitiligo, no definite cure has yet been developed. Over the years, several combination plans were suggested, some with proven efficacy, others with controversial results, and the rest were of denied value. Micro needling could be a method used for transdermal medication delivery to help the absorption of topical drugs, enhance the efficacy and reduce the amount of treatment [8, 9]. Needling followed by topical application of 5- fluorouracil (5- FU) provides a promising, effective, and safe modality of treatment [10]. The aim of the study was to evaluate the efficacy of topical 5%- FU with needling in stable vitiligo.

Patients and Methods.

This is a Prospective study (Before & After) of a group of patients with stable vitiligo attending the Dermatology Department's outpatient clinic at Tishreen University Hospital in Lattakia- Syria during a one year period (April 2019 to April 2020). The following data were recorded: demographic data (age, sex), co-morbidities, type of vitiligo, position, and duration of disease. Exclusion criteria were patients with one of the following: patients younger than 10 years, active Koebner's phenomenon, vitiligo on face, genitalia and intertriginous areas, a previous history of treatment with isotretinoin during the last six months, Hepatitis B&C and pregnancy. The position was cleaned by alcohol, anesthetized with topical lidocaine, then vitiligo area's micro needling was performed and topical 5%- FU was applied with equal amount of antibiotic ointment and a plastic sheet covered the patch. Every patient has received a session every month for a maximum of 3 sessions, and patients were followed for 3 months after the last session. Assessment was done by using clinical photograph and repigmentation was categorized as G0: no pigmentation, poor (G1):<25%, good (G2):25- 50%, very good (G3):50- 75%, and excellent (G4):>75%.

Statistical Analysis

Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations (SD), median, Frequency and percentages. The Wilcoxon test was used to compare two paired groups, and One way Anova to compare between the three groups. Differences of distribution examined by using Fisher exact test. P value <0.05 was considered as statistically significant.

Results.

A total of 31 patients with stable vitiligo who presented to the Department of Dermatology from April 2019 to April 2020 were included in the study. The baseline characteristics of patients are as given in table (1). The median age of patients who enrolled in the study was 36 years, and 67.7% were female. The frequency of comorbid autoimmune diseases was 35.4% with family history of vitiligo in 22.6%.

Table (1) Demographic characteristics of the study population

Variables	
Age (years)	36 (11- 69)
<u>Sex</u>	
Male	10 (32.30%)
Female	21 (67.7%)
<u>Co- morbidities</u>	
Hashimoto's thyroiditis	5 (16.1%)
Diabetes mellitus type1	1 (3.2%)
Diabetes mellitus type2	3 (9.7%)
Alopecia areata	3 (9.7%)
Asthma	3 (9.7%)
Hypertension	2 (6.5%)
hypoparathyroidism	1 (3.2%)
Emotional stress	1 (3.2%)
Addison's disease	1 (3.2%)
Family history of vitiligo	7 (22.6%)

As shown below (Table 2), 61.3% of patients had skin type III. The type of vitiligo was focal in 61.3%, hand and feet were the most common sites of vitiligo involvement (33.7%). The median disease duration was 5.5 years with a previous history of treatment in 74.2%.

Table (2) Distribution of the study population according to different parameters of vitiligo

Variables	
<u>Fitzpatrick skin types</u>	
II	4 (12.9%)
III	19 (61.3%)
IV	8 (25.8%)
<u>Type of vitiligo</u>	
Focal	19 (61.3%)
Generalized	7 (22.6%)
Segmental	4 (12.9%)
Localized	1 (3.2%)
<u>Sites of vitiligo</u>	
Hand & feet	34 (33.7%)
Trunk	25 (24.8%)
Extremities	25 (24.8%)
Neck	17 (16.8%)
Disease duration (year)	5.5 (1- 38)
Previous treatment of vitiligo (n%)	23 (74.2%)

After one month of treatment most of the patients had good to very good improvement. The response to therapy was very good (23.8%) and excellent (63.4%) after 3 months of last session, Table (3).

The adverse effects in our study were: pain, erythema, and itching in 100% followed by ulceration (16.1%). Kobner's phenomenon was not seen in any patient, Table (3).

Table (3) Distribution of the study population according to the response to treatment (micro needling with 5%- FU) and side effects

Response to treatment	After 1 month	After 6 month
G0	6 (5.9%)	2 (2%)
G1	5 (5%)	5 (5%)
G2	39 (38.6%)	6 (5.9%)
G3	49 (48.5%)	24 (23.8%)
G4	2 (2%)	64 (63.4%)

<u>Response to treatment</u>	<u>After 1 month</u>	<u>After 6 month</u>
<u>Side effects</u>		
Pain	31 (100%)	
Erythema	31 (100%)	
Itching	31 (100%)	
Ulceration	5 (16.1%)	
Infection	4 (12.9%)	
Scars	4 (12.9%)	
Hyperpigmentation	3 (9.7%)	
Hypopigmentation	2 (6.7%)	

Excellent response was most often seen in patches over the neck followed by trunk (p:0.001), Table (4).

Table (4) Distribution of the study population according to the response to treatment (micro needling with 5%- FU) and vitiligo position

<u>Variables</u>	<u>Vitiligo position</u>			
	Trunk	Extremities	Hand & feet	Neck
G0	0 (0%)	0 (0%)	2 (5.9%)	0 (0%)
G1	0 (0%)	0 (0%)	5 (14.7%)	0 (0%)
G2	0 (0%)	1 (4%)	5 (14.7%)	0 (0%)
G3	4 (16%)	7 (28%)	11 (32.4%)	2 (11.8%)
G4	21 (84%)	17 (68%)	11 (32.4%)	15 (88.2%)

Discussion

Long term treatment is usually required based upon the clinical course of vitiligo: the ideal topical agent should have good clinical efficacy with a better safety profile. Several studies have shown that micro needling followed by topical application of 5- fluorouracil has promising results in vitiligo.

