Evaluation of intralesional 5% 5-fluorouracil in resistant localized plaque psoriasis

Bharat Bhushan Mahajan, Monika Singla

Department of Dermatology, Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India

ABSTRACT

Background: Psoriasis is a chronic, autoimmune, inflammatory papulosquamous disorder, the treatment of which remains challenging. A variety of therapeutic modalities have been used with varying degree of success. But, there is no such therapeutic modality till date that can prevent the relapse in psoriasis. **Aims:** The present study is being undertaken to evaluate the therapeutic efficacy of intralesional 5% 5-fluorouracil (5-FU) as well as its role in preventing relapse in resistant localized plaque psoriasis. **Study Design:** An open, prospective, randomized-controlled study. **Materials and Methods:** A total of 40 patients of resistant localized plaque psoriasis were enrolled for the study. Intralesional injection of 5% 5-FU was given in a dosage of 0.1 mL/cm^2 of each plaque using an insulin syringe. In all patients, a single plaque was kept as control and was given intralesional injection of distilled water. A total of three injections were given in each plaque at weekly intervals. After that, patients were followed-up regularly at the interval of 2 weeks up to 12 weeks. All the lesions (both treated and control) were assessed clinically as well as photographically at each visit and graded using psoriasis severity index scoring. Results were analyzed statistically at the end of the follow-up period. **Results:** At 12 weeks follow-up, out of 40 patients treated, 4 (10%) patients had clearance (>90% resolution), 19 (47.5%) had excellent (70%-90%) improvement, whereas 12 (30%) patients were moderately (30%-70%) improved, and only 5 (12.5%) patients had mild or no improvement. Results were statistically significant in treated group in comparison to control group. Almost all patients complained of pain at the site of injection which subsided within 1-2 h. A total of 10 (25%) patients had necrosis after one or two injections which healed during the follow-up period within 6-8 weeks. **Conclusion:** Intralesional 5% 5-FU is found to be an effective therapeutic modality in resistant localized plaque psoriasis without much side effects.

Key words: 5-fluorouracil, intralesional, plaque psoriasis

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Address for correspondence:
Dr Monika Singla, Department of Dermatology, Guru Gobind Singh Medical College and Hospital, Sadiq Road, Faridkot - 651 203, Punjab, India.
E-mail: monikasingla483@ymail.com

INTRODUCTION

Psoriasis is a recurrent and progressive papulosquamous disorder that causes significant social and psychological trauma to the patient. It is characterized by the presence of erythematous, sharply demarcated, indurated plaques covered with silvery-white scales. It is a commonly encountered inflammatory disorder with an estimated global prevalence ranging from 0.5% to 4.6%.[1] There is no cure for psoriasis, but there are a variety of treatment modalities that can help improve symptoms and quality of life. A number of studies show that intralesional 5% 5-fluorouracil (5-FU) is an effective modality in various benign, premalignant and malignant cutaneous diseases.

5-FU is an antimetabolite that inhibits deoxyribonucleic acid synthesis as well as ribonucleic acid processing and therefore decreases epidermal proliferation.[2] It has been widely used topically, intravenously, and intralesionally in various dermatological and nondermatological diseases. It is available as a solution, cream and as sustained-release preparation for intralesional use in various concentrations (0.5%, 1%, and 5%). This study was done to evaluate the therapeutic efficacy of intralesional 5% 5-FU as well as its role in preventing relapse in resistant localized plaque psoriasis.

MATERIALS AND METHODS

We performed an open, prospective, randomized, placebo-controlled study enrolling 40 patients of localized plaque psoriasis attending the outpatient clinic in the department of dermatology at GGS Medical College and Hospital, Faridkot.

Patients with generalized psoriasis, in the pediatric or elderly age group, pregnant and lactating females, and patients with known hypersensitivity to 5-FU were excluded from the study.

Patients were diagnosed clinically and a written informed consent was taken from each patient before starting the study. A detailed history and general examination including mucocutaneous examination was conducted in each case. All the routine investigations including complete hemogram, serum biochemical profile, blood sugar, and urinalysis were done for each patient.

Taking all aseptic precautions, 5% 5-FU was infiltrated under the lesion in a dosage of 0.1 mL/cm^2 of the plaque using an insulin syringe. A smaller lesion was injected from a single puncture site but a larger lesion was injected from multiple sites. The total dose of 5-FU did not exceed 150 mg at single sitting. One plaque was selected for intralesional injection of distilled water as control in all patients. Each patient was kept under observation for the next 10-15 min to detect immediate complications like pain, edema, and erythema. Each patient was also observed after 24 h to detect any untoward side effects like persistent pain, sensitivity to 5-FU, or any signs of necrosis.

