Journal of Pakistan Association of Dermatologists. 2022;**32(1)**:9-14.

Original Article

Efficacy and safety of secukinumab in treatment of moderate to severe psoriasis

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Abstract

Objective To assess the effectiveness and safety of Secukinumab in the treatment of Psoriasis.

Methods The study was conducted in the Department of Dermatology, Services Institute of Medical Sciences, Lahore. Eleven patients of Chronic Plaque Psoriasis (moderate to severe), psoriatic arthritis or pustular psoriasis were enrolled after taking informed consent. Their history and examination findings were recorded. The disease severity was assessed by calculating Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI). Patients were given Injection Secukinumab 150mg subcutaneously at week 0, 1,2,3 and 4 and then monthly for 5 months. Patients were followed at 5 and 25 weeks and their post-treatment PASI and DLQI scores were noted and compared. Pre- and post-treatment photographs were also compared. Patients were asked to report any adverse events during therapy.

Results Seven male and four female patients of psoriasis (moderate to severe) with mean age 28.36±5.06 years were enrolled. At week 5, 6 (54.5%) patients achieved PASI 50, while at 25 weeks, four (36.36%) patients achieved PASI 75 and seven sustained PASI 50 response. Ten (90.9%) patients achieved more than 10-points reduction in DLQI score at week 5, while all of them reported 10 to 19-points reduction in DLQI at 25 weeks. Mild headache was reported by four patients while two patients experienced dizziness. These complaints settled after two to three doses.

Conclusion The study results indicate that Secukinumab improves physical and psychosocial life of Psoriatic patients and reduces disease severity along with a good safety profile.

Key words
Secukinumab, Psoriasis, PASI, DLQI.

Introduction

Psoriasis is one of immunologically mediated chronic disorder having a serious effect on physical and psychosocial well being of sufferer. It is associated with much comorbidity too due to the associated joint involvement as well as metabolic syndrome.[1,2] Psoriasis vulgaris manifests on the skin as erythematous, scaly plaques predominantly involving extensor surfaces. Other presentations of the disease include guttate, pustular, erythrodermic and palmoplantar forms. The disease may also involve and damage organs like eyes, cardiovascular system and joints.[3] Various tools have been devised overtime to assess the gravity of disease and effect of treatment. One of them is Psoriasis Area and Severity Index (PASI). It is seen that lowering of PASI by half (PASI 50) and by 75% (PASI 75), after therapy are reliable indicators of overall clinical improvement.[4] Another useful tool is Dermatology Life Quality Index (DLQI), a questionnaire that assesses the effect of illness on patients' personal, social and work related quality of life.[5] Using PASI we can

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grade the severity of Psoriasis as mild <10, moderate 10–20, or severe >20.[6] DLQI grades consequence of ailment on patient's life as no sequel (0-1), mild impact (2-5), moderate impact (6-10), huge impact (11-20) and very huge impact (21-30).[7]

Since Interleukin-17 has a major role in pathogenesis of Psoriasis,[8] Biologics particularly anti-interleukin 17A (IL-17A) agents have been effective in treating skin and joint disease. They have been reported to be safer when compared to other agents.[9,10] Secukinumab, a fully human immunoglobulin, targets and neutralizes IL-17A, a pro-inflammatory cytokine released by helper T-17 cells, which plays a crucial part in mediating the inflammatory pathway in Psoriasis.[10] Secukinumab was the earliest anti-IL-17 biologic which got approval by the European and US drug agencies for treatment of psoriasis.[11] It is available in a 150mg vial or a pre-filled syringe as lyophilized powder which must be reconstituted before subcutaneous administration.[12] The recommended dosage is 300mg in moderate to severe Psoriasis injected subcutaneously weekly for 5 weeks, followed by monthly injections thereafter.[13] Headache was one common adverse effect along with upper respiratory tract infections, diarrhea, joint pains, backache, cough and itching. Serious side effects, however, are rare.[14] No work has been done on this drug in our part of the world. Therefore, this study was planned to assess the clinical effectiveness and safety of the drug in our population.

