Original Article

DOI: 10.7860/JCDR/2023/59172.17381

Dermatology Section

Interleukin-17 Inhibitor in Treatment of Psoriasis during COVID-19 Pandemic: An Ambispective Study

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ABSTRACT

Introduction: Psoriasis is a genetically mediated chronic inflammatory disease that is frequently associated with metabolic co-morbidities. These metabolic co-morbidities have a huge impact in deciding the appropriate immunosupressant of choice in the current scenario of Coronavirus Disease-2019 (COVID-19) pandemic. Treatment of psoriasis especially with biologicals is challenging during covid pandemic, since immunosuppressive therapy might interfere with antiviral immunity.

Aim: To report the safety profile of Interleukin-17 (IL-17) inhibitor, namely injection secukinumab in patients of psoriasis vulgaris during COVID-19 pandemic.

Materials and Methods: An ambispective interventional study was performed on 23 patients of psoriasis who were administered secukinumab at a dose of 300 mg subcutaneously during COVID-19 pandemic. The study was conducted at the Department of Dermatology, Madras Medical College, Chennai, Tamil Nadu, India, among the patients attending the psoriasis clinic between the July 2021 to March 2022. The demographic characteristics of the study group, previous treatment for psoriasis and the relationship between risk of COVID-19 infection and secukinumab were noted. Efficacy of secukinumab was calculated using Psoriasis Area and Severity Index (PASI) scores. Statistical analysis was conducted with Statistical Package for Social Sciences (SPSS) statistics software version 21.0 by Fischer's-exact test.

Results: Out of 23 patients, 17 patients (11 males, six females) completed full course of nine doses (five weekly doses followed by four monthly doses) of secukinumab. The PASI 75 and PASI 90 were achieved in 9 (52.94%) and 5 (29.41%) patients respectively at the end of 12 weeks. None of the patients developed COVID-19 infection during the course of treatment and three months following therapy. Patients with psoriasis who had a history of COVID-19 infection did not show signs of reinfection when started on secukinumab. Both inactivated vaccine (Covaxin) and vector based vaccine (Covishield) were found to be safe in concomitant use with secukinumab.

Conclusion: Secukinumab is found to be safe and effective in psoriasis treatment during COVID-19 pandemic. There is no increased risk of COVID-19 infection or reinfection, COVID-19 associated hospitalisation and mortality among patients with psoriasis administered with secukinumab. The drug can also be safely used with COVID-19 vaccines.

Keywords: Coronavirus disease-19, Psoriasis vulgaris, Psoriasis area and severity index scores, Secukinumab, Vaccine

INTRODUCTION

Psoriasis vulgaris is an inflammatory skin disease affecting 1-3% of the population [1]. It is caused by an inappropriate activation of T-cells and dendritic cells, leading to increase in inflammatory cytokines namely Tumour Necrosis Factor-α (TNF-α), Interleukin-17 (IL-17), Interleukin-23 (IL-23). Secukinumab which is an IL-17 inhibitor has emerged as a promising therapeutic option in chronic plaque psoriasis as well as psoriatic arthritis ensuring high efficacy, long-term maintenance of treatment response and quick onset of action [2].

Coronavirus disease-2019 (COVID-19) caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) virus is a contagious disease with variable presentations ranging from mild upper respiratory infection to severe pulmonary illness, including death. COVID-19 has been thought to worsen chronic inflammatory conditions like psoriasis due to hyperinflamation which is common in both the diseases. The immunological abnormalities seen in patients with COVID-19 are also observed in autoimmune conditions like psoriasis. Many studies have shown that the inflammatory cytokines found in psoriasis patients are similar to those involved in the cytokine storm that results in Acute Respiratory Distress Syndrome (ARDS) in COVID-19 patients [3]. While the efficacy of biologicals in psoriasis is indisputable, the susceptibility to infections due to these drugs has long been a cause of concern [4].

Since, immunosuppressive and immunomodulatory therapy might interfere with antiviral immunity [5], patients under biologicals, particularly those with severe co-morbidities, might be more vulnerable to worse outcomes of COVID-19. Conversely, it has been postulated that overactivation of the immune system and production of proinflammatory cytokines like IL-17 underlies the mechanism of lung injury caused by SARS-CoV-2. Substantially high serum levels of proinflammatory cytokines like IL-17, IL-6 and TNF-α occur in almost all patients with severe COVID-19 [6]. Thus, IL-17 blocking agents could be a safe and effective option in these situations.