Intralesional injection of 5% 5-FU was given weekly for a total of three injections. After that patients were followed-up regularly at intervals of 2 weeks up to 12 weeks. All the lesions injected with 5% 5-FU as well as distilled water were assessed clinically as well as photographically at the baseline, at each visit before the administration of intralesional injection and at each follow-up visit. Psoriasis severity index (PSI) of treated plaques was calculated at each visit which is the summation of erythema, induration, and scale points and ranges between 0 and 12 [Table 1].

The response to treatment taking into consideration erythema, induration, and scaling was graded as shown in Table 2.

Table 1: Psoriasis severity index

	Score	Erythema	Induration	Scale
No sign	0	No redness	No induration	No
Minimal	1	Light pink	Barely palpable	Rare
Mild	2	Pink or bright red	Slight elevation	Poorly defined
Moderate	3	Red	Moderate elevation	Defined
Severe	4	Dark red	Marked ridge	Heavy

Table 2: Grades of improvement evaluated by PSI scores

No response	0-10% improvement
Mild response	10-30% improvement
Moderate response	30-70% improvement
Excellent response	70-90% improvement
Clearance	90-100% improvement

PSI: Psoriasis severity index

Results were analyzed statistically after completion of the follow-up period.

RESULTS

In this study, the age of patients ranged between 20 and 60 years (mean age 39.55 ± 11.26 years); 31 were males (77.5%) and 9 were females (22.5%). The duration of the disease ranged from 1.5 months to 15 years (majority between 1 and 5 years).

After three injections of 5-FU, 57.5% (23/40) patients showed excellent (70%-90%) improvement, 30% (12) patients had moderate (30%-70%) improvement, and only 5 (12.5%) patients did not respond to treatment. At the end of follow-up period of 10 weeks after last injection (12th week), 4 (10%) patients had clearance (>90% resolution), 19 (47.5%) had excellent improvement, whereas 12 (30%) patients were moderately improved; only 5 (12.5%) patients had mild or no improvement. This is in contrast to control plaques in which 27 (67.5%) patients had mild or no improvement [Figure 1]. Clinical photographs of improvement in psoriatic plaques treated with intralesional 5% 5-FU as well as control plaque (treated with distilled water) are shown in Figures 2-4. These differences were statistically significant (*P* value <.001). Most of the patients remained in remission or improved further during follow-up period. Only two patients relapsed with significant increase in PSI scoring which had impact on the grading of improvement from excellent to moderate category.

No clinically significant systemic side effects or treatment-related adverse medical events were observed in our study. Most patients found the injections to be painful. A total of eight (20%) patients developed necrosis in at least one plaque after one injection of 5% 5-FU within 24 h, whereas two (5%) patients developed necrosis after two injections. Necrosis gradually healed within 2-4 weeks leaving hyperpigmentation in all patients and scarring in two patients. Hyperpigmentation was seen in 37 (92.5%) patients after treatment period which gradually disappeared within 8-10 weeks.

DISCUSSION

Psoriasis has become a major psychosocial problem today with cosmetic concern, for which no definite cure is available. Treatment of psoriasis aims to achieve clearing of the psoriatic lesions and preventing their recurrence. During last few years, various new medical and surgical treatments including phototherapy and lasers have been tried. 5-FU is a fluorinated pyrimidine analogue which emerged as a new class of antimetabolite drug in 1957.[3] 5-FU is indicated in various dermatological diseases as both topical as well as intralesional

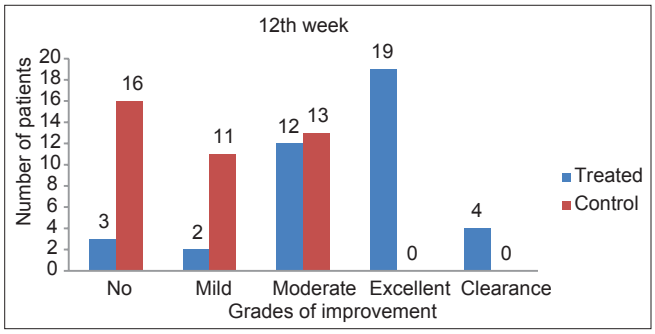

Figure 1: Comparison of grades of improvement between plaques treated with intralesional 5% 5-fluorouracil and kept as control after 12 weeks

