

**EFFICACY OF AND SAFETY OF SECUKINUMAB IN PSORIASIS
VULGARIS; A PROSPECTIVE STUDY**

ABSTRACT

Objective: Psoriasis is an immune mediated inflammatory skin disorder that potentially requires lifelong management. Different therapies treating psoriasis have been recognized wherein Secukinumab is a fully humanized, IL-17A monoclonal antibody that has been approved by US Food and Drug administration for the treatment of moderate to severe plaque psoriasis. Therefore, this study targeted to assess the efficacy of Secukinumab in patients with moderate to severe psoriasis.

Methodology: This was a Prospective interventional multicenter study conducted by using consecutive sampling technique. The duration of study was about one year. The sample size was 138. Adult patients between 18-65 years of either gender with clinical diagnosis of psoriasis vulgaris involving scalp, face, hands, or genital areas, were include. Treatment initiated by the administration of a single dose of 300 mg Secukinumab subcutaneously for 4 weeks then monthly for 52 weeks. Paired t-test was applied to assess the difference in the PASI score at various 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 distribution of disease is concerned, 117(84.8%) patients reported Plaque Psoriasis, 57(41.3%) patients reported Scalp Psoriasis, 9(6.5%) patients reported nail Psoriasis, 11(8.0%) patients reported Palmoplantar Psoriasis, and 5(3.6%) patients reported Erythrodermic psoriasis. For the comparison of Secukinumab treatment under PASI scores, there was statistically significant reduction observed from mean of baseline PASI scores till 1 week ($p < 0.001$), till 2 week ($p < 0.001$), till 4 week ($p < 0.001$), till 8 week ($p < 0.001$). The improvement in mean PASI score from baseline to 1 year was 91 %.

Conclusion: This study concluded that Secukinumab is a highly effective, rapid-acting biological therapy with no obvious adverse effects. Additionally, it was seen that secukinumab significantly reduced the baseline PASI score till 8 week rapidly in moderate and severe psoriasis.

Keywords: Psoriasis vulgaris, PASI score, Secukinumab,

INTRODUCTION

Psoriasis is a chronic, immune mediated inflammatory skin disease with approximately 120-180 million people who are affected worldwide and its occurrence is predicted between 2%-11.8%.[1,2] World Health Organization documented psoriasis as a serious non-transmissible disease in 2014 and the associated WHO report in 2016 put emphasized on better realization of the morbidity related to the disease, globally.[3]

Previous research particularly estimated the occurrence of psoriasis in adults range between 0.27% [4] and 11.4%, [5] with gender, age, geographical location, ethnicity, environmental and genetic factors participating to the differences in the occurrence of the disease.[6] It has been reported that higher occurrence rates were observed at elevated latitude as well as in white population as compared to other racial groups.[7] The Global Burden of Disease group has predicted the occurrence of psoriasis for 21 regions worldwide. [8]

It is characterized by the erythematous, scaly plaques most commonly found on the scalp, elbows, knees, and back. [9] It is now regarded as a systemic disease which is related with metabolic, psychological, arthritic, and cardiovascular comorbidities..[10] Mostly, Psoriasis can arise at any age but frequently it is more prevalent under 35 years of age. [11]

Psoriasis usually affects the skin but joints may also be affected. Inflammation is not only limited to the psoriatic skin but also involve the other organ systems. Psoriasis patients show evidence of hyperlipidemia, hypertension, type 2 diabetes, coronary artery disease, and raised body mass index in comparison with the healthy subjects, [12] these metabolic disturbances were two folds more prevalent in psoriasis patients than healthy individuals [13].

Presently, the impact of psoriasis on psychosomatic and mental wellbeing is an imperative concern due to the influence of the disease on social health and management. Psoriasis patients have an elevated incidence of depression, anxiety and low self esteem. Amazingly, psoriasis management diminishes anxiety symptoms [14]

Generally, Psoriatic patients are divided into two groups: mild or moderate to severe psoriasis, based on the clinical severity of the inflammatory lesion, the proportion of affected area, and life expectancy [15].

