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ORIGINAL ARTICLE

Efficacy of Secukinumab in Moderate to Severe Psoriasis Vulgaris: A Prospective Study

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ABSTRACT

Objective: Psoriasis is a chronic inflammatory skin disorder that potentially needs long-term treatment. Multiple remedies treating psoriasis have been accepted in which Secukinumab is a totally humanized, IL-17A monoclonal used for the treatment of moderate to severe plaque psoriasis. Hence, this study focused to evaluate the effectiveness of Secukinumab in moderate to severely affected psoriasis patients.

Methodology: This was a Prospective interventional multicenter study conducted by using consecutive sampling technique. The ethical approval was approved from the Institutional Review Board. The duration of study was about one year after synopsis approval. A total of 138 adult patients between 18-65 years of both genders with diagnosed cases of psoriasis vulgaris having lesions on scalp, face, hands, and genital areas were included. Treatment started by the single dosage of 300 mg Secukinumab that was administered subcutaneously once weekly for 4 weeks and followed up by once a month for 52 weeks. Paired t-test was used to evaluate the association between baseline and at various weeks of follow ups.

Results: The study results showed that out of 138 patients, 112(81.2%) were males and 26(18.8%) were females and their mean age was 40.47±9.55 years. As far as severity of Psoriasis is concerned, 55(39.9%) were moderately affected while 83(60.1%) were severely affected. Concerning distribution of Psoriasis, Plaque Psoriasis was observed in 117(84.8%) patients, 57(41.3%) reported Scalp Psoriasis, 137(99.3%) reported Pustular psoriasis, and Itching was reported in 120(87.0%) patients. Comparison of baseline PASI scores with different weeks in moderately and severely affected psoriasis patients revealed that there was statistically significant rapid reduction observed from mean of baseline PASI scores till 12 weeks ($p<0.001$),

Conclusion: This study concluded that Secukinumab is an extremely effectual, rapid-acting biological therapy with no evident side effects. Furthermore, it was observed that secukinumab significantly reduced the baseline PASI score till 12 week rapidly in moderately and severely affected psoriasis patients.

Keywords: Psoriasis vulgaris, PASI score, rapid-acting biological therapy, Secukinumab,

INTRODUCTION

Psoriasis is a common long-term inflammatory disorder of skin that manifests as erythematous plaques enclosed by silver scales predominantly involving the skin over the knees and elbows, lumbosacral region and scalp.[1]There is prediction that almost five percent of the total population of world is affected by Psoriasis.[2] In 2014, World Health Organization recognized psoriasis as a severe non-communicable disease,[3] and in 2016, the concomitant WHO report highlighted the morbidity caused by the disease Internationally.[3] Earlier studies specifically projected the incidence of psoriasis in adults ranged between 0.27% [4] and 11.4%,[5] with sexual characteristics, age, geographical site, ethnicity, genetic and environmental factors contributing to the variances in the disease prevalence.[6] It has been also stated that greater occurrence rates were witnessed at higher latitude in addition to white population than other ethnic groups.[7]

Prevalence rate of Psoriasis is ranging from 0.2% to 4.8%. [8]The particular cause of disease is unidentified, but there is HLA antigens association found in many psoriatic patients. Besides genetic predisposition, injury by chemical, mechanical, and radiation encourages psoriatic lesions. Additionally, some drugs such as lithium, chloroquine, steroids, beta-blockers, and NSAIDs can aggravate psoriasis. Usually, summer season recovers psoriasis whereas winter season exaggerates it. Besides these factors, other provoking factors for psoriasis are psychological stress, infections, alcohol intake, smoking, obesity, and hypocalcemia.[9]

The pathophysiology of psoriasis is identified by the penetration of skin by stimulated T cells that encourages multiplication of keratinocytes, results a development of dense plaques. Moreover, further related features are epidermal hyperplasia and Para-keratosis. In addition, the epidermal cells unable to release lipid causing scaly and crusty skin that is a classical sign of psoriasis.[10]

Generally, clinical morphology and lesions site is used to make diagnosis. Histopathology is infrequently required but can assist to distinguish psoriasis from other skin disorders, in case of doubtful diagnosis.[11]The most widely applied assessment tool is Psoriasis Area Severity Index (PASI) that evaluates the severity of this disorder and supports the assessment of treatment effectiveness. The basis of this index is a dichotomous categorization including mild and moderate-severe states of disease. [12]. On the basis of this index, patients who have Psoriasis Area Severity Index (PASI), body surface area (BSA), and Dermatology Life Quality Index (DLQI) values of<10 are characterized as mild psoriasis. Similarly, patients who have values >10 among any of these scales will be labelled as moderate to severe psoriasis. [13,14].