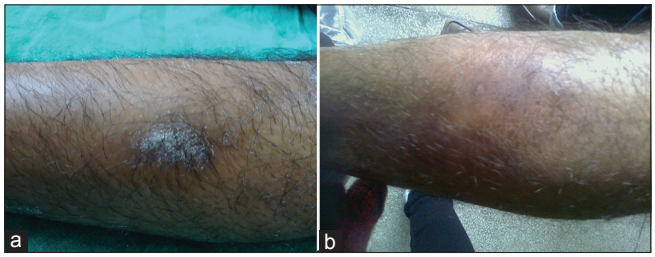

Figure 3: (a) A psoriatic plaque on left leg before injection. (b) The same plaque after three injections after 12 weeks (showing significant improvement)

agent. The advantage of intralesional 5-FU is that it allows higher drug concentration in the lesion for longer duration in comparison to topical 5-FU.

Intralesional 5% 5-FU has been effectively used in various dermatological diseases like keratoacanthomas, basal cell carcinoma, hypertrophic scars, keloids, warts, infantile digital fibromatosis, and psoriasis.[4-17] In our study, the response rate was 87.5% (10% patients with clearance, 47.5% with excellent improvement, and 30% moderate improvement). The results in our study are comparable with a study done by Pearlman *et al*.,[15] which showed favorable response in 82% patients of psoriasis treated with intralesional 5% 5-FU. Similar results were observed in a study by Taheri *et al*.,[17] (70%-90% improvement in 61% patients and > 90% improvement in 33.3% patients).

In our study, there were only local side effects such as pain, necrosis, and hyperpigmentation. These are similar to previous studies related to intralesional 5-FU in which no systemic adverse events were observed.[4-17]

CONCLUSION

From the results of the above study, it may be concluded that intralesional 5% 5-FU is an effective therapeutic modality not only for treatment but also for preventing relapse in localized plaque psoriasis. Further studies with a larger sample size and extended follow-up would be beneficial to delineate the clinical

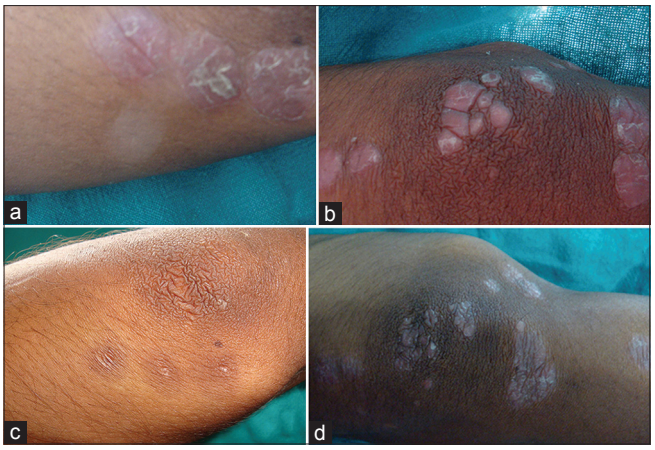

Figure 2: (a) Psoriatic plaques on right elbow before injection at day 0. (b) Psoriatic plaques on left elbow kept as control. (c) Plaques showing improvement after three 5-FU injections after 12 weeks. (d) Control plaques after 12 weeks

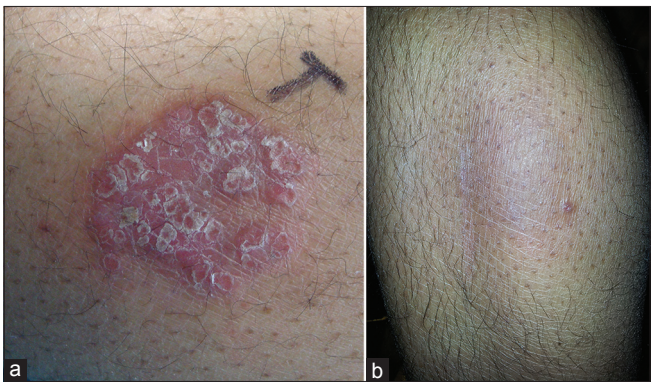

Figure 4: (a) A psoriatic plaque on leg at day 0. (b) The same plaque after three injections of 5- FU after 12 weeks

role and duration of remission with intralesional 5% 5-FU in patients of localized plaque psoriasis.

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