Efficacy of secukinumab in the treatment of moderate-severe plaque psoriasis at a tertiary care teaching hospital in India

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Received: 25 April 2020
Accepted: 2 December 2020

Background: Secukinumab is a fully humanized IL-17A antagonist approved for managing moderate-to-severe plaque psoriasis as well as psoriatic arthritis. This study assessed the speed of action of secukinumab and the improvement in the quality of life in a series of patients.

Methods: We aimed to assess changes in the PASI (Psoriasis Area Severity Index) and DLQI (Dermatology Life Quality Index) following a course of secukinumab injections. Methods: This hospital-based study was conducted in the Department of Dermatology, Venereology and Leprosy of ESIC Medical College & Hospital, Hyderabad, India.

Results: Starting from 8 weeks after initiation of treatment with secukinumab 300 mg, a clinically significant response was observed, with progressive reduction of skin disease indices. Twenty-four patients were included in the study, with a mean age of 42 years. The male to female ratio was 15:9. Thirteen (54.16%) patients achieved PASI 75 at eight weeks. At the end of 52 weeks, 20 (83.33%), 15 (62.5%), and 8 (33.33%) patients maintained PASI 75, PASI 90, and PASI 100, respectively.

Conclusion: Secukinumab is a highly-efficacious, biologic therapy that provides rapid relief with a relatively favorable safety profile in patients with moderate-severe plaque psoriasis. In addition, secukinumab is a preferred treatment for patients with comorbid psoriatic arthritis or arthralgia symptoms due to its ability to arrest the progression of arthritic disease in the early course.

Keywords: biologic therapy, psoriasis, psoriatic arthritis

Iran J Dermatol 2021; 24: 255-261

DOI: 10.22034/ijd.2020.228477.1076

INTRODUCTION

Psoriasis vulgaris is a chronic immune-mediated inflammatory papulosquamous disease characterized by erythematous scaly plaques, with a massive impact on the quality of life of those affected. It has a chronic, relapsing, and remitting course. About 0.2-8.5% of the world population is affected by psoriasis [1]. Roughly 2–3% of people in industrialized countries are affected by psoriasis, which can present in the mild form, affecting only elbows and knees, or as moderate to severe disease, involving large areas of the skin [2]. Psoriasis is also a systemic inflammatory disease with an increased risk of various comorbidities like metabolic syndrome, psoriatic arthritis (PsA), cardiovascular diseases (CVD), obesity, diabetes mellitus, and depression [3–5]. The treatment of patients with psoriasis has evolved

over the past decades. Due to their favorable efficacy and safety, biologics have become the first-line treatment in patients who are suitable candidates for systemic therapy. At present, three classes of biologics are available for this application: the tumor necrosis factor-alpha inhibitors (etanercept, infliximab, and adalimumab), the interleukin (IL)-12/IL-23 inhibitors (ustekinumab), and an IL-17 inhibitor (secukinumab) [6]. The biologics currently used for psoriasis in India are etanercept, infliximab, adalimumab (biosimilar), itolizumab, and secukinumab [7].

Secukinumab is an anti-IL-17A monoclonal antibody approved for treating moderate-to-severe plaque psoriasis with superior efficacy over etanercept and ustekinumab [8,9]. Since 2015, it has been approved by the Food and Drug Administration in the USA and has gained increasing popularity in treating plaque psoriasis. Secukinumab binds to IL-17A, thereby inhibiting its interaction with IL-17 receptors. Preventing the cytokine/receptor interaction neutralizes the bioactivity of IL-17A and inhibits the subsequent release of proinflammatory cytokines, chemokines, and mediators of tissue damage.

Secukinumab has been proven to be highly efficacious in treating moderate to severe psoriasis, with a sustained effect when started early in the course [10-12]. This study was undertaken to evaluate the real-life experience with secukinumab injections in difficult chronic plaque-type psoriasis.

