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Original Article

Short-term effects of secukinumab versus calcipotriol ointment on metabolic function and cytokine levels in patients with moderate-to-severe plaque psoriasis

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Abstract: Objective: To compare the short-term effects of secukinumab versus calcipotriol ointment on metabolic indices and cytokine levels in patients with moderate-to-severe plaque psoriasis. Methods: A total of 147 patients (71 treated with secukinumab and 76 with calcipotriol) were retrospectively enrolled and followed over a 12-week treatment period. The Psoriasis Area and Severity Index (PASI), Dermatology Life Quality Index (DLQI), fasting plasma glucose (FPG), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and serum levels of interleukin-17A (IL-17A), interleukin-22 (IL-22), tumor necrosis factor-α (TNF-α), and interleukin-10 (IL-10) were measured at baseline and week 12. Changes from baseline were compared between the two groups, and their correlations with PASI improvement were analyzed. Results: The secukinumab group achieved significantly higher PASI 75/90/100 response rates and greater reductions in DLQI scores than the calcipotriol group (all $P < 0.001$). In the secukinumab group, FPG, TG, IL-17A, IL-22, and TNF-α levels decreased significantly, whereas HDL-C and IL-10 levels increased significantly (all $P < 0.05$). No significant changes in these indices were observed in the calcipotriol group. Changes in these metabolic and cytokine indices were significantly correlated with PASI improvement in the secukinumab group ($|r| = 0.35$-0.69), whereas no significant correlations were observed in the calcipotriol group. Secukinumab treatment was identified as an independent predictor of PASI 75 response (OR = 13.66), while baseline TG and HDL-C levels showed borderline associations ($P = 0.069$ and 0.086, respectively). Conclusion: Over the 12-week treatment period, secukinumab was associated with greater skin lesion clearance and quality of life improvement than calcipotriol ointment. Secukinumab treatment was also associated with favorable changes in selected metabolic indices (FPG, TG, HDL-C), as well as a more balanced pro- and anti-inflammatory cytokine profile. However, the underlying mechanisms and long-term sustainability of these effects warrant further investigation.

Keywords: Psoriasis, secukinumab, calcipotriol, metabolic function, cytokines

Introduction

Psoriasis is a chronic cutaneous disorder primarily characterized by erythema and scales, with therapeutic strategies centered on managing localized symptoms. Recently, psoriasis has been recognized as a systemic immune-mediated inflammatory disorder, with an estimated global prevalence of approximately 2%-3% [1]. Previous investigations revealed that patients with psoriasis are at increased risk of metabolic syndrome, which consequently elevates their risk of developing atherosclerotic cardiovascular disease through a variety of pathologic pathways [2]. Metabolic abnormalities may also occur in those with mild disease activity [3]. Therefore, metabolic comorbidities have become a major concern in the comprehensive management of psoriasis and should not be overlooked. Whether clinical interventions can effectively alleviate cutaneous inflammation while simultaneously improving metabolic disturbances has become an important consideration in clinical decision-making.

Targeting immune dysregulation is critical to the treatment of psoriasis. Evidence indicates that the IL-23/Th17 axis plays an essential role in the inflammatory pathogenesis of this disease

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[4]. IL-17A, a key downstream effectors of this pathway, promotes keratinocyte proliferation and the recruitment of inflammatory cells [5], and may also impair adipose tissue function and insulin sensitivity [6]. Accordingly, biological agents targeting IL-17A have demonstrated favorable therapeutic efficacy in patients with moderate-to-severe psoriasis. Secukinumab is a high-affinity, human IL-17A monoclonal antibody that selectively binds to and neutralizes IL-17A, thereby reducing neutrophil recruitment and the production of various immune mediators at sites of inflammation. To date, multiple studies have demonstrated favorable clinical outcomes with secukinumab in patients with severe psoriasis [7, 8].

Given the involvement of IL-17A in adipose tissue dysfunction and insulin resistance, the effects of secukinumab on metabolic health warrant further investigation. Evidence from 19 clinical studies indicated that conventional metabolic indices, including BMI, fasting plasma glucose, blood lipid profile, and arterial blood pressure, remained largely unchanged during one year of treatment course. Similarly, emerging metabolic markers such as the fibrosis-4 (FIB-4) index and triglyceride-glucose index, showed no significant changes, whereas inflammatory biomarkers, specifically high-sensitivity C-reactive protein and the neutrophil-to-lymphocyte ratio, decreased significantly [9-11]. These findings suggest that secukinumab may reduce inflammatory biomarkers levels without substantially altering conventional lipid or metabolic indices. However, the clinical importance of maintaining metabolic stability, rather than achieving marked metabolic improvement, during therapy remains to be elucidated.