Psoriasis is a multifaceted syndrome for which a variety of innovative treatment modalities have discovered in the earlier years. Despite of the discovery of novel therapies, psoriasis remains a treatable but still not curable disorder. According to mode of action, remedies treating psoriasis can be grouped into five classes: anti-interleukin-12/23 agents (anti-IL12/23), anti-interleukin-17 agents (anti-IL17), anti-metabolites (AM), anti-T-cell agent (ANT), and anti-tumor necrosis factor- α agent (anti-TNF- α).[16]

Until now, three human monoclonal antibodies targeting IL-17 are accessible. Secukinumab and ixekizumab selectively targets IL-17A causing inhibition of IL-17 receptor's contact with endothelial cells, keratinocytes, osteoblasts and chondrocytes [17]. On the other hand, brodalumab is aimed in opposition to the IL-17 receptor A. Secukinumab was approved for psoriasis in 2015 as the first IL-17A inhibitor. Later on, it was also approved for the active psoriasis arthritic and ankylosing spondylitis [18]. Secukinumab's efficacy in psoriasis vulgaris has been proved to be superior to other numerous biological agents like etanercept and ustekinumab [19].

A combination of glucocorticoids with vitamin D analogues topically along with phototherapy is used to treat mild to moderate psoriasis whereas systemic treatment frequently requires for moderate to severe type of psoriasis.[16] Biological factors targeting IL-17A have revealed higher effectiveness in treating moderate to severe psoriasis. Additionally, it has been reported that anti IL-17A agents has fast mode of action.[20]

The targeted therapies demonstrated high clinical efficiency for the inhibition of IL-23 and IL-17. Some extent of a persistent antipsoriatic effect by these therapies could be established following discontinuation of drug [21,22].

Common undesirable effects due to IL-17 receptor inhibition are nasopharyngitis, headache, arthralgia, and upper respiratory tract infection. Moreover, IL-17 signaling is critical for the

acute defense in opposition to extracellular bacterial and fungal infections. Candidal infections are generally more reported in patients treating by anti-IL17 biological agents such as Secukinumab and ixekizumab than etanercept [18].

A number of researches have documented the recommendation of Secukinumab in treatment of psoriasis, but not any of the researches have been conducted in Pakistan, a South Asian country where the prevalence of moderate to severe psoriasis is highly observed. Therefore, it was imperative to assess the effectiveness and safety of Secukinumab in patients of psoriasis vulgaris.

MATERIAL AND METHODS

This was a Prospective interventional multicenter study conducted by using consecutive sampling technique. The duration of study was about one year after ethical approval of synopsis from the Institutional Review Board. The sample size was 138. Adult patients between 18-65 years of either gender with diagnosed cases of psoriasis vulgaris having psoriatic lesion involving scalp, face, hands, or genital areas, who were unresponsive to other treatments and those patients who were treated only with Secukinumab for minimum four weeks, patients having PASI >10.0 at baseline were included in the study whereas those who were contraindicated or intolerable to conventional treatment, on concomitant systemic therapy like methotrexate, acitretin or cyclosporine, on phototherapy (Ultraviolet B or psoralen plus ultraviolet A) and who did not give consent were excluded.

Baseline demographics of patients for instance age, sex, height; weight, BMI, age at beginning of disease, duration of psoriasis, affected areas by psoriasis and Severity Index (PASI) at baseline and outcome of biological treatment were documented. Treatment initiated by the administration of a single dose of 300 mg Secukinumab subcutaneously once weekly for 4 weeks and followed up by once a month for 52 weeks. Outcome measures of treatment were recorded clinically as PASI scores, with adverse effects both for moderate and severe psoriasis. Patients were followed up for 52 weeks. Data was analyzed using SPSS version 23.0. For quantitative variables mean and standard deviation were documented. Qualitative variables were recorded as frequency and percentages. Paired t-test was applied to assess the association between baseline and at various follow ups. P-value of <0.05 was considered as statistically significant.

RESULTS

A total of 138 patients diagnosed with Psoriasis vulgaris were enrolled for the study wherein 112(81.2%) were males and 26(18.8%) were females; their mean age was 40.47 ± 9.55 years. Mean duration of Psoriasis was 7.95 ± 4.85 years. Mean age at onset of disease was 32.41 ± 10.54 years. Mean baseline PASI scores was reported 54.20 ± 13.49 , 4.42 ± 7.36 at 4 weeks, 0.28 ± 2.07 at 12 weeks, 0.18 ± 1.77 at 24 weeks, 0.04 ± 0.51 at 36 weeks, and 0.0 ± 0.0 at 52 weeks, as shown in Table I.