The dose of secukinumab for treating chronic plaque psoriasis is 300 mg weekly for five weeks, followed by monthly 300 mg doses. A 75% improvement in the Psoriasis Area Severity Index (PASI 75) previously was the primary treatment target; however, the bar has been raised to PASI 90 since the introduction of secukinumab [13]. Several Phase III studies have shown a PASI 75 response in 77%–80% of patients at week 12 and PASI 90 and PASI 100 in 55%–59% and 24%–28% of patients, respectively. Almost 80% of patients maintained PASI 75 till week 52 [9].

PARTICIPANTS AND METHODS

Participants and study design

This hospital-based observational study was conducted in the Department of Dermatology, Venereology and Leprosy of ESIC Medical College & Hospital, Hyderabad, India.

Time period

The study period was between November 2017 and December 2018.

Inclusion criteria

We included adults 18 years and older with moderate-severe plaque psoriasis, who were candidates for systemic therapy and were not responding to topical therapy or methotrexate or developed side effects to methotrexate, and could not comply with regular phototherapy sessions.

Exclusion criteria

We excluded subjects with any other kinds of psoriasis other than chronic plaque psoriasis, subjects with tuberculosis or candidiasis, pregnant or breastfeeding mothers, and those who were not willing to participate.

Objectives of the study

We aimed to assess changes in the PASI (Psoriasis Area Severity Index) and DLQI (Dermatology Life Quality Index) following a course of secukinumab injections.

Demographic and clinical data (age, sex, duration of disease, and comorbidities) for each patient were collected. Past drug history was noted. For all patients, we checked for hepatitis B, hepatitis C, HIV (by serology), and tuberculosis (Mantoux test) at baseline, besides a chest X-ray and assays for complete blood count (CBC), blood urea, creatinine, lipid profile, fasting and postprandial glucose, alanine aminotransferase (ALT), and aspartate aminotransferase (AST). The CBC, ALT, AST, blood urea, and creatinine were re-checked at weeks 4, 12, 24, 36, and 52.

Secukinumab injection was administered in the standard dosing regimen of 300 mg subcutaneously weekly for five weeks followed by once a month for a total of 52 weeks unless cessation became necessary due to adverse effects or poor efficacy. Assessment of severity was done at baseline, week 4, week 12, week 26, and week 52. The primary

endpoint was PASI 75 at week 12. Secondary endpoints were PAS I75 and PASI 100 at week 52 and adverse events during follow-up.

Clinical assessment

Disease severity was assessed at each visit using the PASI [14] – a composite evaluation instrument for psoriasis severity, with subscores for erythema, induration, scaling, and percentage of body-surface area affected. Furthermore, qualitative measures were assessed using the Dermatological Life Quality Index (DLQI) [15] – a validated instrument for dermatologic conditions, where the scores range from 0 to 30 points, with higher scores indicating a greater effect on the quality of life. Drug efficacy was evaluated by observed changes in PASI and DLQI scores since baseline. PASI/DLQI scores were noted at baseline and at an interval of 1 to 6 months. Patients were followed up for another six months.

Statistical method

Statistical analysis was done by IBM SPSS Statistics for Windows, version 23.0. (SPSS Inc., New York, New York, USA). Differences in parametric measures were tested using the t-test, whereas the Wilcoxon signed-rank test was used for nonparametric measures. P-values < 0.05 were considered statistically significant.

Ethical considerations

Written informed consent from patients and Institutional Ethics Committee approval was taken before taking up the study.

RESULTS

Twenty-four patients, including 15 males (62.5%) and 9 females (37.5%), were included in the study. The mean age of the patients was 42.6 years. The average duration of the disease was 6.33 years. Out of 24 patients, comorbidities were noted in 16 (68%), including metabolic syndrome in 14 (58.33%), psoriatic arthritis in 6 (25%), dyslipidaemia in 15 (62.5%), diabetes in 11 (45.83%), and hypertension in 9 (37.5%) cases. All of them were on simultaneous topical therapy with corticosteroids. Each patient had received at least two systemic therapies in the past. The general profile of patients, including their age, sex, past treatment, and comorbidities, is illustrated in Table 1. The baseline PASI of all patients is illustrated in Table 2. The number of cases with baseline PASI < 20 were 7 (29.16%), PASI 20-30 were 8 (33.33%), and > 30 were 9 (37.5%). The mean DLQI at baseline was 14.8.