Secukinumab, Ixekizumab and brodalumab are the three IL-17 blockers available for use. The former two agents are monoclonal Immunoglobulin G1 (IgG1) antibodies that bind specifically to IL-17A and brodalumab is monoclonal IgG2κ antibody against IL-17 receptor. There are a few preliminary reports on COVID-19 patients who were on secukinumab treatment for psoriasis and these patients had a favourable course [7,8]. The present study aimed to report the current status in terms of safety and efficacy in patients receiving secukinumab for moderate to severe psoriasis as well as the actual benefit and risk of IL-17 inhibitor treatment during COVID-19 pandemic.

MATERIALS AND METHODS

This study was an ambispective interventional study conducted in patients who were diagnosed with psoriasis vulgaris clinically and

treated with secukinumab in the Department of Dermatology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India. Patients who attended Psoriasis Clinic of Department of Dermatology between July 2021 to March 2022, were included in the study after obtaining informed consent in regional language (Tamil) and English. Study was submitted for Institutional Ethics Committee clearance (IEC No: 24122021).

Inclusion criteria:

- Patients of age above 18 years of both gender.
- Patients with moderate to severe plaque psoriasis (PASI score between 5-10 and PASI score >10, respectively) with or without joint involvement.
- Patients with resistant psoriatic plaques not responding to conventional immunosuppressants.
- Patients willing for regular follow-up and strict adherence of COVID-19 prevention protocols.

Exclusion criteria:

- Patients with previous history of allergic reactions to secukinumab.
- Patients who were under 18 years of age.
- Pregnant women with psoriasis.
- Patients who did not give consent for the study.

All the patients who fulfilled the inclusion and exclusion criteria and those who were willing to participate in the study were included. Since, all the cases were included no sampling was done.

Study Procedure

All the patients were thoroughly investigated and started on biologicals as per the International guidelines, for initiation and maintenance of biologicals during COVID-19 pandemic [9,10]. Selection of patients was executed after application of inclusion and exclusion criteria. Patients with psoriasis who were treated with injection secukinumab between the month of July 2021 to March 2022 were included in the study. Enrollment of patients for the study was done in December 2021. For patients who were already on treatment (six patients) with secukinumab before the month of December, the details were collected from the previously documented hospital records (case sheets). Since, the duration of treatment with one full course of secukinumab (five consecutive weeky doses and four consecutive monthly doses) is around six months, and all the patients were in regular follow-up except five (lost to follow-up), records of patients who were initiated the drug before the month of enrollment were obtained from the case sheets. These data procured in the retrospective limb of the ambispective study were critically analysed regarding the feasibility of further continuation or sustainment of injection secukinumab in the prospective limb. Data collected in prospective limb- decline in PASI following secukinumab, COVID-19 infection after secukinumab administration, reinfection in vaccinated individuals on secukinumab, if any.

Since, the data was collected in both retrospective and prospective manner, this study was an ambispective study. The duration of prospective limb was about four months and duration of retrospective limb was about five months. Total 23 (16 males and seven females) patients were included in the study of which five patients were lost to follow-up and therapy was stopped in one patient due to continuous high-grade fever. A 17 patients completed a full course of nine doses of secukinumab 300 mg subcutaneous dose (five weekly doses followed by four monthly doses).

For all the patients, detailed history related to the duration of psoriatic lesions, previous medications for psoriasis in the form of oral antimetabolites or biologicals, history of COVID-19 infection with treatment details, vaccination for COVID-19 infection and adverse events following vaccination if any and other co-morbid status were collected.

General examination with Body Mass Index (BMI), systemic examination, dermatological examinations including PASI at each visit were evaluated [11]. Clinical photographs were taken after obtaining informed consent. Relevant baseline investigations were done before starting the drug along with seeking for Cardiology, Hepatology and Thoracic Medicine clearance for administration of Inj. secukinumab. The drug was administered at a dose of 300 mg subcutaneously at 0, 1, 2, 3, 4 (five consecutive) weekly doses and four consecutive monthly maintenance doses.

After completion of maintenance doses (total of nine doses) the patients were followed-up for three months and PASI was assessed to calculate PASI 75 (referring to a 75% or greater reduction in PASI scores from baseline) and PASI 90 (referring to a 90% or greater reduction in PASI scores from baseline) at 12 weeks to evaluate the efficacy of secukinumab.

STATISTICAL ANALYSIS

The data related to patient's age, gender, PASI score, previous treatment, COVID-19 infection and COVID-19 vaccination status were entered in Microsoft excel sheets. Statistical analysis was conducted with Statistical Package for Social Sciences (SPSS) statistics software version 21.0 by Fischer's-exact test.

RESULTS

Total 23 patients were initiated for the treatment with secukinumab during the study period. The overall mean age was 35.06±9.1 years. Total males were 16 (69.6%) and total females were 7 (30.4%). Eight (35%) patients were smokers and 7 (30%) were alcoholics. About 9 (39%) patients suffered from psoriasis for more than eight years [Table/Fig-1]. Ten (43%) patients had co-morbidities with majority being diabetes (17%) and psoriatic arthritis (17%).

