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EFFICACY OF 5-FLUOROURACIL CREAM (5%) WITH NEEDLING IN RECALCITRANT FOCAL STABLE VITILIGO

Dermatology

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ABSTRACT

AIMS AND OBJECTIVES: To evaluate the efficacy and safety of 5-Fluorouracil cream (5%) with needling in cases of recalcitrant focal stable vitiligo. **MATERIALS AND METHODS:** 36 cases of focal vitiligo, stable for more than 1 year and not responded to medical treatment were enrolled. The study was conducted over a period of 6 months from January – June 2019. Under strict aseptic precautions and EMLA application, needling was done. 5-fluorouracil cream (5%) was applied under occlusion. Patients were advised to continue the application once a day for next 14 days. Follow up was done at 1, 3 and 6 monthly intervals. Response was noted in terms of percentage during each visit. Photographic documentation was done. **RESULTS:** Out of 36 patients, 32 completed the study. Out of them, 12 were males and 20 were females. The age-range of the patients was 18-60 years. 12 patients had lesions on upper limbs, 10 had on lower limbs, 6 had over acral areas and 4 had over trunk. At the end of the study, 12 (37.5%) patients had excellent response, 6 (18.75%) had very good response, 4 (12.5%) had good response while 3 (9.38%) had poor response. No response was seen in 7 (21.88%) cases. Maximum repigmentation was seen in truncal lesions and least in acral lesions. 90% experienced pain during procedure and 18.75% experienced immediate burning and erythema. Hyperpigmentation with scarring developed in 6 (18.75%) patients. **CONCLUSION:** Topical 5-fluorouracil (5%) application with needling is a safe, simple procedure with minimal side effects in cases of recalcitrant focal vitiligo and can be one of the treatment modalities.

KEYWORDS

Recalcitrant Focal Stable Vitiligo, 5-Flourouracil Cream (5%), Needling

INTRODUCTION

- Vitiligo is an acquired condition resulting from the progressive loss of melanocytes leading to depigmentation. It is characterized by milky white sharply demarcated lesions.
- It can begin at any age, and the prevalence is probably the same in both sexes.
- Various theories have been suggested for the etiology of vitiligo; the autoimmune theory is currently the leading hypothesis and is supported by strong evidence. It is based on the clinical association of vitiligo with a number of disorders also considered to be autoimmune or autoinflammatory. Among autoimmune diseases, the strongest association is with thyroid disease.
- Histochemical studies show the lack of dopa-positive melanocytes in the basal layer of the epidermis. Electron microscopic studies confirm the loss of melanocytes.
- Focal vitiligo is defined as one or more depigmented macules in one area, but not clearly in a segmental distribution.[1] The pretibial region is the commonest affected area in India,[2] in contrast to the upper limbs in western country.[3]
- Stable vitiligo is defined as a vitiligo with no new lesions, no progression of existing lesions and absence of koebner phenomenon during past one year.[4]
- Medical treatment is the primary mode of therapy to achieve repigmentation. The treatment of choice for focal vitiligo is topical corticosteroids. Other treatment modalities include topical calcineurin inhibitors, topical basic fibroblast growth factor and topical phenol application.
- In patient recalcitrant to medical treatment; various surgical therapies can be used to achieve repigmentation provided the disease is stable. Various surgical modalities include split thickness skin grafting, suction blister grafting and punch excision and grafting.[4]
- Needling followed by topical application of 5-fluorouracil cream (5%) is one of the recent advancements to the treatment modality of vitiligo.[5]
- 5-fluorouracil inhibits pyrimidine metabolism and DNA synthesis. Its FDA approved indications are actinic keratosis, bowen's disease and superficial basal cell carcinoma. Other indications include genital warts, common warts, extramammary paget's disease, darier disease and superficial actinic porokeratosis. Commonly used regimen comprises twice daily application for 2 weeks.[6] Adverse effects include erythema, irritation, burning, pain, pruritus, hypopigmentation and hyperpigmentation.[7]

AIMS & OBJECTIVES

- To evaluate the efficacy and safety of 5-fluorouracil cream (5%) with needling in recalcitrant focal vitiligo.

MATERIALS AND METHODS

- The study was conducted at New Civil Hospital, Surat from January to June, 2019.
- Total 36 patients of recalcitrant focal vitiligo stable for more than one year and who were not on any kind of treatment for at least past 2 months were enrolled for the study.