Llamas-Velasco et al. published a suggestion in 2017, for describing moderate psoriasis on behalf of judgment of six proficient dermatologists belonging to the psoriasis group of the Spanish Academy of Dermatology and Venereology (AEDV). In this suggestion, the classifications of mild, moderate, and severe were demarcated according to PASI and DLQI. The above-mentioned disease classifications were described as:(a) PASI < 7 and DLQI < 5 being considered to be mild psoriasis; (b) PASI < 7 and DLQI ≥ 5 being marked as moderate psoriasis; (c) PASI > 15 with any DLQI value to be identified as severe psoriasis. [15]

As far as treatment is concerned, topical therapy, phototherapy, biologic and non-biologic systemic medicines are used to cure moderate-to-severe psoriasis [16]. Among such existing treatments, phototherapy and biologic agents are most generally used for treating moderate to severe psoriasis [16]. Though multiple factors are involved in the pathogenesis of plaque psoriasis, the interleukin-23/T helper 17 pathway is understood to have a fundamental role in the disease process[17]. In this pathway, overexpression of thisinterleukin-17A (IL-17A) leads to hyperplasia and creates an excessively strong inflammatory reaction in epidermis, resulting to form skin plaques and to cause systemic infection which is a distinctive sign of this disease. Noteworthy, biologic systemic agents like the ones that target IL-17 have been established to be effectual in treating moderate-to-severe plaque psoriasis. Especially, there is cumulative proof that reveals that biologic agents show a remarkable advantage in improving quality of life. [18].

Secukinumab is a totally human IgG1κ anti-IL-17A monoclonal antibody which focuses IL-17A [19]. Secukinumab selectively binds to IL-17A, impeding communication between IL-

17A and IL-17 receptors on endothelial cells, keratinocytes, chondrocytes and osteoblasts resulting a blockage of downstream inflammatory trails that is essential in plaque psoriasis and also other autoimmune inflammatory diseases [20,21]. FDA approved Secukinumab as the first in its class for treating moderate to severe plaque psoriasis and is beneficial for management of active psoriatic arthritis and ankylosing spondylitis too. Several clinical trials supported that secukinumab has superior effectiveness in plaque psoriasis as compared to other biologic medicine that are commonly used for instance ustekinumab and detanercept [22].

A lot of researches have recommended the administration of Secukinumab in management of psoriasis. But in Pakistan where moderate to severe psoriasis is highly prevalent, there is insufficient researches available. Therefore, it was imperative to assess the efficacy and safety profile of Secukinumab in those patients who are affected with moderate and severe psoriasis vulgaris.

MATERIAL AND METHODS

This is a prospective interventional multicenter study piloted by using consecutive sampling technique. The ethical approval was approved from the Institutional Review Board. Duration of study was about one year after synopsis approval. The sample size was calculated by open epi software keeping 50% proportion of patients reporting to opds with psoriasis. A total of 138 adult patients between 18-65 years of both genders with diagnosed cases of psoriasis vulgaris having lesions on scalp, face, hands, or genital areas, and patients who were resistant to other treatment options and who were treated only with Secukinumab for the duration of at least 4 weeks, those patients with PASI >10.0 at baseline were included in the study while those in which the drug is contra-indicated or intolerant to conventional treatment, or associated systemic therapy such as acitretin or cyclosporine, methotrexate on phototherapy (Ultraviolet B or psoralen plus ultraviolet A) and who were not interested to participate in this study were excluded.

Basic demographic characteristics of patients such as age, sex, weight, height, BMI, age at commencement of disease, duration of psoriasis, affected parts by psoriasis and Severity Index (PASI) at baseline and effects of biological management were noted. The basis of this index is a dichotomous categorization including mild and moderate-severe states of disease. [12]. On the basis of this index, patients who have Psoriasis Area Severity Index (PASI), body surface area (BSA), and Dermatology Life Quality Index (DLQI) values of<10 are characterized as mild psoriasis. Similarly, patients who have values >10 among any of these scales will be labelled as moderate to severe psoriasis. Treatment initiated by the single dosage of 300 mg Secukinumab that was administered subcutaneously once a week for 4 weeks. This was followed up by once a month for 52 weeks. Outcome measures of treatment were documented clinically as PASI scores both for moderate and severe psoriasis. Patients were followed up for 52 weeks.