The efficacy of secukinumab is depicted in Table 3. Thirteen (54.16%) patients achieved PASI 75 at eight weeks. Eighteen (75%) out of 24 patients achieved PASI 75, seven (29.16%) achieved PASI 90,

Table 1. Baseline characteristics and summary of 24 cases of moderate-severe plaque psoriasis on secukinumab

Demographics	
Total number of cases	24
Age, mean years	42.6
Males	62.5% (15)
Females	37.5% (9)
Duration of disease, average years	6.33
Comorbidities	68% (16)
Metabolic syndrome	58.33% (14)
Psoriatic arthritis	25% (6)
Diabetes	45.83% (11)
Hypertension	37.5% (9)
Dyslipidemia	62.5% (15)

Table 2. Baseline PASI

Baseline PASI (mean SD)	
% of subjects with PASI <20	29.16% (7)
% of subjects with PASI >20 <30	33.33% (8)
% of subjects with PASI >30	37.5% (9)
Baseline DLQI (mean SD)	14.8

Table 3. PASI & DLQI during the course of treatment

	Week 8	**Week 12**	**Week 24**	**Week 52**
PASI				
PASI 75	54.16% (13)	75% (18)	83.33% (20)	83.33% (20)
PASI 90	25% (6)	29.16% (7)	45.83% (11)	62.5% (15)
PASI 100	0	8.33% (2)	2.08% (5)	33.33% (8)
DLQI				
DLQI mean	9.8	5.6	3.2	2.4

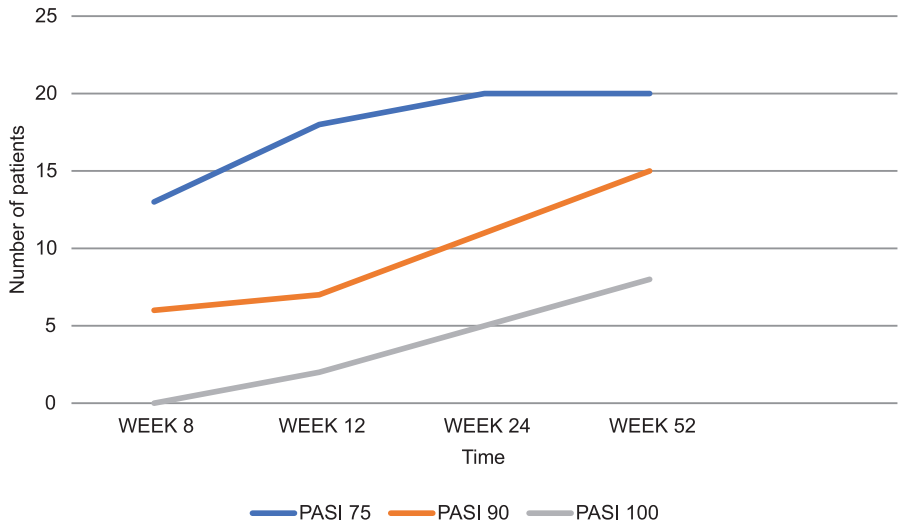

Figure 1. Number of patients achieving PASI 75, PASI 90, and PASI 100 over time

and 2 (8.33%) achieved PASI 100 at 12 weeks. At the end of 52 weeks, 20 (83.33%), 15 (62.5%), and 8 (33.33%) patients maintained PASI 75, PASI 90, and PASI 100, respectively (Figure 1). The DLQI, which was 14.8 at baseline, gradually reduced to 9.8 at week 8, 5.6 at week 12, 3.2 at week 24, and 2.4 at week 52 (Table 3). The reductions in PASI and DLQI by each subsequent visit were statistically significant ($P < 0.001$). In patients with concomitant arthritis, there was a significant improvement in the condition and generalized well-being.