Inclusion criteria

- Patients giving informed written consent
- Focal vitiligo, stable for more than one year
- Vitiligo recalcitrant to medical management

Exclusion criteria

- Patients less than 18 years of age
- Vitiligo involving face and genitalia
- Pregnant and lactating women
- History of keloidal tendency and bleeding diathesis

- A detailed history regarding the onset, duration and course of the disease, family history, associated skin and systemic problems, history of treatment taken so far and its outcome were recorded.
- Complete hemogram, bleeding and clotting profile was done. Baseline liver and renal function tests and RBS were done. HBsAg, HCV and HIV investigations were also carried out.
- The patients were explained about post procedure sequelae and possible side effects.

Procedure

- EMLA cream was applied over the stable vitiligo lesion for 45 minute.
- Under strict aseptic precautions needling was done with a 26 gauge hypodermic needle until minute pin-point bleeding developed.
- 5-fluorouracil cream (5%) was applied under occlusion. The patients were made to sit for 1 h after application so as to check for any side effects. Systemic antibiotic was given and post procedure care was advised.
- Patients were asked to apply 5-FU cream (5%) once a day for next 14 days.
- Follow up examination was done at 1, 3 and 6 monthly intervals.

Response was noted in terms of percentage during each visit.
- Photographic documentation was done and response to treatment was graded as following table.

Table-1: Grading of response

Repigmentation (%)	Grade
0% repigmentation	No response
<25% repigmentation	Poor response
25-50% repigmentation	Good response
50 -75% repigmentation	Very good response
>75% repigmentation	Excellent response

RESULT

- Out of 36 patients, 32 completed the study. Out of them, 12 were males and 20 were females. The male to female ratio was 1:7. The patients' age in our study ranged from 18 years to 60 years.

Table-2: Age and sex distribution of patients

Age-group	Male	Female	Total
18-30	7	10	17
31-40	2	6	8
41-50	2	2	4
51-60	1	2	3
Total	12	20	32

- The duration of vitiligo ranged from 1.5 years to 10 years with a mean duration of 3.5 years. The average duration of different kinds of treatment taken was 2 years.
- Out of the 32 patients, 12 had lesions on upper limbs, 10 had lesions on lower limbs, 6 had lesions over acral areas (4 had lesions over hands and 2 had over feet) and 4 had lesions over trunk.

Table-3: Result

	At the end of 1 month	At the end of 3 month	At the end of 6 month
No response	18 (56.25%)	9 (28.13%)	7 (21.88%)
Poor response	14 (43.75%)	6 (18.75%)	3 (9.38%)
Good response	0	8 (25.00%)	4 (12.5%)
Very good response	0	4 (12.50%)	6 (18.75%)
Excellent response	0	5 (15.63%)	12 (37.5%)
Total no. of cases	32	32	32

- At the end of one month, repigmention in the form of poor response was seen in 14 (43.75%) patients.
- At the end of 3 months 23 (71.87%) patients showed repigmentation. Out of them, 5 (15.63%) patients showed excellent response, 4 (12.50%) patients showed very good response, 8 (25%) had good response while 6 (18.75%) had poor response. No response was seen in 9 (28.13%) patients.
- At the end of 6 months, no pigmentation was seen in 7 (21.88%) patients and repigmentation was seen in 25 (78.13%) patients. Out of them, 12 (37.5%) patients showed excellent response, 6 (18.75%) patients showed very good response, 4 (12.5%) had good response while 3 (9.38%) had poor response.
- Maximum repigmentation was seen in truncal lesions and least was seen in acral lesions. Less repigmentation was seen in lesions with leucotrichia and lesions over bony prominence. These findings are in concordance with the literature.[8]
- 90% patients experienced pain during the procedure.
- Immediate complications in the form of burning and erythema were noticed in 6 (18.75%) patients.
- Late complications in the form of hyperpigmentation with scarring developed in 6 (18.75%) patients.

DISCUSSION

- Application of 5-FU after therapeutic wounding, as a treatment for vitiligo, was introduced by Tsuji and Hamada in 1983.[9]
- A strong inflammatory reaction will develop after needling followed by application of topical 5-FU. Due to this, there is local edema, which increases the intercellular spaces of the basal layer for a long time.
- Active melanocytes with frequently vacuolated cytoplasm are found migrating from pigmented to the achromic epidermis through these enlarged intercellular spaces.[10]
- Further, the inflammatory mediators such as leukotrienes C4 and D4 are locally released, which stimulate melanocyte proliferation and migration.[11]
- The metalloproteinase-2 synthesized by the keratinocytes during the epidermis remodeling process has been found to help in melanocyte migration. This favourable milieu, which persists for a long time, could explain the successful migration of melanocytes from the pigmented area to the achromic area.

CONCLUSION

- Greater than 50% repigmentation was seen in more than half of the patients.
- Needling with 5-FU application is effective in recalcitrant focal vitiligo.
- It is safe, simple and outpatient procedure with minimum side effects. Further studies are required to confirm the effectiveness of this procedure.

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