



A STUDY OF THERAPEUTIC EFFICACY OF MICRO NEEDLING WITH TOPICAL 5-FLUOROURACIL SOLUTION IN MANAGEMENT OF LOCALISED STABLE VITILIGO.


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ABSTRACT

Background: Vitiligo affects 1% of the world's population with a higher incidence in dark-skinned individuals. Many medical treatments have been attempted with partial success, but recent focus has been on surgical techniques. The aim of this study was to evaluate the therapeutic efficacy of microneedling combined with topical 5-fluorouracil solution. **Methods:** A total of 102 lesions in 50 patients with localized stable vitiligo were treated. Microneedling combined with topical 5-fluorouracil solution was used which is available in the form of solution in concentration of 50mg/ml. The procedure was repeated after every 15 days up to 6 months and the patients were followed up for total 9 months. **Results:** The patients response to treatment (repigmentation) was graded as G1 <25% repigmentation (Poor), G2 25%-50% repigmentation (Fair), G3 50%-75% (Good), G4 >75% (Excellent). Results at the end of study are out of 102 lesion in grade 1 is 6 (5.88%), grade 2 is 12 (11.76%), grade 3 is 26 (25.49%), grade 4 is 28 (27.45%). **CONCLUSION:** Microneedling combined with 5-fluorouracil is efficient and better treatment in localised stable vitiligo.

Keywords :- Vitiligo, 5-fluorouracil, Microneedling, Repigmentation.

Access this article online		
Home page: http://www.mcmed.us/journal/abs	Quick Response code 	
DOI: http://dx.doi.org/10.21276/abs.2018.5.1.4		
Received:25.11.2017	Revised:12.12.2017	Accepted:05.01.18

INTRODUCTION

Vitiligo is an acquired disorder characterized by circumscribed depigmented macules and patches that result from a progressive loss of functional melanocytes affecting approximately 0.5%- 2% of general population world-wide, without predilection for sex or race[1]. The age of onset of vitiligo is variable, but it peaks in second and third decades. The depigmentation has predilection for acral areas and around body orifices (mouth, eye, and nose and anogenital region)[2]. The precise cause of vitiligo is unknown. There are 3 major Hypothesis for pathogenesis of vitiligo that is not exclusive of each Other: Biochemical/ Cytotoxic,

Neural and Autoimmune [3]. As none of the three hypotheses is sufficient to explain, fully the mechanism of vitiligo, convergence theory is proposed [4]. Current treatment modalities aim to stimulate melanocyte proliferation or interfere with inflammatory factors affecting melanocyte structure or function. No single treatment method has yet been found that is consistently effective with relatively few side effects [5]. Current repigmentation therapies include corticosteroids, topical immunomodulators, Photo (chemo) therapy, surgery[2]. In previous studies topical 5-FU is combined

with dermabrasion [6] and Erbium: YAG Laser ablation [7], it was found to be effective.

This aim of this study was to evaluate the therapeutic efficacy of microneedling combined with topical 5-fluorouracil solution, in the management of localized stable vitiligo. Although the Food and Drug Administration (FDA) has not yet approved topical 5-fluorouracil for use in vitiligo. We studied the effect of topical 5 fluorouracil solution after microneedling of the skin to use its properties of repigmentation.

MATERIAL AND METHODS

102 lesions in fifty patients having localized stable vitiligo were included in the study. The inclusion criteria were as follows: patients age between 5-60 year should not have more than five patches of vitiligo; the patches should be stable, i.e. should not have any increase or decrease in pigmentation or size over the 6 months; the sizes of the patches should be less than 10 cm in diameter; no local and systemic therapy for at least 6 months before inclusion in study and no active infection should be present on the patches or on the body. Patients with a patch size of more than 10 cm in diameter, keloidal tendency, active infection, bleeding disorders, or immunocompromise were not included in the study.

A dermaroller with a size of 1.5 mm were used for the procedure, sites at which dermaroller is not applied insulin syringe is used for microneedling. After surgical preparation of patches local anesthesia was given with lignocaine intradermally and subcutaneously. Microneedling of vitiligo area was performed with 1.5 mm derma-roller from one border to another by multiple, parallel side to side and top down strokes. This was followed by appearance of multiple tiny, punctuate, bleeding point. Haemostasis was achieved by compressing normal saline-soaked piece of gauge on treated area, followed by application of 5-fluorouracil solution which is available in market as ampules in strength of 50mg/ml, topically and rubbing over affected area about 2 min. After which occlusive dressing was done and kept for 1 day. A third generation cephalosporin cefixime and NSAIDS with topical antibacterial (mupirocin cream 2%) was given for next 5-7 days. The patients were followed up after 15 days and procedure was repeated every 15 days till

repigmentation is achieved or upto 6 month with total seating not exceeding more than 12. After completion of treatment patients were examined every 1 month upto 3 month for appearance of pigmentation and complication if any. The patient's response to treatment (pigmentation) was graded as follows: G1 < 25% repigmentation (poor); G2 25–50% repigmentation (fair); G3, 50–75% repigmentation (good); G4, > 75% repigmentation (excellent). The results were analyzed statistically after a follow-up of 3 months.