Adverse effects of mild nature were noticed only in four (16.67%) patients. These were rhinosinusitis (4.16%), diarrhea (4.16%), and injection site itching (8.33%), none of which required a stoppage of therapy. The upper respiratory tract infection was treated using a short course of oral antibiotics. There was no abnormality of laboratory parameters detected in the follow-up investigations. Pre-therapy and Post-therapy images of two patients depicting rapid clearance of the disease are illustrated in Figures 2 and 3.

DISCUSSION

Psoriasis is a chronic papulosquamous disease with a relapsing course associated with comorbid conditions, causing significant morbidity and negatively impacting the quality of life. In patients of moderate-severe plaque psoriasis who cannot be managed with topical treatment alone, systemic agents are added. Biologics are tried in a subset of patients who do not respond to systemic agents alone. They are proven to reduce the PASI and DLQI of patients significantly.

Secukinumab is a fully humanized monoclonal anti-IL-17 antibody. Phase III studies and pooled data analysis show that secukinumab has a favorable safety profile, and patients achieved sustained remission while on secukinumab [16]. Though the trial data for the efficacy of secukinumab are promising, the availability of real-life data is limited.

In our study of 24 patients, the mean age was 42.6 years with a male to female ratio of 15:9.

The average duration of the disease was 6.33 years. In our study, 16 patients (68%) had comorbidities, out of which dyslipidemia was seen in 15 (62.5%), metabolic syndrome in 14 (58.33%), diabetes in 11 (45.83%), hypertension in 9 (37.5%), and psoriatic arthritis in 6 (25%). At baseline, the PASI was < 20 in 7 cases (29.16%), 20-30 in 8 cases (33.33%), and > 30 in 9 cases (37.5%). In the study by Neema *et al.* [17], the baseline PASI was 17.3. In our study, 13 (54.16%) patients achieved PASI 75 after eight weeks. Eighteen (75%) out of 24 patients achieved PASI 75, seven (29.16%) achieved PASI 90, and 2 (8.33%) patients achieved PASI 100 at 12 weeks. At the end of 52 weeks, 20 (83.33%), 15 (62.5%), and 8 (33.33%) patients maintained PASI 75, PASI 90, and PASI 100, respectively. In the study of Neema *et al.* [17], 15 (75%) patients achieved PASI 75 at four weeks; 17 (85%) achieved PASI 75,