Descriptive characteristicts		Frequency	Percentage (%)
Age group (years)	18-24	3	13.04%
	25-34	8	34.78%
	35-44	8	34.78%
	45-54	4	17.39%
Gender	Male	16	69.6%
	Female	7	30.4%
Duration of lesion (years)	≤8 years	14	60.87%
	>8 years	9	39.13%
History of COVID-19 infection	Yes	4	17.39%
	No	19	82.61%
COVID-19 vaccination-Covishield/Covaxin	Yes	5	21.74%
	No	18	78.26%
History of smoking	Yes	8	34.78%
	No	15	65.22%
History of alcohol consumption	Yes	7	30.43%
	No	16	69.57%
Obese	Yes	2	8.69%
	No	21	91.30%
Loss to follow-up		5	21.74%

[Table/Fig-1]: Demographic characteristics of the study population (N=23).

History of COVID-19 infection before starting treatment was present in 4 (17%) patients. Three of them were treated with oral azithromycin 500 mg OD for five days and one patient was given injection dexamethasone 8 mg intravenous twice a day for five days. Five (22%) patients were administered with COVID-19 vaccine during the course of treatment of which 3 (13%) received Covishield and 2 (9%) received Covaxin. None of these patients reported adverse events following vaccination. Total 18 (78%) patients were neither vaccinated nor they had protective antibody to COVID-19 due to previous infection.

Nearly half of the patients, 12 (52%) had previous methotrexate therapy for psoriasis while tab. cyclosporine and tab. apremilast

were second most commonly used drugs 4 (17% each) and one patient was on infliximab (3%). General examination and systemic examination were normal in all the patients.

The mean PASI score at baseline was 16.2. There was statistically significant mean difference (p-value <0.05) between PASI at the beginning of treatment with subsequent doses [Table/Fig-2]. PASI 75 was seen in 9 (52.94%) cases and PASI 90 in 5 (29.41%) cases at the end of 12 weeks [Table/Fig-3]. Factors such as age, gender, duration of lesion, history COVID-19 infection, COVID-19 vaccination status, history of smoking and history of alcohol intake were not significant factors influencing PASI 75 or PASI 90 at 12 weeks [Table/Fig-4,5].

The percentage reduction in PASI was around 90% at the end of first month after treatment with 100% clearance of lesion in 10 (58.8%) patients [Table/Fig-6]. On follow-up for three months complete remission of lesions was noted in (52%) cases and relapse in (17%) cases and most common site being trunk. One patient had exacerbation of lesions over extensor aspect of legs during treatment with secukinumab and was started on tab. azathioprine 50 mg once daily for the same.

The [Table/Fig-7a,b,8a,b,9a,b] show complete remission of back lesions with resultant post inflammatory hyperpigmentation in three patients following five weekly doses of secukinumab 300 mg.

Paired samples test									
		Paired differences					t	df	Sig. (2-tailed)
					95% Confidence interval of the difference				
PASI		Mean	Std. Deviation	Std. Error mean	Lower	Upper			
Pair 1	5th dose	10.9824	10.4286	2.5293	5.6204	16.3443	4.342	16	0.001
Pair 2	6th dose	14.6118	11.0361	2.6767	8.9375	20.2860	5.459	16	<0.0001
Pair 3	7th dose	16.9882	11.5311	2.7967	11.0595	22.9170	6.074	16	<0.0001
Pair 4	8th dose	18.7353	11.3218	2.7459	12.9142	24.5564	6.823	16	<0.0001
Pair 5	9th dose	19.9882	11.3936	2.7634	14.1302	25.8463	7.233	16	<0.0001
Pair 6	First month after last dose	19.9647	12.2757	2.9773	13.6531	26.2763	6.706	16	<0.0001

[Table/Fig-2]: PASI scores at various stages of treatment.

Outcome variables at 12 weeks		Frequency	Percentage
>75% reduction in PASI	Yes	9	52.94%
	No	8	47.06%
>90% reduction in PASI	Yes	5	29.41%
	No	12	70.59%

[Table/Fig-3]: Percentage of study population who achieved PASI 75 and PASI 90 at 12 weeks.

Study variables		PASI-75		p-value
		Yes	No	
Age (years)	<35	3	6	0.109
	≥35	6	2	
Gender	F	1	4	0.111
	M	8	4	
Duration of lesion (years)	≤8	4	5	0.399
	>8	5	3	
History of COVID-19 infection	Yes	2	1	0.547
	No	7	7	
COVID-19 vaccination	yes	2	1	0.547
	No	7	7	
History of smoking	Yes	3	3	0.627
	No	6	5	
History of alcohol consumption	Yes	4	1	0.183
	No	5	7	

[Table/Fig-4]: Association between PASI 75 and demographic variables.