Although secukinumab has demonstrated favorable results, calcipotriol ointment, a vitamin D3 derivative, remains one of the most widely used topical drugs for mild-to-moderate plaque psoriasis [12]. It can bind to vitamin D receptor in keratinocytes, thereby inhibiting cell division, promoting differentiation, and modulating the local immune microenvironment. Basic research has shown that calcipotriol can reduce IL-36α/γ expression in psoriatic lesions and thus inhibit the IL-23/IL-17 inflammatory cascade [13]. A study examining calcipotriol in combination with acitretin reported a reduction in serum glucose concentrations, although this effect was primarily attributed to acitretin-mediated regulation of glucose transporter expression [14]. Overall, current studies have neither established a direct effect of topical calcipotriol on systemic metabolic disturbances, nor provided sufficient head-to-head comparisons with biologic agents such as secukinumab regarding metabolic outcomes. In patients with moderate-to-severe psoriasis, it therefore remains unclear whether topical therapy provides systemic metabolic benefits beyond improving cutaneous lesions, whether the metabolic improvement associated with biologic therapy occur secondary to inflammation resolution, and whether two therapeutic approaches differ in their effects on metabolic health.

To address this gap, we conducted a retrospective chart review of patient with moderate-to-severe plaque psoriasis. Clinical outcomes, metabolic indices, and serum cytokine levels after 12 weeks of treatment with secukinumab or calcipotriol ointment were compared. Factors associated with treatment response were also identified. These findings can support treatment selection for patients with moderate-to-severe plaque psoriasis.

Materials and methods

Study design and patient source

This was a single-center retrospective observational study. Electronic medical records of patients with moderate-to-severe plaque psoriasis who were treated at Longgang Central Hospital of Shenzhen between January 2023 and April 2025 were reviewed. This study was approved by the Ethics Committee of Longgang Central Hospital of Shenzhen.

Potentially eligible patients were screened according to the predefined inclusion and exclusion criteria. A total of 147 eligible patients were include and divided into two groups according to actual treatment received: the secukinumab group (n = 71) and calcipotriol group (n = 76).

A *post hoc* power analysis was performed using G*Power version 3.1.9.7 (Kiel University, Germany). Based on estimated 12-week PASI 75 response rates of 87% and 42% in the two groups, respectively, and a two-sided alpha level of 0.05, the achieved statistical power was 0.99.

Inclusion criteria: (1) age ≥ 18 years, regardless of sex; (2) a confirmed diagnosis of chronic plaque psoriasis according to *Guideline for the Diagnosis and Treatment of Psoriasis in China* (2023 edition) [15], with a disease history ≥ 6 months; (3) moderate-to-severe disease at baseline, characterized by at least one of the following criteria: Psoriasis Area and Severity Index (PASI) score ≥ 10, body surface area (BSA) involvement ≥ 10%, or Dermatology Life Quality Index (DLQI) score ≥ 10 [16]; (4) continuous treatment for at least 12 weeks with either secukinumab monotherapy or calcipotriol ointment monotherapy; and (5) complete clinical and laboratory data, including metabolic indicators and cytokine levels, available at baseline and week 12.

Exclusion criteria: (1) treatment with any biologic agent or systemic immunosuppressant within the three months before treatment; (2) concomitant atopic dermatitis, systemic lupus erythematosus, other inflammatory cutaneous conditions, or acute infections; (3) a history of malignancy, severe cardiovascular or cerebrovascular disease, or uncontrolled endocrine disorders; (4) pregnancy or lactation; (5) concomitant use of antidiabetic agents, lipid-lowering agents, or other medications or supplements that could affect metabolic parameters, including traditional Chinese herbs and dietary supplements, during the treatment period; (6) suboptimal therapeutic compliance (< 80% adherence to the prescribed regimen) or failure to complete the 12-week follow-up.