RESULTS

Fifty patients having 102 lesion were included in the study. In which 28(56%) were female and 22(44%) were male with a female to male sex ratio of 1.27: 1. The maximum numbers of patients were in age group between 16- 25 years. A family history of vitiligo was positive in only 3(6%) patients. The distribution of vitiligo lesions varied over the body, but the most common distribution was in lower limb, back and face. A total of 102 lesions are treated. Taking G3 and G4 as the desirable outcome, the efficacy of microneedling with topical 5-fluorouracil was 52.94% at 9 month.

All 102 patches showed mild to profuse serous discharge at 24 hour postoperatively. None of the patches showed any or allergic reaction at 10 days postoperatively. Only 8 lesion during treatment have secondary infection, 1 lesion have hypertrophic scarring. The time taken for healing (Re-epithelialization) of the patch was treated with 5-fluorouracil is around 5-7 days. Marked hyperpigmentation was seen in 6 patches treated with microneedling combined with 5-fluorouracil, which persisted up to 3 months of follow-up. Only 1 patch show relapse in follow up of 3 month which show grade 1 pigmentation during treatment. When difference in degree of repigmentation from 0 week to 2 weeks of follow up was compared statistically, it was found to be statistically significant, when results after 2 weeks were compared with those at 4, 6, 8, 10, 12 weeks and 3 month they were found to be statistically highly significant. Similarly, when results after 4 weeks follow up compared with those after 6, 8, 10, 12 week and 2 month, they were found to be highly significant. This indicates that repigmentation started from 2 weeks onward was significant.

Table 1. Showing status of repigmentation in 102 lesions in 50 study cases after two weeks

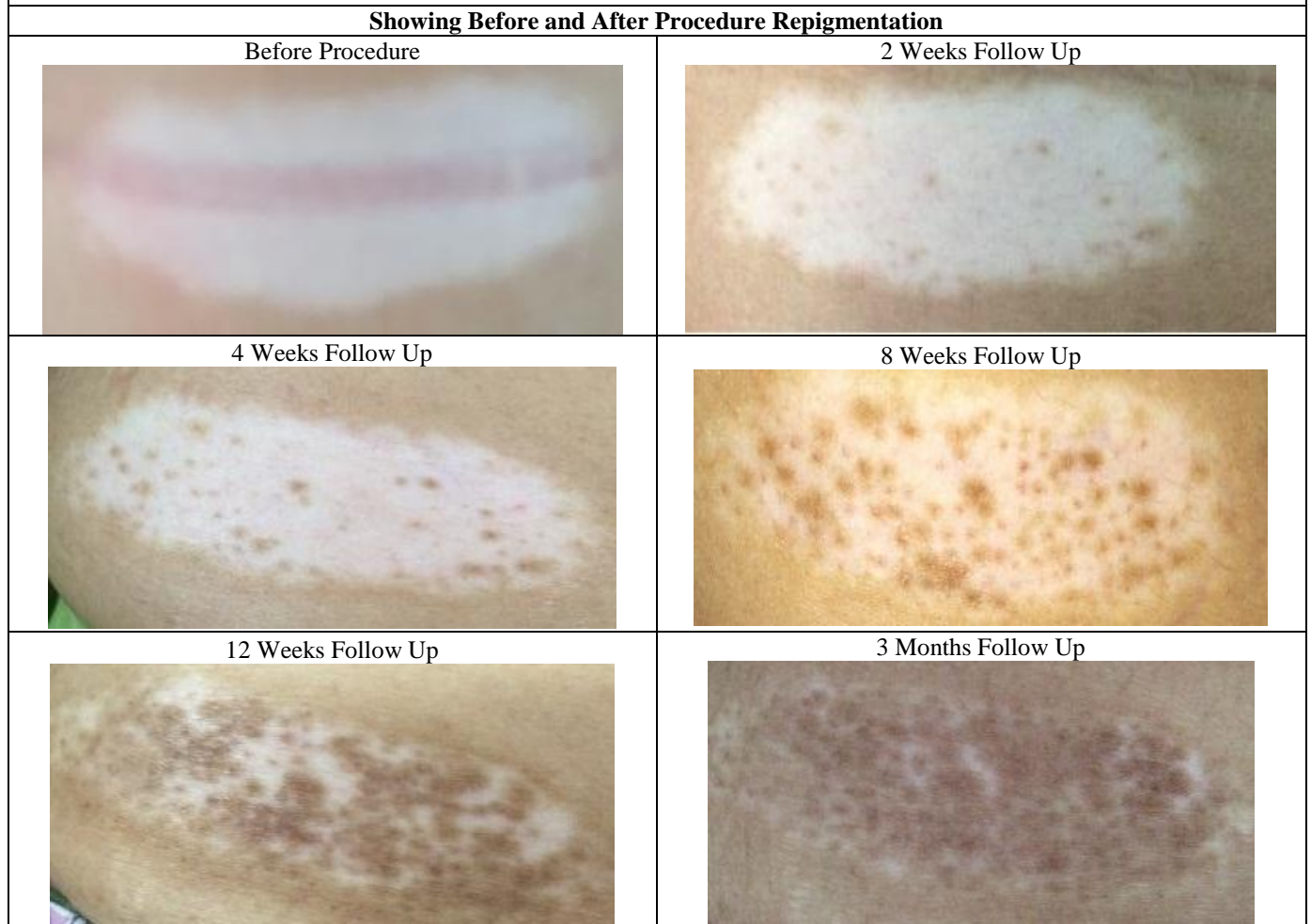
Percentage (%) of repigmentation	Grade of repigmentation	Total no. of lesion	Percentage
>25%	1	11	10.78%
25-50%	2	-	-
50-75%	3	-	-
>75%	4	-	-
No Improvement	-	91	89.22%
Total		102	100%