Study variables		PASI-90		p-value
		Yes	No	
Age (years)	<35	2	6	1
	≥35	3	6	
Gender	F	1	5	0.6
	M	4	7	
Duration of lesion (years)	≤8	4	7	0.600
	>8	1	5	
History of COVID-19 infection	Yes	1	6	0.3382
	No	4	6	
COVID-19 vaccination	yes	1	4	0.580
	No	4	5	
History of smoking	Yes	2	6	1
	No	3	6	
History of alcohol consumption	Yes	3	5	1
	No	2	7	

[Table/Fig-5]: Association between PASI 90 and demographic variables.

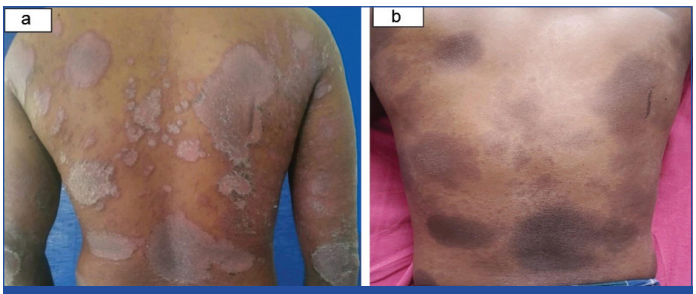
Further, the drug was extremely effective in treating cases with nail, scalp and joint involvement, which often fails to improve with conventional treatments. In this study, we found an excellent response in scalp lesions with complete resolution of psoriatic plaques after five weeks of secukinumab injections in one of the patients without any relapse [Table/Fig-10a,b]. Noteworthy, result was seen in the same patient with diffuse geographic lesions over the trunk clearing to leave behind residual postinflammatory hyperpigmentation [Table/Fig-11a,b].

DISCUSSION

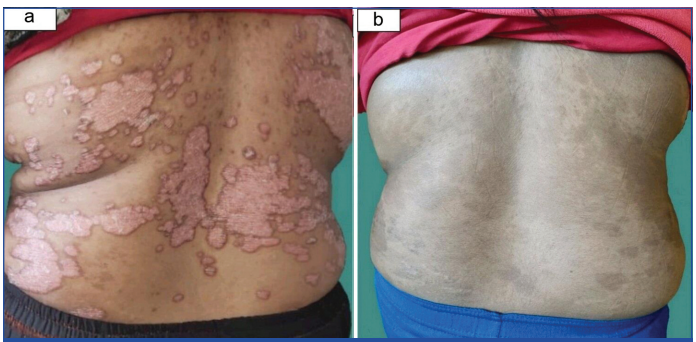
Psoriasis is cnow considered a systemic disease not merely confined to the skin alone. Metabolic syndrome is also being increasingly associated with it. It includes insulin resistance, systemic hypertension, dyslipidaemia, abdominal obesity all of which result in increased risk of cardiovascular morbidities. Both genetic predisposition and immune mediated mechanism underlie the pathogenesis of metabolic syndrome in psoriasis patients. Mediators of Th1 and Th17 pathway like TNF-α and IL-6 involved in psoriasis antagonize insulin signaling and cause abnormal adipokine expression resulting in insulin resistance and obesity. Hyperinsulinaemia, one of the components of metabolic syndrome, increases severity of inflammation in psoriatic plaques. Additionally genetic factors like PSORS4 CDKAL1 and APOE4 are common for both psoriasis and metabolic syndrome [10]. Risk of atherosclerosis is more in psoriasis patients due to endothelial dysfunction occurring in the background of chronic inflammation leading to cardiovascular co-morbidities [12]. All these co-morbidities can worsen the outcome of COVID-19 pneumonia. Since, these co-morbidities associated with activation of proinflammatory cytokine pathway like Th1 and Th17, administration of IL-17 inhibitor will have a positive outcome.

