

## Efficiency of 5 fluorouracil solution application using dermaroller in the treatment of vitiligo

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### **ABSTRACT:**

**Introduction:** Vitiligo is a common acquired condition, resulting from the progressive loss of melanocytes (1). Vitiligo affects 0.5–1 % of the world's population, It can appear at any age. The prevalence is probably the same in sexes, but higher prevalence is suggested in dark-skinned individuals (1,2). Vitiligo Is a major dermatologic challenge considering the many available therapeutic modalities (5). **Case report:** We present two patients who were treated with 5FU and microneedling using a dermaroller over a period of 3 months. Both patients are in their 3rd decade of life, diagnosed with vitiligo several years ago. The treated lesions were stable and unchanged over time. We present the results of the treatment together with the pathohistological finding of treated and untreated lesions. **Conclusion:** After needling and application of topical 5-fluorouracil, patohistology report shows a strong inflammatory reaction and minor edema. New promising therapeutic modalitie is topical 5-fluorouracil (5-FU), which probably stimulates repigmentation in vitiligo by direct over stimulation of proliferation of the melanocytes and an increase in the number of melanosomes in the keratinocytes.

**Keywords:** Microneedling, 5-fluorouracil, repigmentation, vitiligo

### **INTRODUCTION:**

Vitiligo is a common acquired condition, resulting from the progressive loss of melanocytes (1). Its clinical characteristics are well-defined milky white macules which are localized or in general distribution and often coalesce in large depigmented lesion (2). Vitiligo affects 0.5–1 % of the world's population, It can appear at any age. The prevalence is probably the same in sexes, but higher prevalence is suggested in dark-skinned individuals (1,2). Vitiligo has a profound impact on the quality of life of both children and adults (3,4).

Vitiligo is a major dermatologic challenge considering the many available therapeutic modalities (5). Surgical modalities alone, or combined to medical management induce best results in process of repigmentation (5,6). New promising medical management modalities is topical 5-fluorouracil (5-FU), which stimulates repigmentation in vitiligo by direct overstimulation of proliferation of the melanocytes and an increase in the number of melanosomes in the keratinocytes (7). So, the

aim of our study is to estimate the efficacy of topical 5-FU applied on a stable vitiligo patch, with manual microneedling, using a dermaroller.

### **MATERIALS AND METHODS:**

We were working with 2 patients with stable vitiligo lesions. Every patient was clinically assessed, and we took thorough medical and family history. We outlined all the investigated patches on a transparent sheet and photographed. The treatment lasted for a three months, from November 2019 to January 2020, and three months of follow up with clinical assessment of the threatened lesion.

The treatment was performed every two weeks, so we managed to do 6 treatments in three months. The whole procedure was performed in sterile conditions, after cleansing the skin, the dermaroller with 192 needles with diameter of 1,5mm, is used. After crossing the place with the roller with endpoint of blood spotting, 5-Fluorouracil is applied (50mg/ml). The dose of 5-

Fluorouracil solution used in one session depends of the skin change, but the maximum dose was 10mL.

One month after the last treatment we took a biopsy of the treated area and a biopsy of another vitiligo change to compare the pathohistological finding after the treatment. Skin samples were taken from the margin under local anaesthesia with 4 mm punches.

### **Case Reports:**

#### **Patient N° 1:**

A 21year old female patient diagnosed with Hashimoto's syndrome a few years earlier, with regular Levothyroxine therapy and normalized thyroid values, has been treated for a stable vitiligo lesion. She was

diagnosed with vitiligo 10 years ago and local corticosteroid cream treatment has so far shown no results. Several smaller and one larger lesion ( diameter 4cm) on the right upper arm of the flexor side have been treated in this patient. After the first treatment, hyperpigmentation of the edges of the lesions was observed, after the 4th treatment we noticed the appearance of new pigmented islands inside the lesions. The change has continued to show progress, but very slowly and with little intensity. After 3 months of treatment, the patient still has hyperpigmentation of the edges and a slight reduction in the hypopigmented surface. During the whole treatment, the patient did not complain of any side effects.



**Fig 1. Vitiligo lesion before the treatment, Fig 2. Vitiligo lesion one month after the last treatment**

#### **Patient N° 2:**

A 29 year old male patient diagnosed with vitiligo at age of 9 without other comorbidities was treated for stable abdominal lesion (diameter 9cm) with a dermaroller and 5 fluorouracil. After the first few treatments, there was a marked hyperpigmentation of the edges of the change, after the 5th treatment we noticed a decrease in the size

of the change, a change in the shape and appearance of new pigmented islands in the hypopigmented zone, 3 months after treatment, the lesion is still subject to change, completely altering its shape by releasing new pigments into the lesion from the edges. The patient did not complain of side effects during all treatments.