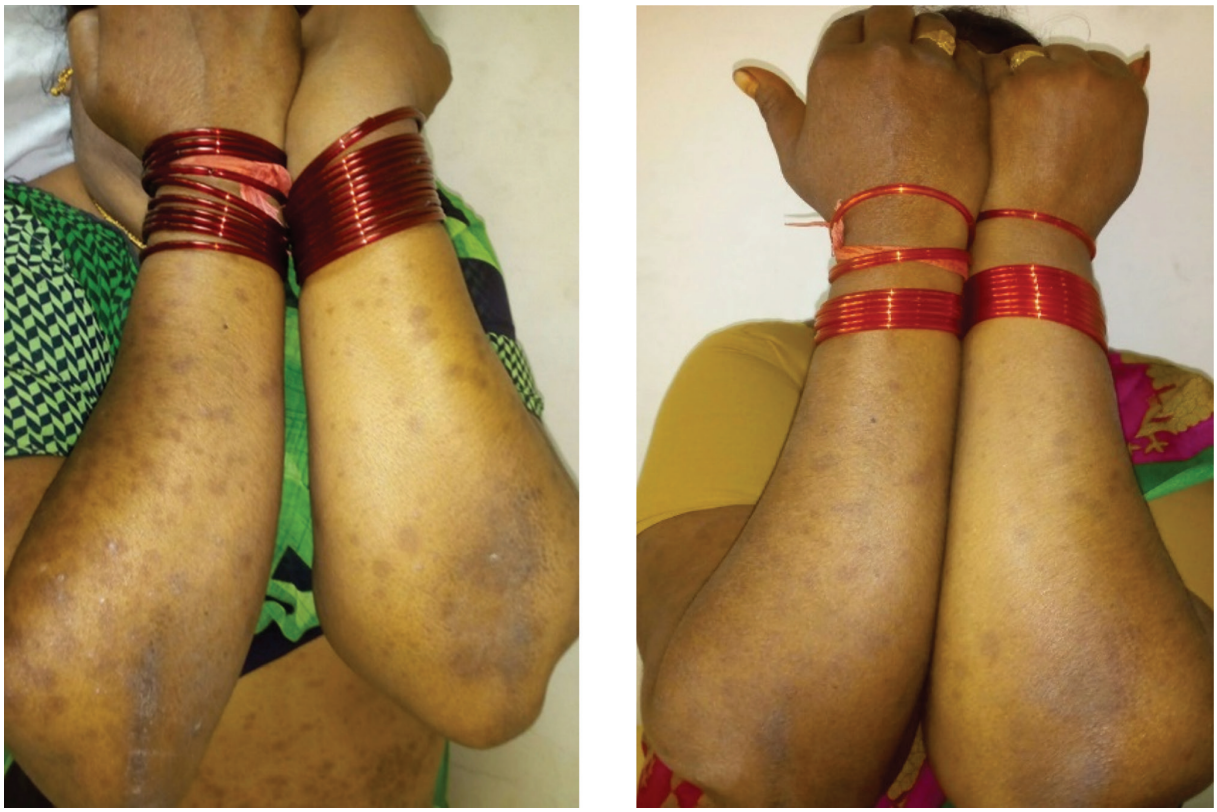

Figure 2. A patient at weeks 8 (left) and 16 (right)