PASI scores at base line and percentage reduction during follow-up												
	4th week		8th week		12th week		16th week		20th week		24th week	
PASI at baseline	5th dose	% reduction	6th dose	% reduction	7th dose	% reduction	8th dose	% reduction	9th dose	% reduction	First month after last dose	% reduction
15	8.1	46	6	60	5.2	65.33	4	73.33	3.1	79.33	2.8	81.33
28.2	28.2	0	14	50.35	7.1	74.82	3.5	87.59	1	96.45	0	100
11.5	2.5	78.26	1.8	84.35	1	91.30	1	91.30	0.4	96.52	0	100
14.8	11.1	25	9.5	35.81	9	39.19	1	93.24	0	100	0	100
30	19	36.67	10	66.67	4	86.67	0.9	97	0.4	98.67	0	100
28	12.9	53.93	5	82.14	1.2	95.71	0	100	0	100	0	100
12.8	10	21.88	10	21.88	10	21.88	8.4	34.38	5	60.94	6.2	51.56
11.4	8.1	28.95	8.1	28.95	7.5	34.21	6	47.37	4	64.91	2.1	81.58
13.2	6.5	50.76	1	92.42	0	100	0	100	0	100	0	100
26.1	18.5	29.12	12	54.02	7.5	71.26	5.6	78.54	1.4	94.64	0.4	98.47
25.5	19.1	25.10	15	41.18	10.4	59.22	7	72.55	4	84.31	4	84.31
40	3.8	90.50	0	100	0	100	0	100	0	100	0	100
35.5	3.1	91.27	0.5	98.59	0	100	0	100	0	100	0	100
16.5	12	27.27	11.3	31.52	9	45.45	7.8	52.73	6	63.64	5.8	64.85
11	5.5	50	4	63.64	4	63.64	5.2	52.73	7.1	35.45	13.6	-23.64
39.6	15	62.12	11.6	70.71	7.1	82.07	5.4	86.36	2.1	94.70	0	100
15.2	4.2	72.37	6.1	59.87	2.5	83.55	0	100	0	100	0	100

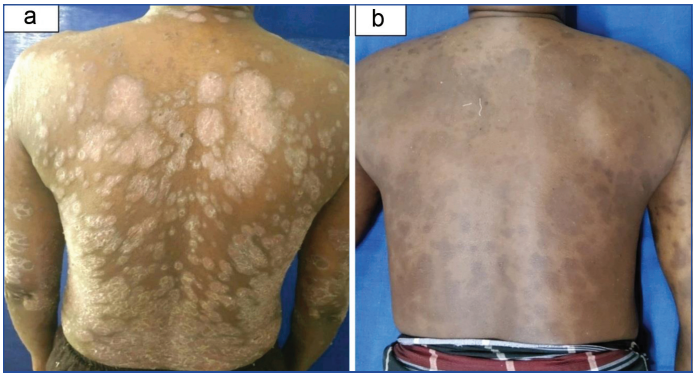
[Table/Fig-6]: PASI scores at baseline and percentage reduction during follow-up for each patient.



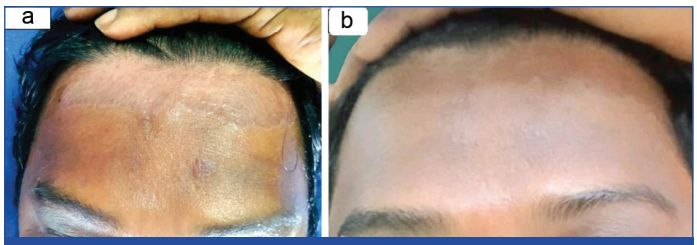
[Table/Fig-7]: a) Extensive erythematous scaly plaques at the back before the initiating secukinumab; b) Post inflammatory hyperpigmented patches in the same patient after completing 5 doses of secukinumab.



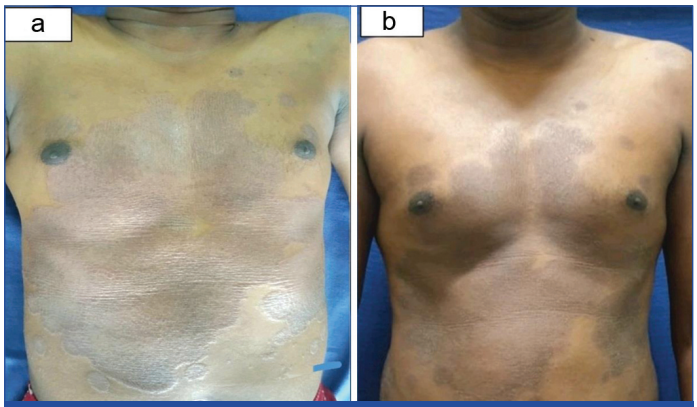
[Table/Fig-8]: a) Multiple indurated erythematous raised plaques at the back in a 21 years female before starting secukinumab; b) Resolution of psoriatic plaques with postinflammatory hyperpigmentation after initial four doses of secukinumab.



[Table/Fig-9]: a) Extensive well defined and coalescing plaques with severe scaling before secukinumab therapy; b) Complete clearance of plaques with residual pigmentation after secukinumab therapy.



[Table/Fig-10]: a) Corona psoriatica lesions before and b) After secukinumab therapy.



[Table/Fig-11]: a) Geographic plaques of psoriasis over trunk; b) Resolving plaques with minimal scaling and hyperpigmentation after treatment with secukinumab.