Only 6(4.3%) patients showed history of Cardiovascular Disease, 19(13.8%) patients showed history of Diabetes mellitus. 32(23.2%) patients showed history of hypertension, 30(21.7%) patients were smokers. as shown in Table II.

As far as distribution of disease is concerned, 117(84.8%) patients reported Plaque Psoriasis, 57(41.3%) reported Scalp Psoriasis, 9(6.5%) reported nail Psoriasis, 11(8.0%) reported Palmoplantar Psoriasis, and 5(3.6%) reported Erythrodermic psoriasis while 137(99.3%) reported Pustular psoriasis. (Table III)

There was statistically significant reduction observed from mean of baseline PASI scores till 1 week ($p < 0.001$), till 2 week ($p < 0.001$), till 4 week ($p < 0.001$), and till 8 week ($p < 0.001$), as shown in Table IV. Additionally, no significant side effects were observed.

Table I: 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
At 4 weeks	4.42±7.36
At 12 weeks	0.28±2.07
At 24 weeks	0.18±1.77
At 36 weeks	0.04±0.51
At 52 weeks	0.0±0.0

Table II: Frequency of Gender and History

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-morbrids	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 III: Frequency of areas of involvement 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	137	99.3
	No	1	0.7
Psoriatic Arthritis	Yes	1	0.7
	No	137	99.3

Table IV: Association of comparison of baseline PASI scores with different weeks in psoriasis patients.

Variable	Mean±SD vs Mean±SD	p-value
Baseline vs At 4 weeks	54.20±13.49vs4.42±7.36	<0.001
Baseline vs At 12 week	54.20±13.49vs 0.28±2.07	<0.001
Baseline vs At 24 weeks	54.20±13.49vs0.18±1.77	<0.001
Baseline vs At 36 weeks	54.20±13.49vs0.04±0.51	<0.001
Baseline vs At 52 weeks	54.20±13.49vs0.0±0.0	<0.001

DISCUSSION

The present study demonstrated that Secukinumab treatment led to rapid and sustained improvement in PASI scores with 90% response rate. The safety profile of Secukinumab remained favorable through 1 year with no adverse event.

A Prospective, cross-sectional study conducted in Lahore analyzed the study wherein sample size involved 56 males (64.4%) and 31 females (35.6%) thereby proved the male predilection in their study. [23] These findings were similar with our study and showed that 112(81.2%) were males and 26(18.8%) were females thereby proved male predominance.

Similarly, another research reported gender distribution of Psoriasis patients that was 71% males and 29% females.[24] Further researches conducted in Pakistan have revealed unpredictable statistics. One research from Jinnah Hospital, Lahore has reported 42% females and 58% males.[25] One more study from Liaquat University of Medical and Health Sciences has

revealed 56% males and 44% females.[26]As far as our study is concerned, male predominance was obvious and showed that 112(81.2%) were males and 26(18.8%) were females.

Likewise, one study reported the mean age of affected patients was 39.8 years.[24] Further analysis based on Pakistani population have shown similar findings.[26,27] Another current research conducted in Korea has also revealed analogous findings.[28]In Iran Research, the reported mean age was 33.3 years at onset of disease.[29] Our study was inconsistent with the above mentioned researches and observed the mean age of affected Psoriasis patient was 40.47 ± 9.55 years.

Concerning area of involvement, one more study observed 46% patients involved joints whereas another study from Jinnah hospital Lahore proved joint involvement was observed in 35% patients.[30] On the other hand, an Iranian study included 150 patients that reported joint involvement in 73% cases.[27]The present study was not in agreement with the above cited studies as there was only 1(0.7%) patient involved joints.

Similarly, one research found involvement of nail in 29% psoriasis patients.[24] Likewise, another small sample size study based completely on nail involvement has reported a rate of occurrence of 54%.[27]Our study was not supported the above studies and showed that Nail Psoriasis was found only in 9(6.5%) patients. Our data was conflicted with above researches as it was smaller sample size study.