Table 2. Showing status of repigmentaion in 102 lesions in 50 study cases after eight weeks.

Percentage(%) of repigmentaion	Grade of repigmentaion	Total no.of lesion	Percentage
>25%	1	18	17.64%
25-50%	2	22	21.56%
50-75%	3	25	24.50%
>75%	4	05	04.90%
No improvement	-	32	31.37%
Total		102	100%

Table 3. Showing status of repigmentaion in 102 lesions in 50 study cases after three months.

Percentage(%) of repigmentaion	Grade of repigmentaion	Total no.of lesion	Percentage
>25%	1	6	5.88%
25-50%	2	12	11.76%
50-75%	3	26	25.49%
>75%	4	28	27.45%
No Improvement	-	30	29.41%
Total		102	100%

Graph 1. Showing Grades of Repigmentation At 2nd, 4th, 6th, 8th, 12th Week and 3rd Month Post Operatively In A Group of Lesions

DISCUSSION

Vitiligo is a major socio-psychological problem, especially in dark-skinned individuals. The treatment of vitiligo has undergone an evolutionary change down the ages. During the last few years, several surgical techniques have been developed to replenish the melanocyte population in depigmented skin conditions. The present study was designed to evaluate efficacy of micro needling combined with topical 5-fluorouracil solution in 102 patches, in localised stable vitiligo. Repigmentation usually started after 2-3 sittings. Usually, repigmentation occurred as small, brown, perifollicular macules, which then enlarged and coalesced. This began from the margins and spread centripetally; however, in some patches, repigmentation occurred diffusely from the beginning. In treated patch, re-epithelialization takes place from the remnants of dermal appendages: sebaceous glands, hair follicles, and sweat glands. It was observed that hairy areas healed with perifollicular pigmentation, which indicates that the follicular reservoir population of melanocytes migrates to the epidermal surface during wound healing after microneedling, and further propagates centrifugally around the hair follicle. In nonhairy areas, the treated area healed with perilesional hyperpigmentation at the borders with migration of this pigment for a few millimeters

towards the center, thus indicating that peripheral epidermal melanocytes are stimulated during surface epithelialization. Topical 5-fluorouracil induces the repigmentation of vitiligo possibly by the overstimulation of follicular melanocytes, which migrate to the surface during epithelialization, resulting in hyperpigmentation [8]. Hyperpigmentation is a known side-effect of 5-fluorouracil, and is observed during the treatment of skin tumors and psoriasis [9]. The efficacy of microneedling with topical 5-fluorouracil was 52.94 at 9 months. Marked hyperpigmentation was seen in 6 patches treated with microneedling combined with 5-fluorouracil, which persisted up to 3 months of follow-up. Hyperpigmentation is a known side-effect of 5-fluorouracil, observed during the treatment of skin tumors and psoriasis. Hypertrophic scarring seen in 1 patch. Hypertrophic scarring is a known side-effect of the topical application of 5-fluorouracil [10]. Depigmentation of the patches, together with marginal depigmentation, persisted in our study. The reason for depigmentation at the lesions may be the impending total exhaustion of melanocytes or the total absence of melanocyte reservoirs in the affected lesions. The results of our study showed that microneedling combined with topical 5-fluorouracil may be used as efficient treatment modality in localised stable vitiligo.

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Cite this article:

Ankit Kumar Singrodia, Rajesh Dutt Mehta, Bhikam Chand Ghiya, PrasoonSoni, Pooja Goswami, AasthaChawla. A Study Of Therapeutic Efficacy Of Micro Needling With Topical 5-Fluorouracil Solution In Management Of Localised Stable Vitiligo. *Acta Biomedica Scientia*, 2018;5(1):17-20. DOI: <http://dx.doi.org/10.21276/abs.2018.5.1.4>



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