Treatment regimens

In the secukinumab group, secukinumab (Cosentyx®, Novartis Pharma Schweiz AG) was administered by subcutaneous injection at an initial dose of 300 mg once weekly over five straight weeks, followed by 300 mg once every 4 weeks. All patients completed at least 12 weeks of treatment.

In the calcipotriol group, calcipotriol ointment (Daivonex®, Leo Pharma A/S, Denmark) was applied evenly to psoriatic lesions twice daily, with the total weekly dose not exceeding 100 g. Treatment records indicated that all included patients achieved ≥ 80% adherence to the prescribed regimen.

During the treatment period, patients in both group were prohibited from using other external medications (e.g., corticosteroids or calcineurin inhibitors), systemic therapies (e.g., methotrexate, cyclosporine, acitretin), or phototherapy. Moisturizers use was documented but was not considered an exclusion criterion.

Data collection and outcome measures

Baseline demographic and clinical data were obtained from the electronic medical records, including age, sex, disease duration, body mass index (BMI; kg/m^2), smoking status, alcohol consumption, previous treatments, and comorbidities such as hypertension and diabetes. Clinical and laboratory variables were evaluated at baseline, before intervention initiation, and after 12 weeks of treatment.

Furthermore, assessors blinded to intervention assignments examined anonymized biochemical test results and numerical scores. After data entry, the treatment-group labels remained concealed from the statistical analyst and were disclosed only after the prespecified analyses had been completed.

Primary outcome measure

The PASI [17] was used to assess psoriasis severity based on the extent of BSA involvement and the severity of clinical signs, including erythema, induration, and scaling. The total score ranges from 0 to 72, with higher scores indicating greater disease severity. In this study, all PASI assessment were performed by the same trained dermatologist, who recorded both the total score and individual component scores. PASI 75, PASI 90, and PASI 100 responses were defined as reductions of ≥ 75%, ≥ 90%, and 100%, accordingly, in the total PASI score from baseline.

Secondary outcome measures

The DLQI [18] was used to evaluate patients' quality of life. The questionnaire comprises 10 items, each scored from 0 to 3, yielding a total score of 0-30; a higher score indicates a more substantial decline in the quality of life. Participants completed the questionnaire during their clinical assessment, after which research staff reviewed it for completeness.

Metabolic biomarkers: After an overnight (≥ 8-hour) fast, cubital venous blood samples were collected from each participant between 7:00 and 8:00 a.m. Biochemical analyses were performed in the hospital's clinical lab using a Beckman AU5800 automated biochemical analyzer (Beckman Coulter, Inc., USA). Daily internal quality-control measurements were performed, and the inter-assay coefficients of variation were consistently below 5%. The analytical methods were as follows:

(1) Fasting plasma glucose (FPG) was measured using the hexokinase method (Beckman AU5800 automated biochemistry analyzer, Beckman Coulter, Inc., USA); (2) Triglycerides (TG) were measured using the glycerol phosphate oxidase-peroxidase assay; (3) Total cholesterol (TC) was measured using the cholesterol oxidase method; (4) High-density lipoprotein cholesterol (HDL-C) was measured using a targeted blocking testing approach; (5) Low-density lipoprotein cholesterol (LDL-C) was measured using a direct selective detergent method.

All assays were performed in accordance with the manufacturers' instructions. Quality-control results remained within the acceptable ranges throughout the study period.

For cytokine measurements, 5 mL of fasting elbow vein blood was collected. After standing at room temperature for 30 minutes, the collected blood samples were centrifuged at 3,000 rpm for 10 min to separate the serum. Serum aliquots were stored at -80°C until batch analysis. Serum concentrations of IL-17A, IL-22, TNF-α, and IL-10 were measured using enzyme-linked immunosorbent assay (ELISA) kits purchased from R&D Systems, Inc. (Minneapolis, MN, USA), in strict compliance with manufacturer guidelines supplied by the manufacturer's instructions.

Safety monitoring: Adverse events occurring during the course of treatment were documented, including injection-site reactions (e.g., erythema, swelling, and pain), upper respiratory tract infections, oral candidiasis, application-site reactions (e.g., erythema, desquamation, pruritus, stinging), and serious adverse events. The severity of adverse events was graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0 [19].

