CASE REPORT

Apremilast in unstable non segmental vitiligo: A case series

Sumir Kumar,[1] MD, Jaskirat Kaur,[2] MD, B. K. Brar,[3] MD

[1]Associate Professor, [2]Post Graduate resident, [3]Professor and Head
Department of Dermatology, Venereology and Leprology, Guru Gobind Singh Medical College and Hospital, Faridkot-151203, Punjab, India

ABSTRACT

Though a number of innovative modalities have been tried in vitiligo, none of them provide satisfactory results for all patients. Both stability and repigmentation are equally important in the treatment of vitiligo. Multiple inflammatory mediators are involved in the pathogenesis of vitiligo. Apremilast, a novel phosphodiesterase 4 inhibitor interrupt this pathological cascade by modulating the expression of various cytokines. We herein report our experience in the 10 patients of unstable non segmental vitiligo. Marked to complete repigmentation in our patients demonstrated apremilast to be a novel, safe and effective treatment armamentarium in treatment of vitiligo. It has left the academic scholars and pharmaceutical companies to go through the less trodden path of searching a meanigful wonder drug for vitiligo folk.

KEYWORDS: Apremilast, unstable, vitiligo

INTRODUCTION

Vitiligo is associated with the huge social stigma in Asian skin. Despite of a number of treatment modalities being tried in vitiligo, search for newer molecules continue to endure because of shortcomings of the already persisting treatment modalities. Apremilast is an orally administered immunomodulator that modulates expression of multiple pro-inflammatory and anti-inflammatory molecules by virtue of inhibiting phosphodiesterase 4 enzyme. It has been approved by the US Food and Drug administration for the management of chronic plaque psoriasis and psoriatic arthritis.[1] Since then it is being used in a number of dermatological indications like Atopic dermatitis, Alopecia areata, Behcet's disease, and so on. Vitiligo, like psoriasis has deregulated immune pathogenesis, attibuted to T helper 1 cytokines in both the diseases.[2] We tried to solve the dilemma faced by researchers to prove the efficacy of scientifically promising drug in the ten cases of unstable vitiligo vulgaris.

CASE HISTORY

A total of 10 patients were enrolled from OPD with unstable non segmental vitiligo. The mean duration of vitiligo ranged from 5±0.5 years. The mean age of patients ranged from 22 to 50 years. All patients had tried various treatment modalities (such as oral corticosteroids, oral photochemotherapy, NB-UVB) and stopped them all 6 months back. Baseline

Correspondence: *Dr Jaskirat kaur, OPD block, 1st Floor, Department of Dermatology, Venereology and Leprology, Guru Gobind Singh Medical College and Hospital, Sadiq road, Faridkot-151203, Punjab, India - Tel.: 9646703202 - jaskiratkaur93@yahoo.com jaskiratkaur99930@gmail.com*

haematological investigations in all the patients were within the normal limit. The patients were prescribed 30 mg apremilast twice daily for a total of 4 months. No other systemic or topical treatment was given along with. The patients were followed four weekly up to a total of 36 weeks. Follow up was done by Vitiligo Area Severity Index (VASI), Dermatological life quality index (DLQI) and photographically. Hematological investigations were also done at 4 weekly intervals. Any adverse effects seen during the study period were recorded. The results were assessed statistically at end of the follow up period. Most of our patients showed stabilization and repigmentation in the form of hyperpigmented macules, which coalesce over a course of few weeks to form patches. Fig. 1 & 2 shows course of repigmentation in 3 of our patients. Most of our cases showed hyperpigmentation in the repigmented patches before they could achieve likeable matching pigmentation. The drug showed very minor side effects like nausea, vomiting, headache, diarrhea etc which improved over a course of 1 week in most of the patients. 1 patient withdrew from the study due to these adverse events. Mean reduction in VASI was 6.9%, which was statistically significant (p=0.046), in contrast our patients did not achieved proportional reduction in DLQI. Table 1 describe the statistical results of the study. Hematological investigations remained within normal range in all patients. None of our patients showed relapse during the follow up period.