Data was analyzed by using SPSS version 23.0. Quantitative variables were documented as mean and standard deviation. Qualitative variables were documented as frequencies and percentages. Paired t-test was used to evaluate association between baseline and at various weeks of follow ups. P-value of <0.05 was taken to be statistically significant.

RESULTS

Total 138 patients diagnosed with moderate and severe Psoriasis vulgaris were registered for the study wherein their mean age was 40.47±9.55 years. Mean age at onset of disease was 32.41±10.54 years. Mean duration of Psoriasis was 7.95±4.85 years. Mean baseline PASI scores was reported 54.20±13.49, as shown in Table I.

Out of 138 patients, 112(81.2%) were males and 26(18.8%) were females. 30(21.7%) patients were smokers. As far as severity of Psoriasis is concerned, 55(39.9%) were moderately affected while 83(60.1%) were severely affected. Only 6(4.3%) patients showed history of Cardiovascular Disease, 19(13.8%) patients were Diabetics and 32(23.2%) patients were hypertensive, as shown in Table II.

Concerning distribution of Psoriasis, Plaque Psoriasis was observed in 117(84.8%) patients, 57(41.3%) reported Scalp Psoriasis, Itching was reported in 120(87.0%) patients, Nail Psoriasis was observed in 9(6.5%) patients, Palmoplantar Psoriasis reported in 11(8.0%) cases, 1(0.7%) reported Pustular psoriasis, and 5(3.6%) patients reported Erythrodermic psoriasis, as shown in Table III.

Comparison of baseline PASI scores with different weeks in moderately affected psoriasis patients revealed that there was statistically significant rapid reduction observed from mean of baseline PASI scores till 12 weeks (p<0.001), as shown in Table IV.

Table 1: Demographic characteristics of Psoriasis patients (n=138)

Variable	Mean±SD n(%)
Age (years)	40.47±9.55
Duration of Psoriasis (years)	7.95±4.85
Age at Onset of disease (years)	32.41±10.54
Baseline (Psoriasis Area and Severity Index scores)	54.20±13.49

Table 2: Frequency of Gender, severity and History of comorbidities.

Variable			n	(%)
Gender		Male	112	81.2
		Female	26	18.8
Smoking		Yes	30	21.7
		No	108	78.3
Specify Severity		Moderate	55	39.9
		Severe	83	60.1
Co-morbids	Diabetes Mellitus	Yes	19	13.8
		No	119	86.2
	Hypertension	Yes	32	23.2
		No	106	76.8
	Cardiovascular Disease	Yes	6	4.3
		No	132	95.7

Table 3: Frequency of distribution of involved areas in psoriasis.

Variable		n	(%)
Itching	Yes	120	87.0
	No	18	13.0
Joint Involvement	Yes	1	0.7
	No	137	99.3
Plaque Psoriasis	Yes	117	84.8
	No	21	15.2
Scalp Psoriasis	Yes	57	41.3
	No	81	58.7
Nail Psoriasis	Yes	9	6.5
	No	129	93.5
Palmoplantar Psoriasis	Yes	11	8.0
	No	127	92.0
Erythrodermic psoriasis	Yes	5	3.6
	No	133	96.4
Pustular psoriasis	Yes	1	0.7
	No	137	99.3
Psoriatic Arthritis	Yes	1	0.7
	No	137	99.3

Table 4: Association of comparison of baseline PASI scores with different weeks in moderately affected psoriasis patients

Variable	Mean±S.DvsMean±S.D	p-value
Baseline vs Weeks4	43.10±11.27vs3.90±9.68	<0.001
Baseline vsWeeks12	43.10±11.27vs0.18±1.34	<0.001
Baseline vsWeeks 24	43.10±11.27vs0.0±0.0	<0.001
Baseline vsWeeks36	43.10±11.27vs0.0±0.0	<0.001
Baseline vsWeeks52	43.10±11.27vs0.0±0.0	<0.001

Comparison of baseline PASI scores with different weeks in severely affected psoriasis patients revealed that there was statistically significant rapid reduction observed from mean of

baseline PASI scores till 4,12, 24 and 36 weeks (p<0.001),as shown in Table V.