Statistical analysis

All statistical analyses were performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was verified using the Shapiro-Wilk test. Normally distributed variables are presented as mean ± standard deviation (SD), whereas non-normally distributed variables are presented as the median and interquartile range (IQR). Between-group comparisons were performed using the independent-samples t-test or Mann-Whitney *U* test, as appropriate. Within-group comparisons between baseline and week 12 were performed using the paired *t*-test or Wilcoxon signed-rank test, as appropriate.

Categorical variables were summarized as frequencies and percentages and were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. Spearman's rank correlation analysis was used to assess the correlations between changes in individual indicatorsand the percentage improvement in PASI within each treatment group. Fisher's Z transformation was applied to compare the correlation coefficients between the two groups.

Variables with $P < 0.10$ in the univariable analyses were entered into a multivariable logistic regression model using forward stepwise selection to identify independent predictors for achieving PASI75. The results were reported as odds ratios (OR) with corresponding 95% confidence intervals (CIs). The proportion of missing data for each individual variable was < 5%; therefore, a complete-case analysis was performed without imputation. All statistical tests were two-tailed with a significance level set at $\alpha = 0.05$, and P values < 0.05 were considered significant.

Results

Baseline demographic and clinical characteristics

No statistically significant differences were observed between the two groups in terms of baseline age, sex distribution, disease duration, BMI, smoking status, alcohol consumption, comorbidities, initial PASI score, DLQI score, metabolic indices, or cytokine levels (all $P > 0.05$; **Table 1**).

Table 1. Comparison of baseline characteristics between the two groups

Variable	Secukinumab group (n = 71)	Calcipotriol group (n = 76)	Statistic	*P*
Age (years)	46.5 ± 12.3	48.2 ± 13.0	t = -0.822	0.412
Male n (%)	43 (60.6)	45 (59.2)	χ^2 = 0.026	0.872
Disease duration (years)	8.0 (4.0-14.5)	8.5 (4.0-15.0)	Z = -0.471	0.637
BMI (kg/m^2)	25.7 ± 3.2	25.3 ± 3.5	t = 0.727	0.468
Smoking history, n (%)	22 (31.0)	24 (31.6)	χ^2 = 0.006	0.938
Alcohol consumption, n (%)	15 (21.1)	18 (23.7)	χ^2 = 0.141	0.708
Hypertension, n (%)	19 (26.8)	21 (27.6)	χ^2 = 0.012	0.912
Diabetes, n (%)	11 (15.5)	13 (17.1)	χ^2 = 0.071	0.791
Baseline PASI	14.2 ± 3.4	13.9 ± 3.1	t = 0.558	0.577
Baseline DLQI	12.5 ± 4.0	11.9 ± 3.8	t = 0.924	0.357
Baseline FPG (mmol/L)	5.90 ± 1.15	5.82 ± 1.09	t = 0.425	0.672
Baseline TG (mmol/L)	2.08 ± 0.80	2.00 ± 0.78	t = -0.648	0.524
Baseline TC (mmol/L)	4.78 ± 0.85	4.73 ± 0.81	t = 0.369	0.713
Baseline HDL-C (mmol/L)	1.04 ± 0.29	1.07 ± 0.31	t = -0.606	0.545
Baseline LDL-C (mmol/L)	3.02 ± 0.74	2.95 ± 0.70	t = 0.584	0.562
Baseline IL-17A (pg/mL)	58.6 ± 12.9	57.2 ± 12.4	t = 0.662	0.509
Baseline IL-22 (pg/mL)	43.0 ± 10.2	41.8 ± 9.9	t = 0.722	0.471
Baseline TNF-α (pg/mL)	25.7 ± 6.1	24.9 ± 5.8	t = 0.811	0.418
Baseline IL-10 (pg/mL)	8.3 ± 2.4	8.6 ± 2.5	t = -0.738	0.462

Notes: BMI, body mass index; PASI, Psoriasis Area and Severity Index; DLQI, Dermatology Life Quality Index; FPG, fasting plasma glucose; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; IL-17A, interleukin-17A; IL-22, interleukin-22, TNF-α, tumor necrosis factor-alpha; IL-10, interleukin-10.