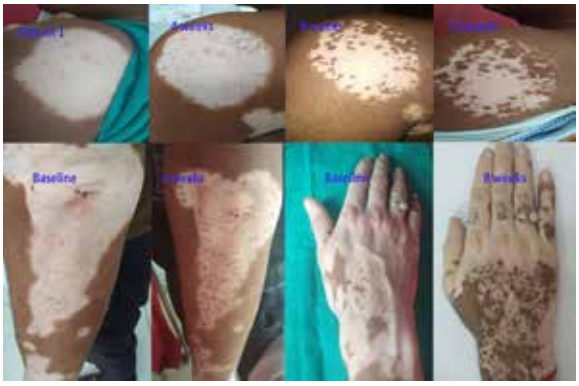

Fig. 1 Shows multiple sites of a vitiligo patient and improvement at succesive intervals.

Fig. 2 Shows depigmented patches in 2 vitiligo patients and almost significant repigmentation in them.

Table 1 Showing statistical profile of the study

S. No	Age	Sex	Type of vitiligo	Percentage reduction in VASI score	Percentage reduction in DLQI score
1	45	M	Unstable NSV	25	8.3
2	26	M	Unstable NSV	8.5	0
3	19	F	Unstable NSV	16.6	0
4	60	F	Unstable NSV	90	16.6
5	29	M	Unstable NSV	12.5	16.6
6	34	F	Unstable NSV	50	0
7	27	M	Unstable NSV	70	8.3
8	29	F	Unstable NSV	43	0
9	38	F	Unstable NSV	45	8.3

DISCUSSION

Vitiligo is an acquired disorder of melanogenesis that occur due to complex interaction between environmental and genetic factors, leading to the melanocyte destruction and characteristic depigmented lesions. Vitiligo is observing an era of therapeutic shutdown, where all the possible treatment modalities have been exhausted for many of the distressed patients. In such a scenario of therapeutic foreclosure, "Apremilast" could act as a new ray of hope.

PDE-4 normally degrades cyclic adenosine monophosphate (cAMP) to 5 - adenosine monophosphate. With inhibition of this enzyme, accumulation of cAMP within the cell occurs.[3] As a result of this pro inflammatory molecules like TNF-α, IL23 are decreased and anti-inflammatory like IL10 are increased. Melanocytes culture from vitiligo skin have shown to express high level of IL6 and IL17.[4] Apremilast also reduces the activity of nitric oxide synthetase, thereby and act as antiinflammatoy.[5] The absolute bioavailability of apremilast is around 70%. Its concentration in plasma reaches maximum after 2.5 hours.[6] Mild to moderate renal and severe hepatic dysfunction does not effect its metabolism. The drug does not show any organ specific or cumulative toxicity. It has been off label used in lichen planus, atopic dermatitis, alopecia areata, sarcoidosis etc with varying efficacy. Its role in vitiligo was yet to be elucidated, and we have succesfully elaborated the potential effect of this molecule in vitiligo. The drug is highly efficacious for inducing both stability and repigmentation. Resistant acral lesions also showed satisfactory response to the treatment. Most of our patients did not achieved much improvement in DLQI, this could be attributed to non specificity of this index.

Our experience demonstrated unexplored effective, safe and steroid sparing novel therapeutic alternative in patients with vitiligo. In our opinion, it may also be used as bridging or maintenance therapy after induction or can simply be combined with other agents. We are highly optimistic that this novel molecule will ultimately be a game changer for millions of vitiligo patients seeking treatment.

REFERENCES

1. Fala L. Otezla (Apremilast), an oral PDE4 inhibtor, receives FDA approval for treatment of patients with active psoriatic arthritis and plaque psoriasis. Am Heath Drug Benefits. 2018; 8:105-10.
2. Sharquie K E, Salman H A, Yseen K. Psoriasis and vitiligo are close relatives. Clin Cosmet Investig Dermatol. 2017; 10:341-45.
3. Papp K, Reich K, Leonardi CL. Apremilast, an oral phosphodiesterase 4 (PDE 4) inhibitor in patients with moderate to severe plaque psoriasis: Results of a phase III, Randomized controlled trial (Efficacy and Safety Trial Evaluating the Effects of Apremilast in psoriasis ESTEEM 1). J Am Acad Dermatol. 2015; 73:37-49.
4. P. Schafer. Apremilast mechanism of action and application to psoriasis and psoriatic arthritis. Biochem Pharmacol. 2012; 83:1583-90.
5. Lowes MA, Farinas SM, Krueger JG. Immunology of Psoriasis. Annu Rev Immunol. 2014; 32:227-55.
6. Afra TP, Razmi TM, Sunil Dogra. Apremilast in Psoriasis and beyond: big hope on a small molecule. Indian Dermatol Online J. 2019; 10 (1):1-12.