**Fig 3. Vitiligo lesion before treatment**



**Fig 4. Vitiligo lesion after last treatment**

### **Hystopathological Assessment:**

#### **Technique:**

Punch biopsies of 4mm were taken from two patients with sampling from treated and non-treated areas. Samples were fixed 24 hrs in 10% formaldehyde solution. The tissue was processed in tissue processor Thermo Fisher Scientific Citadel 2000, and embedded in paraffin wax. Sections of 4 microns thickness were made, and after deparaffinization, stained with H&E in automated slide strainer Thermo Fisher Scientific Gemini AS. The sections were examined under lite microscope Nikon Eclipse E600 and images were captured with photomicroscope.

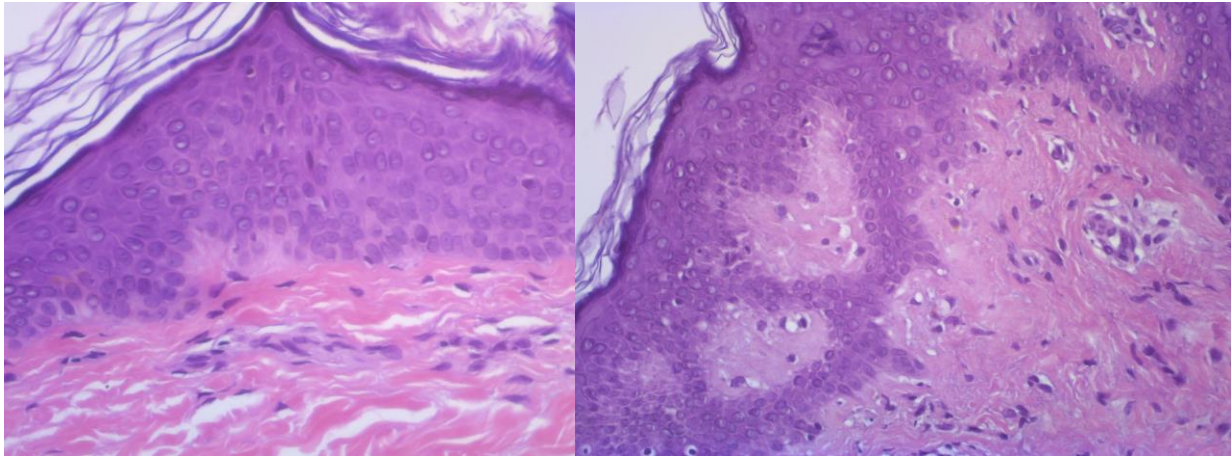
#### **RESULTS:**

Patient N<sup>o</sup>.I a 21 year old female with taken sample from right upper arm flexor side from the treated area, and right upper arm extensor side non treated area.

a.) Non-treated area: light hyperkeratosis, discrete thickening of the epidermal layer with shortened and

flattened epidermal papillae were present, with reduction of melanocytes in the basal layer. Some of the remaining melanocytes did not contain melanin pigment in their cytoplasm. Rare scattered apoptotic cells in the basal area of the epidermis were observed, but also some of them incorporated in-between keratinocytes and migrating upwards toward the middle area. There were no significant changes in the dermis (Fig.5).

b.) Treated area: marked hyperkeratosis was present, with slight spongiotic change and no changes in the thickness of the epidermal layer. Slight reactive changes in keratinocytes were also present. There were slight changes in the present melanocytes, with a discreetly visible melanin pigment in the cytoplasm. Apoptotic cells with identical distribution were still present. Elastotic change in the papillary dermis and completely discreet sparsely granulated free melanin pigment in barely visible foci was observed with edema around small capillary vessels in dermis and no other significant changes (Fig 6.)