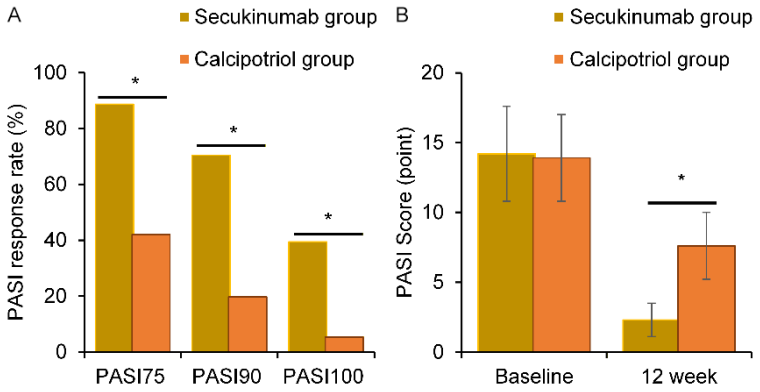


Figure 1. Comparison of PASI response rates between the two groups after 12 weeks of treatment. (A) The proportion of PASI responders, (B) PASI values. *P < 0.05. PASI: Psoriasis Area and Severity Index.

PASI response rates at week 12

Following a 12-week intervention, the PASI 75, PASI 90, and PASI 100 achievement rates in the secukinumab group were 88.7% (63/71), 70.4% (50/71), and 39.4% (28/71), respectively. These rates were markedly higher than those observed in the calcipotriol cohort (42.1% [32/76], 19.7% [15/76], and 5.3% [4/76], respectively; all P < 0.001). The mean PASI score was 2.3 ± 1.2 in the secukinumab group, which was significantly lower than 7.6 ± 2.4 in the calcipotriol group (P < 0.001; **Figure 1**).

Improvement in quality of life at week 12

In the secukinumab group, the mean DLQI score decreased from 12.5 ± 4.0 at baseline to 2.8 ± 2.1 at week 12 (P < 0.001). In the calcipotriol group, DLQI score decreased from 11.9 ± 3.8 at baseline to 8.1 ± 3.0 at week 12 (P < 0.001). The improvement in DLQI score was significantly greater in the secukinumab group than in the calcipotriol group (P < 0.001; **Figure 2**).

Changes in metabolic indices at week 12

After 12 weeks of treatment, FPG and TG levels decreased significantly, whereas HDL-C levels increased significantly in the secukinumab

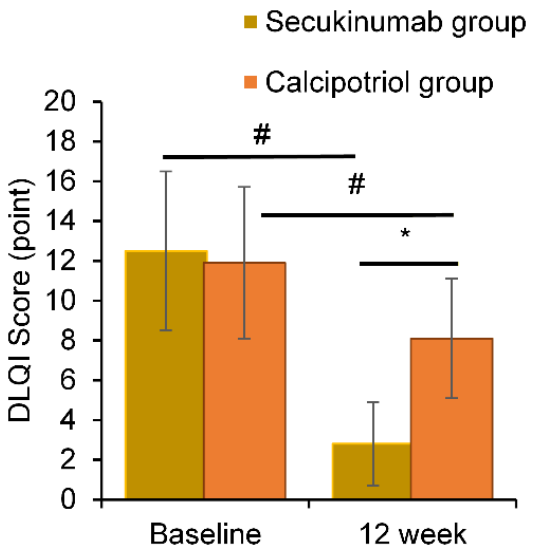


Figure 2. Comparison of DLQI scores between the two groups before and after treatment. $^{*}P < 0.05$; $^{\#}P < 0.05$. DLQI: Dermatology Life Quality Index.

group (all $P < 0.05$). No significant changes were observed in TC or LDL-C levels (both $P > 0.05$). In the calcipotriol group, no significant differences were observed in these metabolic indices before and after treatment (all $P > 0.05$). The changes in FPG, TG, and HDL-C differed significantly between the two groups ($P < 0.05$). Details are shown in **Figure 3**.

Changes in cytokine levels at week 12

After 12 weeks of treatment, serum IL-17A, IL-22, and TNF-α levels decreased significantly, whereas IL-10 increased significantly in the secukinumab group (all $P < 0.001$). No significant changes in these cytokines were observed in the calcipotriol group (all $P > 0.05$). The inter-group differences were statistically significant (all $P < 0.001$; **Figure 4**).