Methods

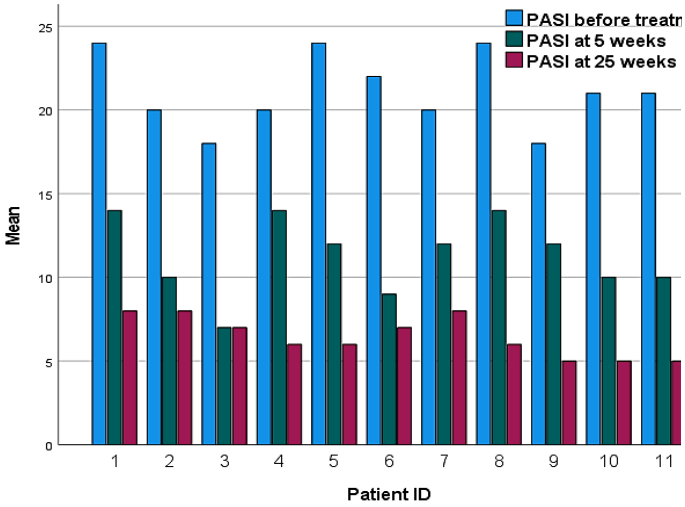
After taking approval from Ethical Review Board, eleven patients of moderate to severe Psoriasis were enrolled after written, informed consent. Complete history and clinical examination was done. Contraindications for the use of biologics i.e. pregnancy, active infections, tuberculosis, HIV, hepatitis B, C and hypersensitivity to Secukinumab, were excluded. PASI and DLQI were calculated. Pre-treatment photographs were taken. Patients received Injection Secukinumab 150mg subcutaneously at week 0, 1, 2, 3, 4 and then monthly for 5 months. Patients were followed up at week 5 and 25 and their post-treatment photographs, PASI and DLQI scores were compared. Any adverse events reported during therapy were recorded

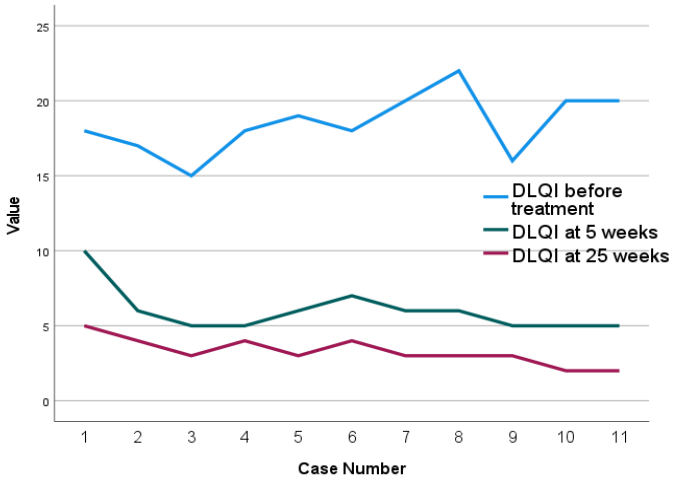
Results

Data was entered and analyzed in SPSS 27. Mean age of the patients was 28.36 ± 5.06 years. Seven patients were male while four were female. Disease duration varied from less than six months in 6 patients to more than 2 years in five patients. Out of eleven patients, three suffered from chronic plaque psoriasis alone, six had chronic plaque psoriasis along with psoriatic arthritis and two had pustular psoriasis. Among those with joint involvement, two patients had mono- or oligoarthritis, two had involvement of distal interphalangeal joints and two had involvement of axial skeleton. Five patients had moderate Psoriasis while six patients had severe disease.

Response: After 4 weeks of treatment, 6 (54.5%) patients achieved PASI 50, while at 25 weeks; four (36.36%) patients achieved PASI 75 (Responders) and seven sustained PASI 50 response (Partial responders). As far as their quality of life was concerned, 10 (90.9 %) patients achieved more than 10-points reduction in DLQI score at week 5, while all of them reported 10 to 19-points reduction in DLQI at week 25.

Safety: Four patients reported headache and two complained of dizziness. They were managed





Graph 1 & 2 Reduction in PASI and DLQI scores before treatment and at 5 and 25 weeks follow up.