Various conventional therapeutic approaches are already in use for psoriasis. The invention of biologicals like TNF-alfa inhibitors (infliximab, adalimumab, etanercept), IL-17 inhibitors (secukinumab, ixekizumab, brodalumab) made the treatment of psoriasis revolutionary. Secukinumab (monoclonal antibody to IL-17A) is widely used in India for management of psoriasis and psoriatic arthritis [13]. Secukinumab was approved for use in psoriasis in 2015 in adults and in 2021 for children more than six years [14]. Efficacy is particularly notable in patients who do not respond to conventional treatments. We had several patients with previous treatment with methotrexate (50%), other biologicals like infliximab (3%) who did not show much response to these drugs. Since, IL-17 modulates the progression of secondary IgA nephropathy, use of secukinumab can protect against associated renal damage in chronic psoriasis patients. The drug has shown cardioprotective effects by increasing the Flow Mediated Dilation (FMD) which is a marker of endothelial function in

psoriasis patients thus reducing the risk of atherosclerosis [15]. It is also safe for use in latent Tuberculosis (TB) and does not seem to cause increased risk of TB reactivation [16].

Various trials suggested that, secukinumab is beneficial in patients with demyelinating disorders like multiple sclerosis by reducing the lesional activity in Magnetic Resonance Imaging (MRI) due to IL-17A blockage [17]. Since, it blocks IL-17A and selectively targets the key factor pathogenesis of psoriasis, it allows meeting the goals of psoriasis management without the need to augment treatment regimens with additional agents [18].

The superiority of IL-17 inhibitors is more pronounced in terms of the proportion of patients who achieve PASI 90 and PASI 100. This is significant because these efficacy endpoints are more substantial than PASI 75 from a patient's perspective, as demonstrated by a study finding that, patients who achieve PASI 90 and PASI 100 experience greater improvement in quality of life than PASI 75 responders [19]. In ERASURE (Efficacy of Response and Safety of Two Fixed Secukinumab Regimens in Psoriasis) study, 82% and 59% patients achieved PASI 75 and PASI 90 respectively after 12 weeks therapy with secukinumab 300 mg [2]. However, according to current study observations, around 52% and 29% cases only achieved PASI 75 and PASI 90 at the same time interval. PASI 100 was attained after one month of administering nine doses in 58.8% cases. But one sixth (17%) of the study group showed relapse within three months.

Besides considering the benefits of secukinumab, its side effects cannot be deflected on a long run. The role of IL-17 in host defense against pathogens raised concerns about the risk of infections under IL-17 Inhibitors (IL-17I). Overall, IL-17I and IL-17 receptor inhibitors boost an impressive safety profile despite an elevated risk of mucocutaneous *Candidiasis* and respiratory tract infections [20,21]. It is contraindicated for use in Interstitial Bowel Disease (IBD) and Human Immunodeficiency Virus (HIV) patients. The most common adverse effects of secukinumab include upper respiratory tract infections and headache. Others that should be closely monitored include infections, hypersensitivity reactions, neutropaenia, and rare cases of new or worsening IBD. In present study group, none of the patients reported any such side-effects. Psoriasis by itself is frequently associated with cardiometabolic co-morbidities, such as obesity and diabetes, that are risk factors leading to poor prognosis in the case of COVID-19 [22]. The usage of biologicals may increase the susceptibility to COVID-19 infection due to its immunosuppressive action. However, considering that cytokine storm following COVID-19 infection is the leading cause of pulmonary inflammation and subsequent respiratory failure, targeting these cytokines by use of specific biological can be protective in COVID-19 pneumonia and death. In COVID-19 affected patients, a high Th17 cells activation could result from a virus-driven increased production of IL-6 by the immune system [23,24]. Acute Respiratory Distress Syndrome (ARDS) occurs in 81% of fatal cases of COVID-19. In ARDS, IL-17 augments the destruction of the lung parenchyma through maladaptive neutrophil recruitment, by stimulating the production of proinflammatory mediators and through the prevention of apoptosis [25,26].

A study by Ekinci AP et al., found that, despite living in the same house with a COVID-19 positive household, two patients who had been taking IL-17 inhibitor secukinumab did not develop suspicious symptoms of COVID-19 suggesting a possible protective effect of anti IL-17 agents [27]. In this study, five patients who were on secukinumab maintenance dose, had family members with COVID-19 infection for which they were suggested home isolation. These five patients did not develop COVID-19 infection during and after secukinumab therapy despite living with COVID-19 infected relatives in the same household. A population-based study by Kridin K et al., in Israel which involved 680,2,153 and 138,750 patients treated with IL-17I, methotrexate and nonsystemic/non immunomodulatory drugs respectively, concluded that there was no increased risk of COVID-19 infection, among patients with psoriasis treated by IL-17I [28]. Findings in this study were consistent with these studies as no patient on secukinumab developed symptoms of COVID-19 infection or tested positive for COVID-19 by Reverse Transcription Polymerase Chain Reaction (RT-PCR) during the course of treatment for six months and a follow-up of three months.