Correlations between changes in measured indices and PASI improvement

Spearman's correlation analyses were performed separately for the two groups, and the resulting correlation coefficients were compared. The results showed that, in the secukinumab group, ΔFPG, ΔTG, ΔHDL-C, ΔIL-17A, ΔIL-22, ΔTNF-α, and ΔIL-10 were all significantly correlated with the percentage improvement in PASI ($|r| = 0.35$-0.69, all $P < 0.01$). Between-group comparisons showed significant differences in the correlation coefficients for ΔFPG, ΔTG, ΔHDL-C, ΔIL-17A, and ΔIL-10 (all $P < 0.05$). By contrast, the between-group differences in the correlation coefficients for ΔIL-22 ($P = 0.089$) and ΔTNF-α ($P = 0.052$) were not significant (**Table 2**).

Factors associated with a PASI 75 response

(1) Univariable analysis: Univariate logistic regression analyses were performed with a PASI 75 response at week 12 as the dependent variable (1 = yes, 0 = no), and treatment group, demographic factors, disease duration, BMI, smoking status, alcohol consumption, co-morbidities, baseline PASI, DLQI, metabolic markers, and cytokine levels as independent variables (**Table 3**). The results showed that secukinumab treatment (OR = 10.83), baseline PASI score (OR = 0.87), and baseline IL-17A level (OR = 1.42 per 10 pg/mL) were strongly associated with PASI 75 response (all $P < 0.05$). Baseline TG (OR = 0.68, $P = 0.069$) and HDL-C (OR = 1.56 per 0.3 mmol/L, $P = 0.086$) showed marginal importance. All other variables had $P \geq 0.10$.

(2) Multivariable analysis: Variables with $P < 0.1$ in the univariable analyses (treatment group, baseline PASI score, baseline IL-17A, TG and HDL-C levels) were included in the following multivariable logistic regression model. The results show that secukinumab treatment was independently associated with a higher likelihood of achieving a PASI75 response (OR = 13.66, 95% CI: 6.92-26.98; $P < 0.001$), whereas a higher baseline PASI score was associated with a lower likelihood of achieving this response (OR = 0.91, 95% CI: 0.84-0.99; $P = 0.032$). Baseline IL-17A was not retained in the final model ($P = 0.123$). The Hosmer-Lemeshow test showed good model fit ($\chi^2 = 5.12$, $df = 8$, $P = 0.745$), and the overall classification accuracy was 84.5%.

Safety assessment

No serious adverse events were documented during the 12-week treatment period. All documented adverse events were grade 1-2 according to CTCAE version 5.0, and no Grade 3 or higher events occurred.

In the secukinumab group, 8 patients (8/71; 11.3%) experienced adverse events, including 4 cases (5.6%) of injection-site reactions (Grade 1), 3 cases (4.2%) of upper respiratory