Globally, a number of associated comorbidities with psoriasis have been reported. Hypertension, Diabetes, psychological disorder of varying degree and cardiovascular diseases have been related with psoriasis although in low frequency as shown in some study.[24]. As far as our study is concerned, 19(13.8%) psoriasis patients showed history of Diabetes mellitus along with 32(23.2%) patients showed history of hypertension.

Interestingly, one of the studies conducted in Japan analyzed the efficacy of secukinumab in psoriasis vulgaris and psoriatic arthritis using Psoriasis Area and Severity Index score (PASI). It was observed that mean PASI score was enhanced from baseline (14.7 ± 12.3) to week 12 (1.78 ± 3.3), which was sustained till week 24 (1.59 ± 3.0). [31] As far as our study is concerned, it was found that mean PASI score was significantly improved from baseline (54.20 ± 13.49) to week 8 (1.20 ± 5.77) and sustained till 52 weeks.

Furthermore, above mentioned research demonstrated the Absolute PASI score and proposed that absolute PASI score of less than or equal to 3 [32,33] and less than or equal to 2 [34] shows

success of treatment by secukinumab, regardless of baseline PASI score. In our study, it was reported that reduction in PASI score from baseline to week 8 in moderate and severe psoriasis patients indicated the successful treatment by the administration of secukinumab.

A lot of biological agents are accessible for management of plaque psoriasis, but these remedies differ in effectiveness and safety profile. Generally, IL-23 and IL-17 inhibitors reveal superior effectiveness as compared to TNF- α inhibitors, whereas further analysis on the mode of action of biologic agents revealed that IL-17 A inhibitors work rapidly as compared to TNF- α inhibitors and ustekinumab.[35] Importantly, secukinumab caused PASI 75 rapid response in 25% of cases in duration of 3 weeks, therefore proving accomplishment of 50% reduction in PASI score in 3.0 weeks.[36] Our study was consistent with the above study and showed that quick reduction in PASI score was achieved from baseline 54.20 ± 13.49 to week 8 1.20 ± 5.77 under treatment of secukinumab in psoriasis patients whereas our study did not compare the secukinumab with other IL-17 inhibitors.

Though, the most fast-acting IL-17 inhibitor, brodalumab, has a distressing effect such as depression. Even though the definite factor for depression with use of brodalumab is vague,[37] On the other hand, Secukinumab has no alarming sign for depression and suicidal tendency. Hence, patients are occasionally more willing to initiate secukinumab treatment, instead of brodalumab or TNF- α inhibitors.[36] Our study demonstrated that there was no reported adverse effects of secukinumab therapy thereby proved its superior clinical efficacy and effectiveness over the other biological therapies.

About 40% of psoriasis patients might grow psoriatic arthritis in their lifespan. Therefore, it is imperative to treat symptoms related to joints along with skin to prevent irreparable joint destruction. Hence, Secukinumab is one of six biological agents (that includes etanercept, adalimumab, infliximab, ustekinumab, and ixekizumab) recently accepted for the management of psoriatic arthritis along with psoriasis vulgaris,. Secukinumab gives superior effectiveness following 52 weeks of treatment, but this biological agent might impede radiographic joint injury in psoriatic arthritis patients till 2 years.[38] Consequently, secukinumab presents an enduring treatment alternate for psoriatic arthritis patients that not only slow the damage to the joints but also prevents further damaging as well. Our study was inconsistent with the above cited studies and reported that there was only 1(0.7%) patient showed the joint involvement thereby our study comprehensively focused the skin symptoms associated with psoriasis.

The large sample size of the study has assured that we have treated extensive range of psoriatic patients. However the study might not be immune from selection bias due to non probability sampling technique. Further studies with probability sampling technique are recommended to generalize the results

CONCLUSION

This study concluded that Secukinumab has superior efficacy with excellent skin clearance. Thus it offers the potential for equal or improved therapeutic effects as compared to other biologics and is a valuable addition to our current antipsoriatic armamentarium. Additionally, it was seen that secukinumab significantly reduced the baseline PASI score till 8 week rapidly and sustained clearance till 52 weeks.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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