National Psoriasis Foundation COVID-19 task force guidelines for management of psoriasis during pandemic suggests that patients with psoriatic disease should receive the seasonal inactivated (e.g., killed) influenza vaccine. While this vaccine will not protect against SARS-CoV-2, influenza vaccine lowers the risk of infection from seasonal influenza, which is of special importance to the individual and public health during the COVID-19 pandemic [29].

The IL-17A inhibitor secukinumab has been proven not to affect the humoral response to influenza vaccination in patients of psoriatic arthritis [30]. It has been reported that there is no contraindication for use of IL-17 inhibitors with Moderna (mRNA 1237 vaccine) and Pfizer BioNtech (BNT162b2) vaccines [31]. According to current observation, it was found that secukinumab does not seem to affect seroconversion or modify the efficacy when used simultaneously with Covaxin and Covishield, since no patient developed COVID-19 infection following vaccination. To our best knowledge, this study was the first of its kind to report the safety of secukinumab with COVID-19 vaccines available in India. The availablity of various choices of safe and effective drugs help the treating practitioner handle these challenges and provide an improved quality of life, free of morbidities to the patient.

Limitation(s)

The main limitation of this study was a relatively small sample size and more number of drop outs (26% of the participants). This was an ambispective observational study without any comparison group. A larger multicentre study is needed to determine the optimal treatment with safety for psoriasis during life threatening pandemics like COVID-19.

CONCLUSION(S)

It is obvious that injection secukinumab has a wide safety margin even during the pandemic times in that the patients who were initiated early on secukinumab before the advent of pandemic era are able to continue treatment with the drug. Vaccination of all types was not a contraindication for the continuation of secukinumab injection for treating psoriasis. The drug was found to have a smooth impact on the quality of life of patients even during the pandemic without warranting either deferring of vaccination or termination of treatment postvaccination. Thorough prebiological work-up, strict adherence to safety precautions during COVID-19 pandemic and following COVID-19 appropriate behaviour will ensure 100% successful implementation of the therapeutic efficacy IL-17 inhibitor during COVID-19 pandemic.

REFERENCES

[1] Schön MP, Boehncke WH. Psoriasis. N Engl J Med. 2005;352(18):1899-12.
[2] Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths CEM, Papp K, et al. Secukinumab in plaque psoriasis—results of two phase 3 trials. N Engl J Med. 2014;371(4):326-38.
[3] Zeng F, Huang Y, Guo Y, Yin M, Chen X, Xiao L, et al. Association of inflammatory markers with the severity of COVID-19: A meta-analysis. Int J Infect Dis. 2020;96:467-74.
[4] Kamata M, Tada Y. Safety of biologics in psoriasis. J Dermatol. 2017;45(3):279-86.
[5] Schoot TS, Kerckhoffs AP, Hilbrands LB, van Marum RJ. Immunosuppressive drugs and covid-19: A Review. Front Pharmacol. 2020;11.
[6] Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with coronavirus 2019(COVID-19) in Wuhan, China. Clin Infect Dis. 2020;71(15):762-68.
[7] Galluzzo M, Tofani L, Bianchi L, Talamonti M. Status of a real-life cohort of patients with moderate-to-severe plaque psoriasis treated with secukinumab and considerations on the use of biological agents in the COVID-19 ERA. Expert Opin Biol Ther. 2020;20(8):829-30.