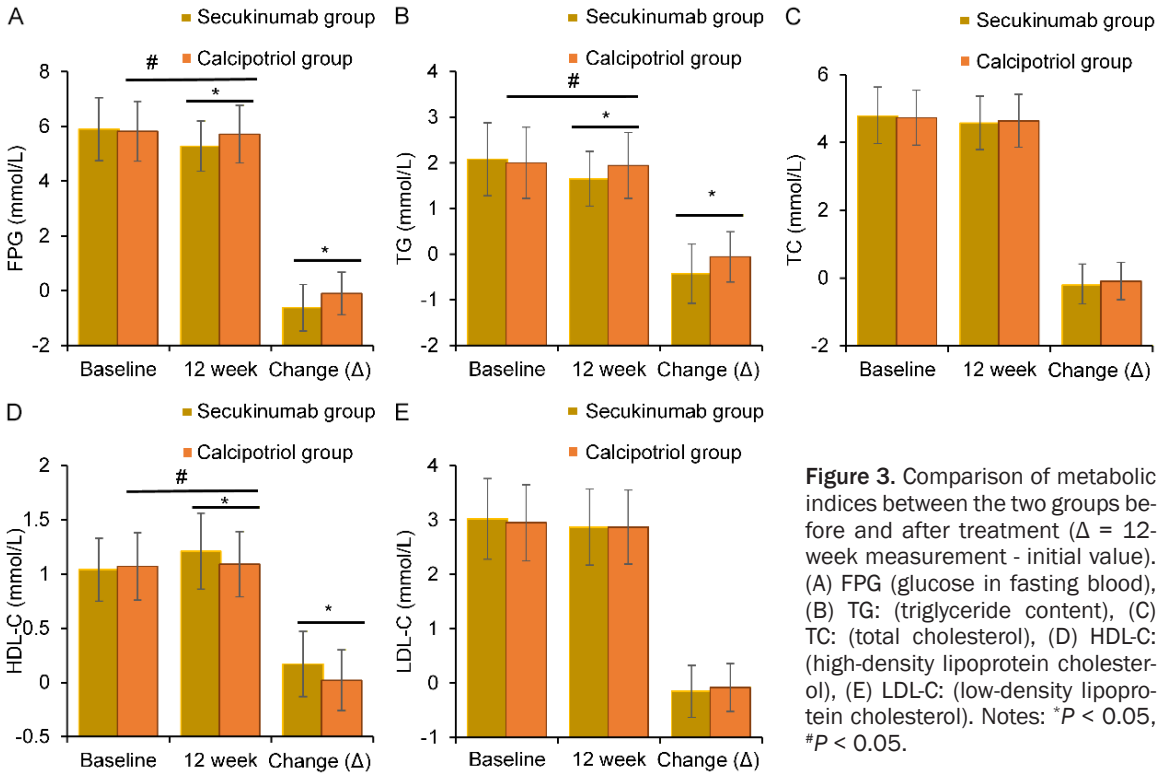


Figure 3. Comparison of metabolic indices between the two groups before and after treatment (Δ = 12-week measurement - initial value). (A) FPG (glucose in fasting blood), (B) TG: (triglyceride content), (C) TC: (total cholesterol), (D) HDL-C: (high-density lipoprotein cholesterol), (E) LDL-C: (low-density lipoprotein cholesterol). Notes: $^{*}P < 0.05$, $^{\#}P < 0.05$.

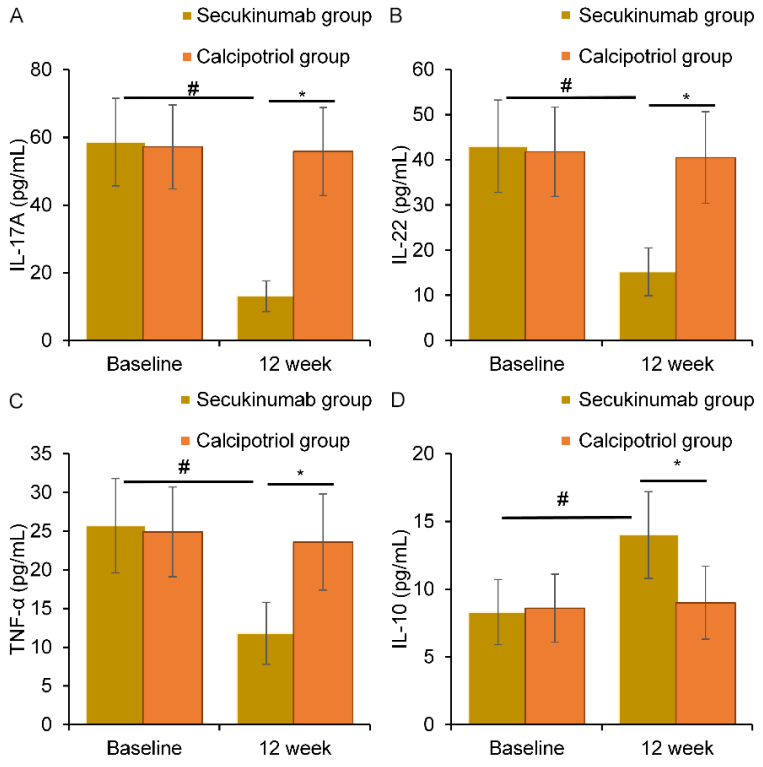


Figure 4. Comparison of serum cytokine levels between the two groups after 12 weeks of treatment. (A) IL-17A (interleukin-17A), (B) IL-22 (interleukin-22), (C) TNF-α (tumor necrosis factor-alpha), (D) IL-10 (interleukin-10). Notes: $^{*}P < 0.05$, $^{\#}P < 0.05$.

tract infections (Grade 1) and 1 case (1.4%) of oral candidiasis (Grade 1). In the calcipotriol group, 10 of 76 patients (13.2%) experienced application-site irritation, including 7 patients (9.2%) of grade 1 and 3 patients (3.9%) of grade 2. The grade 2 events resolved after the frequency of application was reduced. No hospitalization or treatment discontinuation occurred due to adverse events.