Table 1 Efficacy end-points achieved according to Type of Psoriasis

		Type of Psoriasis					
		Plaque Psoriasis		*Plaque Psoriasis with Psoriatic Arthritis*		*Pustular Psoriasis*	
		Count	*Row N %*	*Count*	*Row N %*	*Count*	*Row N %*
PASI50 achieved at 25 weeks	Yes	3	27.3%	6	54.5%	2	18.2%
	No	0	0.0%	0	0.0%	0	0.0%
PASI75 achieved at 25 weeks	Yes	1	25.0%	2	50.0%	1	25.0%
	No	2	28.6%	4	57.1%	1	14.3%
Reduction in DLQI >10-points at 5 weeks	yes	3	30.0%	5	50.0%	2	20.0%
	no	0	0.0%	1	100.0%	0	0.0%
Reduction in DLQI >10-points at 25 weeks	Yes	3	27.3%	6	54.5%	2	18.2%
	No	0	0.0%	0	0.0%	0	0.0%

conservatively and settled after two to three doses.

Discussion

Various treatment modalities have been employed in the past considering the severity of Psoriasis, patient preferences, cost of therapy and safety profile. These include topical agents, phototherapy, methotrexate, retinoids, cyclosporine and some natural and herbal agents. Most of these therapeutic options are associated with significant end organ damage. Therefore, more recently Biologics have been introduced that selectively inhibit small molecules, receptors and enzymes leading to effective clearance of disease and favorable safety profile.[15] Secukinumab is a fully human monoclonal antibody against interleukin-17. Phase III trials have shown promising results in moderate to severe psoriasis.[16] Not much work has been done in our part of the world on Secukinumab, so we conducted this study to obtain real life data on the drug's effectiveness and safety.

Neema S. et al[17] retrospectively analyzed twenty patients in India, who received injection Secukinumab for Psoriasis, and reported that 85% patients achieved PASI 75 at 12 weeks. These results were much higher than our results (36.36%), probably because they used 300mg of the drug while we used half the dose, in order to keep the cost of the drug and safety profile under control. Mean age of their patients was also

Figure 1 Week 0 Week 5 Week 25

Figure 2 Week 0 Week 5 Week 25

Figure 3 Week 0 Week 5 Week 25

higher (46 years) than our patients (28.36±5.06 years). Lin Cai et al[18] reported that 87.2% Chinese patients on 150mg Secukinumab achieved PASI 75 at 12 weeks. Higher mean age (40.5±10.8 years) and ethnic differences were probably responsible for the variation from our results. Another Indian study[19] reported 55.9% patients achieving PASI 75 in 12 weeks in Secukinumab 150mg subgroup. However, 80% patients achieved PASI 50 at 52 weeks, while all our patients achieved PASI 50 at 25 weeks. Again the mean age of the patients was 45 years.

Pariser D et al[20] studied efficacy of Secukinumab in North American population and reported a 10-point reduction in DLQI scores, similar to our results. Augustin M et al[21] also reported normalization of DLQI scores after Secukinumab in moderate to severe Psoriaisis. These results were consistent with our

observations as patients' quality of life significantly improved along with reduction in erythema and scaling at week 5 and sustained at week 25 **(Figure 1-3)**.

As far as safety of the drug is concerned, only four patients reported headache and dizziness which was relieved after two to three doses. However, longer term Phase II and III trials have reported upper respiratory tract infections, fever and diarrhea as commonest, while Candidiasis, inflammatory bowel disease and cardiac events as lesser commonly seen effects.[16,19] This difference from our results can be attributed to much larger number of patients followed for much longer duration and ethnic variations. Moreover, we studied smaller number of patients with more severe, resistant and complicated disease as 73% of our patients had psoriatic arthritis or pustular psoriasis.

Due to lack of published data on the safety and effectiveness of Secukinumab in Pakistan, our study can pivot ways for further large scale studies as Secukinumab may prove to be a preferred treatment option for patients having recalcitrant disease not responding to other treatment options.

Limitations of Study: Small sample size is the main limitation of the study.

Strength of Study: This is first real-life data with 25 weeks follow up from Pakistan.

Conclusion

The study results indicate that Secukinumab significantly improves quality of life of Psoriatic patients and reduce the severity of disease along with a good safety profile.

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