[8] Di Lernia V, Bombonato C, Motolese A. Covid-19 in an elderly patient treated with secukinumab. Dermatol Ther. 2020;33(4):e13580.
[9] Guidance on the use of immunosuppressive agents [Internet]. American Academy of Dermatology. [cited 2022 Nov 6]. Available from: https://www.aad.org/member/practice/coronavirus/clinical-guidance/biologics.
[10] Davidovici BB, Sattar N, Jörg PC, Puig L, Emery P, Barker JN, et al. Psoriasis and systemic inflammatory diseases: Potential mechanistic links between skin disease and co-morbid conditions. J Invest Dermatol. 2010;130(7):1785-96.
[11] Clinical Review Report: Guselkumab (Tremfya):(Janssen Inc.): Indication: For the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy [Internet].
[12] Azfar RS, Gelfand JM. Psoriasis and metabolic disease: Epidemiology and pathophysiology. Curr Opin Rheumatol. 2008;20(4):416-22.
[13] De Simone C, Di Giorgio A, Sisto T, Carbone A, Ghitti F, Tondi P, et al. Endothelial dysfunction in psoriasis patients: Cross-sectional case-control study. Eur J Dermatol. 2011;21(4):510-14.
[14] Cosentyx [Prescribing Information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2021.
[15] von Stebut E, Reich K, Thaçi D, Koenig W, Pinter A, Körber A, et al. Impact of secukinumab on endothelial dysfunction and other cardiovascular disease parameters in psoriasis patients over 52 weeks. J Invest Dermatol.. 2019;139(5):1054-62.
[16] Elewski BE, Baddley JW, Deodhar AA, Magrey M, Rich PA, Soriano ER, et al. Association of secukinumab treatment with tuberculosis reactivation in patients with psoriasis, psoriatic arthritis, or ankylosing spondylitis. JAMA Dermatology. 2021;157(1):43-51.
[17] Havrdová E, Belova A, Goloborodko A, Tisserant A, Wright A, Wallstroem E, et al. Activity of secukinumab, an anti-IL-17A antibody, on brain lesions in RRMS: Results from a randomized, proof-of-concept study. J Neurol. 2016;263(7):1287-95.
[18] Cather JC, Crowley JJ. Use of biologic agents in combination with other therapies for the treatment of psoriasis. Am J Clin Dermatol. 2014;15(6):467-78.
[19] Farahnik B, Beroukhim K, Zhu TH, Abrouk M, Nakamura M, Singh R, et al. Ixekizumab for the treatment of psoriasis: A review of phase III trials. Dermatol Ther(Heidelb). 2016;6(1):25-37.
[20] Saunte DM, Mrowietz U, Puig L, Zachariae C. Candida infections in patients with psoriasis and psoriatic arthritis treated with interleukin-17 inhibitors and their practical management. Br J Dermatol. 2017;177(1):47-62.
[21] Wan MT, Shin DB, Winthrop KL, Gelfand JM. The risk of respiratory tract infections and symptoms in psoriasis patients treated with interleukin 17 pathway-inhibiting biologics: A meta-estimate of pivotal trials relevant to decision making during the COVID-19 pandemic. J Am Acad Dermatol. 2020;83(2):677-79.
[22] Gisondi P, Bellinato F, Chiricozzi A, Girolomoni G. The risk of COVID-19 pandemic in patients with moderate to severe plaque psoriasis receiving systemic treatments. Vaccines. 2020;8(4):728.
[23] Coperchini F, Chiovato L, Croce L, Magri F, Rotondi M. The cytokine storm in COVID-19: An overview of the involvement of the chemokine/chemokine-receptor system. Cytokine Growth Factor Rev. 2020;53:25-32.
[24] Kimura A, Kishimoto T. IL-6: Regulator of Treg/th17 balance. Eur J Immunol. 2010;40(7):1830-35.
[25] Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-COV-2 pneumonia in Wuhan, China: A single-centered, retrospective, Observational Study. Lancet Respir Med. 2020;8(5):475-81.
[26] Muir R, Osbourn M, Dubois AV, Doran E, Small DM, Monahan A, et al. Innate lymphoid cells are the predominant source of IL-17A during the early pathogenesis of acute respiratory distress syndrome. Am J Respir Crit Care Med. 2016;193(4):407-16.
[27] Ekinci AP, Pehlivan G, Gökalp MO. Surveillance of psoriatic patients on biologic treatment during the COVID-19 pandemic: A single-center experience. Dermatol Ther. 2020;34(1):e14700.
[28] Kridin K, Schonmann Y, Solomon A, Damiani G, Tzur Bitan D, Onn E, et al. Risk of COVID-19 infection, hospitalization, and mortality in patients with psoriasis treated by interleukin-17 inhibitors. J Dermatolog Treat. 2022;33(4):2014-20.
[29] Gelfand JM, Armstrong AW, Bell S, Anesi GL, Blauvelt A, Calabrese C, et al. National psoriasis foundation covid-19 task force guidance for management of psoriatic disease during the pandemic: Version 2-advances in psoriatic disease management, covid-19 vaccines, and covid-19 treatments. J Am Acad Dermatol. 2021;84(5):1254-68.
[30] Frieder J, Kivelevitch D, Menter A. Secukinumab: A review of the anti-il-17a biologic for the treatment of psoriasis. Ther Adv Chronic Dis. 2017;9(1):05-21.
[31] Simonetti O, Rizzetto G, Molinelli E, Diotallevi F, Radi G, Cirioni O, et al. Safety and efficacy of vaccines during COVID-19 pandemic in patients treated with biological drugs in a dermatological setting. Healthcare. 2021;9(4):401.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 20, 2022
- Manual Googling: Nov 08, 2022
- iThenticate Software: Nov 17, 2022 (20%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jul 19, 2022**
Date of Peer Review: **Oct 18, 2022**
Date of Acceptance: **Nov 18, 2022**
Date of Publishing: **Jan 01, 2023**