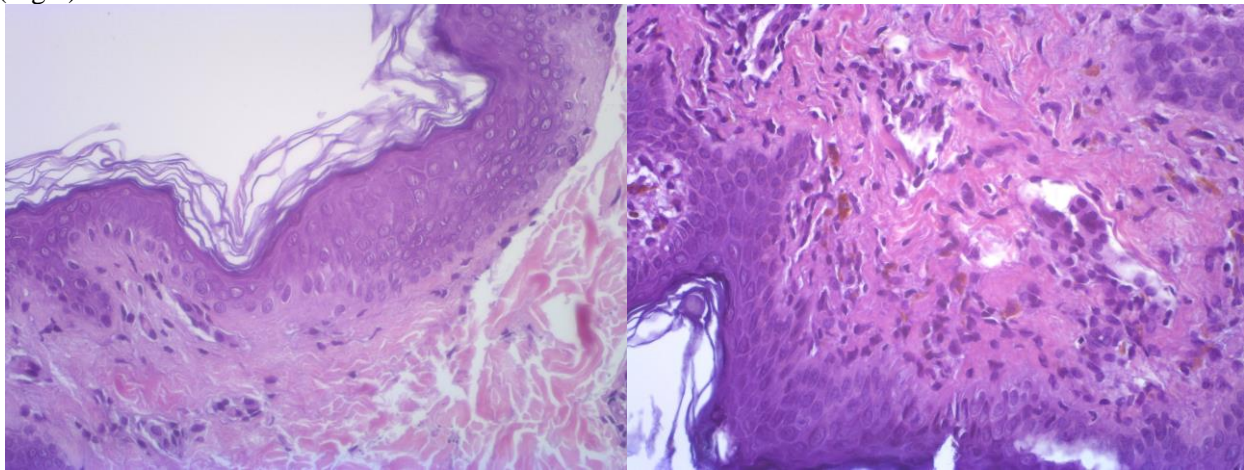


**Fig 5. Untreated area - H&E staining (x400) Fig 6. Treated area - H&E staining (x400)**

Patient N<sup>o</sup>.II 29 years old male patient with sample taken from abdominal area 10cm under the umbilicus from treated area, and sample taken from lower right lateral side of the back from non treated area.

a.) Non-treated area: Discrete hyperkeratosis, slightly thinning of the epidermal layer with elongated epidermal papillae and segmental reduction of the melanocytes in the basal area was observed. Some of the remaining melanocytes did not contain melanin pigment in their cytoplasm. Also individual apoptotic cells are noticed, mostly situated in the basal area of the epidermis. Broadened dermal papillae without significant changes in the papillary and reticular layer of the dermis were present (Fig 7).

b.) Treated area: marked hyperkeratosis with focally emphasized thinning of the epidermal layer and elongated epidermal papillae were present with slight reactive changes in keratinocytes. Here we noticed focal discrete small groups of active melanocytes with presence of intracytoplasmic melanin pigment. Apoptotic cells are still present in the basal area but are significantly reduced in number. There is a significant inflammatory response with lymphocytic infiltration and elastotic activity in the papillary dermis. Also focally we noticed marked changes, with single and small grupes of melanofages, as well as melanin pigment incontinence (Fig 8).



**Fig 7. Untreated area - H&E staining (x400)**

**Fig 8. Treated area - H&E staining (x400)**

## **DISCUSSION:**

5FU is a drug used to treat cancer. In dermatology it is most commonly used as a topical cream for the treatment of actinic keratosis and skin cancers, with application twice a day for several weeks has proven to be quite effective. Irritation, tingling, redness, and

hyperpigmentation have been described as the most common side effects of topical use of 5FU. It is hyperpigmentation that has attracted the most attention and given the idea to many doctors to use the drug as a treatment for other diseases. It was first used as a vitiligo treatment in 1983 (8).

There are several ways in which this drug can be used to pigment hypopigmented changes. The use of the drug as a topical cream or in the form of a solution in combination with a dermaroller, dermabrasion and CO2 laser are opportunities that give patients hope (7-10). In the study of Kumar et al. an excellent response in the form of repigmentation of the area affected (75%-90% depending on the site) was obtained (8).

In the study of Santosh et al. improvement was seen in about 60% of the patients with some erythema and hyperpigmentation developing on the margins of vitiligo patches, and after 3 months they had almost complete pigmentation in small patches. Larger ones had less pigmentation and 40% did not have any pigmentation from the previous state (10).

Shashikiran et al. reported more than 75% repigmentation in 49% of the patches. 50–75% repigmentation was seen in 26% of the patches and 25–50% repigmentation in 11% of the patches, whereas 14% of the patches responded poorly with less than 25% repigmentation. The rate of pigmentation was rapid in approximately 8% of the patches, which developed 100% repigmentation within the first month (11).

After needling and application of topical 5-fluorouracil we are witnesses of a strong inflammatory reaction and minor edema. Due to this reaction we believe that this is the main reason for causing the whole process of melanocyte proliferation and repigmentation.

Based on histopathological findings In both patients reaction was observed, reactive changes in keratinocytes, intracytoplasmic melanin pigment, which is more discreet in patient N<sup>0</sup> I and slightly more pronounced in patient N<sup>0</sup> II, elastotic activity changes in papillary dermis was also seen. Significant inflammatory reaction in the papillary dermis has also been reported in patient N<sup>0</sup> II. Clinically, the improvement is markedly greater in patients number two, the histopathological finding confirms this. We concluded that topical 5% fluorouracil needling is an easy, efficacious, safe method of repigmentation in vitiligo not responding to the medical treatment.

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