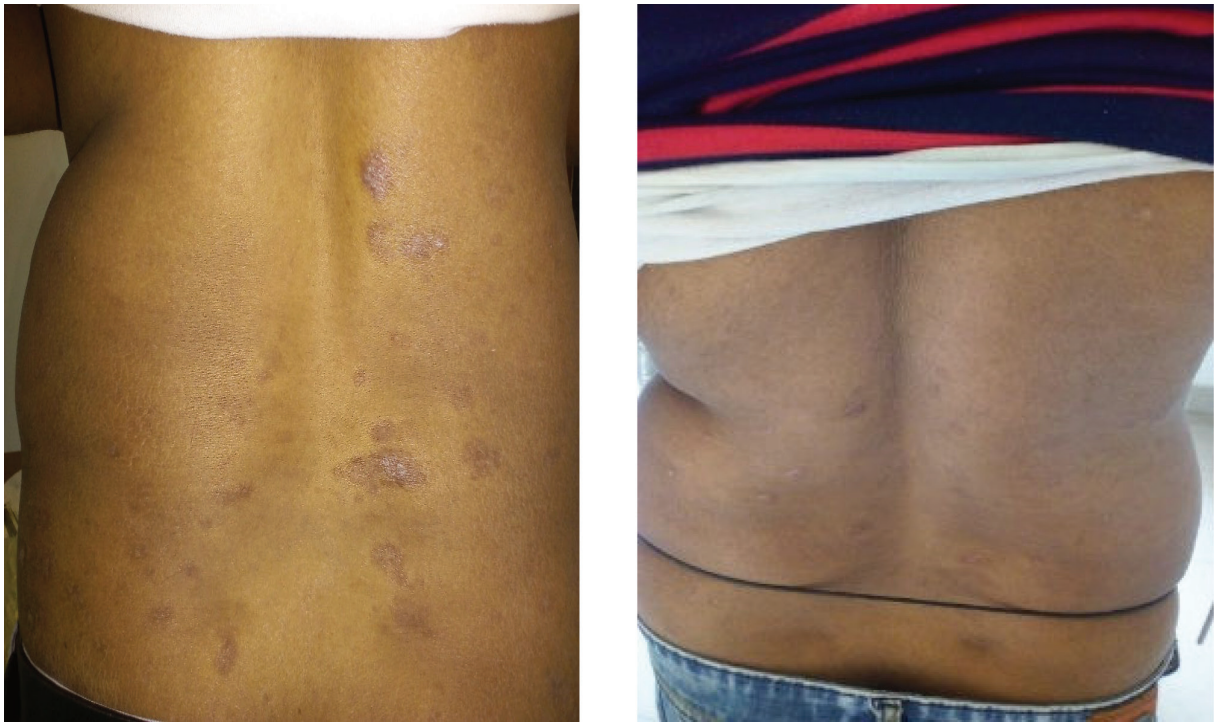

Figure 3. A patient at weeks 4 (left) and 52 (right)

13 (65%) achieved PASI 90, and 10 (50%) achieved PASI 100 at 12 weeks. At the end of 52 weeks, 18 (90%), 10 (50%), and 7 (35%) patients maintained PASI 75, PASI 90, and PASI 100, respectively. Galluzzo *et al.* [18] conducted a multi-centric real-life study in Italy, including 107 patients and a 52-week observation period. At week 4, 58% of patients achieved PASI 75, 35.5% PASI 90, and 22.4% PASI 100. At week 52, data were available for 35.5% (38/107) of patients. About 92.1% (35/38), 81.6% (31/38), and 78.9% (30/38) of patients maintained PASI 75, PASI 90, and PASI 100, respectively. The baseline DLQI in our study was 14.8, which gradually declined to 9.8 at eight weeks and then to 2.4 at 52 weeks. In a study by Singh *et al.* [19], the baseline DLQI was 15.31, reducing to 2.56 at the end of 12 weeks. In the FIXTURE [20] study, DLQI reduction at 12 weeks was 10.9% of baseline. These results were comparable to our study.

In the study by Chaudhari *et al.* [21] and in the EXPRESS II study by Menter *et al.* [22], secukinumab's efficacy at week 12 was better than other biologics like infliximab. In comparison to etanercept, a study conducted by Gordon *et al.* [23] and a study by Tyring *et al.* [24] showed 33% and 47% treated with 25 mg etanercept, respectively, which is less compared to secukinumab at week 12. A study by Chopra *et al.* [25] investigated the biosimilar efficacy of adalimumab, revealing that after 16 weeks, about 93% of patients achieved PASI 75, and 55% reported complete remission, i.e., PASI 100. About 14% of their patients were PASI 90, and 24% were PASI 75 responders. In another phase III trial [26], 71% of adalimumab-treated patients had achieved PASI 75 at 16 weeks; PASI 90 and 100 scores were reported in 45% and 20% of patients, respectively. These results are comparable to secukinumab, though we achieved PASI 75 and PASI 100 in a greater percentage of patients compared with other drugs.

In our study, adverse effects of mild nature were noticed only in four (16.67%) patients. These were rhinosinusitis (4.16%), diarrhea (4.16%), and injection site itching (8.33%). In the study by Galluzzo *et al.* [18], nearly 9.3% (10/107) of patients experienced adverse effects, the most common of which was mucocutaneous candidiasis. In the study by Neema *et al.* [17], thirty percent of patients (6/20) developed adverse effects during therapy, out of which two required discontinuation of treatment.

CONCLUSION

Secukinumab is a treatment of choice for chronic plaque-type psoriasis that is resistant to systemic treatment alone in the scenario of the Indian subcontinent. Secukinumab is a highly-efficacious biologic therapy that provides rapid relief with a relatively favorable safety profile. It can be considered in patients requiring rapid clearance of their psoriasis and in patients with psoriasis located in difficult-to-treat areas, such as the scalp, palms, soles, or nails. In addition, secukinumab is a preferred treatment for patients with comorbid psoriatic arthritis or arthralgia symptoms due to its ability to arrest the progression of arthritic disease in the early course. Efficacy is maintained long-term compared to other systemic therapy and other biologics. More real-life studies are required.

Conflicts of Interest: None declared.

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