Table 5: Association of comparison of baseline PASI scores with different weeks in severely affected psoriasis patients

Variable	Mean±S.DvsMean±S.D	p-value
Baseline vs Weeks4	61.55±9.13vs4.77±5.34	<0.001
Baseline vs Weeks12	61.55±9.13vs0.36±2.44	<0.001
Baseline vs Weeks 24	61.55±9.13vs0.31±2.28	<0.001
Baseline vs Weeks36	61.55±9.13vs0.07±0.65	<0.001
Baseline vs Weeks52	61.55±9.13vs0.0±0.0	<0.001

DISCUSSION

Long-term treatment with biological agents is required in most of the cases of moderate-to-severely affected psoriasis patients to control their disease. The present study exhibited the effectiveness and safety of subcutaneously administered drug Secukinumab to treat moderate to severely affected psoriasis patients.

One research demonstrated that prior to start secukinumab treatment, most of the patients had one-third of their bodies covered with psoriatic lesions and their average PASI score was 23.5. Their quality of life was also very affected. In spite of disease severity, administration of secukinumab successfully and congruously controlled the psoriasis for five years. Averagely, degree and disease severity were enhanced by almost 90% through 5 years.[23] Another recently recommended treatment objectives regarding psoriasis suggested by the National Psoriasis Foundation (BSA ≤1) demonstrated that up to three-quarters of patients also attained better response,[24] Also a Canadian expert task-force also achieved improved response (PASI ≤3).[25] The present study was inconsistent with the above reported research and revealed that PASI score was significantly reduced (p<0.001) in moderately affected patients just in 24 weeks similarly severely affected psoriasis patients PASI score improved significantly by 36 weeks.

Worldwide, a lot of accompanied comorbidities with psoriasis have been described. In some research, Diabetes, hypertension, psychological disorder of variable degree and low frequency of cardiovascular diseases have been associated with psoriasis.[26]. The present study was corroborated with above cited research and indicated that 19(13.8%) psoriasis patients were Diabetics and 32(23.2%) patients were hypertensive thereby proving the accompanied comorbidities with psoriasis

However, the rapid-acting IL-17 inhibitor, brodalumab, has a disturbing outcome like depression. Although, the causative factor to develop depression with usage of brodalumab is ambiguous[27]. Alternatively, Secukinumab doesnot causes depression and suicidal ideation. Therefore, patients are frequently agreed to start secukinumab treatment, rather than brodalumab or TNF-α inhibitors [28]. Our study was in agreement with the above researches revealing no undesirable effects of secukinumab therapy were observed thereby showed its superior clinical efficiency and value over the other biological therapies.

Similarly, one research revealed that Secukinumab proved rapid, powerful, and persistent recovery from disease with a superior and comparable safety profile for moderate to severe psoriasis regardless of racial and ethical differences. It was also proved that the superior efficacy profiles of secukinumab was achieved in week 52 [29].These results were similar to the previous researches from the overall populations[30,31].As far as the present study is concerned, efficacy profiles of secukinumab was very high proving that moderately affected patients were significantly reduced PASI score within 24 week while severely affected patients reduced their PASI score within 36 week.

Concerning distribution of involved area, one research conducted in Jinnah hospital Lahore reported that35% patients showed joint involvement.[32] Moreover, an Iranian study examined 150 patients wherein 73% cases reported joint involvement.[33]The present study was not supported the above cited studies as there was only 1(0.7%) psoriatic patient involved joints.

Likewise, one more research revealed that 29% psoriasis patients reported nail involvement.[26] Similarly, additional small sample sized study reported occurrence rate of nail involvement was 54%.[33]Our study showed inconsistency with the above reported researches and revealed that Nail Psoriasis was observed only in 9(6.5%) patients.

The larger sample size of the study has confirmed that we have treated broad range of psoriatic patients. Though, the study might not be exempted from selection bias owing to non-probability sampling technique. More researches with probability sampling technique are suggested to simplify the outcomes.

CONCLUSION

Our Study predicted that Secukinumab is highly effective with outstanding skin clearance. Thus it offers the potential for equal or better therapeutic effects in contrast to other biologics and is an important addition to our current antipsoriatic therapies. Moreover, the baseline PASI score till 8 week was significantly reduced after the therapy and sustained clearance was achieved till 52 weeks

Ethics approval and consent to participate: The ethical approval was approved from the Institutional Review Board of Hamdard University

Conflict of Interest and Funding: There was no any conflict of interest.

Authors' contributions

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