Our study demonstrated that vitiligo was more frequently in females. Focal vitiligo was the most common morphological type, and most common sites affected were hand and feet followed by trunk and extremities. The associated autoimmune disease was found in 35.4%, with a family history of vitiligo in 22.6%. The response rates to needling followed by topical application of (5- FU) after 3 months of the last session vary between excellent (63%) and very good (23.8%), depending on the location of vitiligo, with excellent results for neck and trunk. Side effects of the treatment were: pain, erythema, and itching in all cases followed by ulceration, infection and scars.

Needling induces inflammatory response and local edema leading to increased intercellular spaces of the basal layer in which active melanocytes migrate from pigmented epidermis through these

spaces. The inflammatory mediators help in melanocyte migration and proliferation. It was postulated that 5- FU could exert repigmentation in vitiligo by direct stimulation of melanocytes and an increase in the number of melanosomes in the keratinocytes [11, 12]. These results are comparable to the findings reported by previous studies.

Vimala *et al.*, (2012) demonstrated that micro needling combined with 5- FU is efficient in treatment stable vitiligo in which total repigmentation was observed in 71.4% and partial repigmentation in 28.6% without any significant side effects [13].

Gandhi *et al* (2018) demonstrated that response to micro needling combined with 5- FU was excellent in 49% and very good in 26%. Side effects were: pain 100%, erythema (52%), itching (52%) and Kobner's phenomenon (1%) [14].

Ghiya *et al* (2019) also found that micro needling combined with 5% fluorouracil is efficient in stable vitiligo. The patient's response to treatment was excellent in 60% and very good in 12%. Side effects of treatment were: hyperpigmentation (48%), hypertrophic scarring (28%), and infection (12%) [15].

Zahra *et al* (2020) demonstrated that needling with 5% fluorouracil is effective and safe in treatment vitiligo. Initiation of repigmentation started at 1 month in 65%, improvement was excellent in 47% and very good in 46.2% at the end of 6 months. Side effects were: pain (40%), erythema (66.6%), itching (33.3%) and ulceration (6.6%) [16].

In summary, needling with 5% FU appears to be effective and safe treatment in vitiligo.

References

- 1- Migayron L, Seneschal J (2020). Vitiligo, from physiopathology to emerging treatments: a review. *Dermatol Ther.*10:1185- 1198.
- 2- Picardo M and Taieb A (2019). Vitiligo. Springer Nature Switzerland AG.382- 397.
- 3- Zhang Y, Cai Y, Shi M (2016). The prevalence of vitiligo: A meta- analysis. *PLOS One.*11:1- 17
- 4- Frisoli M, Essien K, Harris J (2020). Vitiligo: Mechanism of pathogenesis and treatment. *Annu Rev Immunol.*38:621- 648.
- 5- Rodrigues M, Ezzeddine K, Hamzavi I (2017). Vitiligo Working Group. New discoveries in the pathogenesis and classification of vitiligo. *J Am Acad Dermatol.*77:1- 13.
- 6- Boniface K, Seneschal J, Picardo M (2018). Vitiligo: Focus on clinical aspects, immunopathogenesis, and therapy. *Clin Rev Allergy Immunol.*54:52- 67.
- 7- Passeron T (2020). First step in a new era for treatment of patients with vitiligo. *Lancet.*396:74- 75.
- 8- Kumar A, Bharti R, Agarwal S (2019). Micro needling with dermaroller 192 needles along with 5- fluorouracil solution in the treatment of stable vitiligo. *J Am Acad Dermatol.* 81:67- 9.
- 9- Salloum A, Bazzi N, Maalouf D, Habre M (2020). Micro needling in vitiligo: A systematic review. *Dermatol Ther.*33:14297.

- 10- Tsuji T, Karasek MA (1986). Differential effects of 5- fluorouracil on human skin melanocyte and malignant melanoma cells in vitro. *Acta Derm Venereol.*66:474- 8.
- 11- Singh A, Yadav S (2016). Micro needling: Advances and widening horizons. *Indian Dermatol online J.* 7:244- 54.
- 12- Gauthier Y, Anbar T, Lepreux S (2013). Possible mechanisms by which topical 5- fluorouracil and dermabrasion could induce pigment spread in vitiligo skin: an experimental study. *ISRN Dermatol.*8:49- 52.
- 13- Vimala.R, Ramasamy. P. Efficacy of dermabrasion along with topical 5- fluorouracil in 25 patients of vitiligo. *MD Dermatology*, The Tamil Nadu Dr. M.G.R. Medical University, 2012.
- 14- Gandhi S, Shashikiran A, Muruges S (2018). Efficacy of topical 5% fluorouracil needling in vitiligo. *Indian Journal of Dermatology.* 223- 227.
- 15- Ghiya B, Prasoon S, Mehta R (2016). Comparative evaluation of the therapeutic efficacy of micro needling alone or micro needling combined with topical 5- fluorouracil in localized stable vitiligo. *Adv Hum Biol.* 6:25- 28.
- 16- Zahra F, Adil M, Mohtashim M (2020). Efficacy of topical 5% fluorouracil with needling versus 5% fluorouracil alone in stable vitiligo: A randomized controlled study. *Journal of cutaneous and Aesthetic Surgery.*13: 197- 203.