Discussion

This study provided evidence regarding therapeutic differences in metabolic indices and cytokine levels between secukinumab and calcipotriol ointment in patients with moderate-to-severe plaque psoriasis. After a 12-week treatment period, secukinumab was associated with greater improvements in skin lesions and qual-

Table 2. Correlation between 12-week changes in indices and the percentage improvement in PASI in each treatment group, with between-group comparisons of correlation coefficients

Indicator changes (Δ)	*Sikuximab group (n = 71)*		*Carbotriol group (n = 76)*		*Comparison of P-values between groups*
	r (95% CI)	*P*	*r* (95% CI)	*P*	
ΔFPG	-0.48 (-0.65 - -0.27)	< 0.001	-0.08 (-0.30 - 0.15)	0.491	0.014
ΔTG	-0.35 (-0.54 - -0.13)	0.003	-0.10 (-0.32 - 0.13)	0.401	0.038
ΔHDL-C	0.44 (0.23 - 0.62)	< 0.001	0.06 (-0.17 - 0.28)	0.622	0.022
ΔIL-17A	0.69 (0.54 - 0.80)	< 0.001	0.12 (-0.11 - 0.34)	0.311	0.006
ΔIL-22	0.51 (0.31 - 0.68)	< 0.001	0.09 (-0.14 - 0.31)	0.453	0.089
ΔTNF-α	0.47 (0.26 - 0.64)	< 0.001	0.13 (-0.10 - 0.35)	0.271	0.052
ΔIL-10	-0.53 (-0.69 - -0.33)	< 0.001	-0.07 (-0.29 - 0.16)	0.560	0.029

Notes: Δ = 12-week value minus baseline value. PASI: Psoriasis Area and Severity Index; FPG: fasting blood glucose; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; IL-17A: interleukin-17A; IL-22: interleukin-22; TNF-α: tumor necrosis factor-alpha; IL-10: interleukin-10.

Table 3. Univariable logistic regression analysis of factors associated with a PASI 75 response

Variable	*OR (95% CI)*	*P*
Treatment group (Sikuximab group vs. Cabozantriol group)	10.83 (4.98-23.56)	< 0.001
Baseline PASI (for every 1 point increase)	0.87 (0.78-0.97)	0.012
Baseline TG (every 1 mmol/L increase)	0.68 (0.45-1.03)	0.069
Baseline HDL-C (every 0.3 mmol/L increase)	1.56 (0.94-2.58)	0.086
Baseline IL-17A (every 10 pg/mL increase)	1.42 (1.06-1.91)	0.019
Other variables	-	*P* > 0.10

Notes: PASI: Psoriasis Area and Severity Index; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; IL-17A: interleukin-17A.

ity of life compared to calcipotriol ointment. Secukinumab treatment was also associated with reductions in FPG, TG, IL-17A, IL-22, and TNF-α levels and elevation in HDL-C and IL-10 levels, whereas no significant changes in these indices were detected in the calcipotriol group. Moreover, changes in metabolic indices and cytokine levels were significantly associated with PASI improvement in the secukinumab group. Nevertheless, the causal relationship requires further validation in prospective studies.

Regarding the effects of secukinumab on metabolic biomarkers, findings from previous prospective studies and clinical trials have been inconsistent, although most studies have reported no significant changes in conventional glucolipid metabolic indices after treatment. Gisondi et al. [20] found that secukinumab had no significant effects on metabolic indices, the hepatic steatosis index, or the lipid accumulation product during 12 months of follow-up. Similarly, Cingöz and Gençoğlan [11] observed no significant changes in TC, LDL-C, HDL-C, or the atherogenic index after ≥ 6 months of treatment. A cross-sectional study by Kokolakis et al. [21] also found no significant differences in metabolic status between biologic-treated patients and healthy controls.

In contrast, the present study demonstrated significant reductions in FPG and TG levels and an increase in HDL-C levels after 12 weeks of secukinumab therapy. This discrepancy may partly reflect differences in baseline population characteristics. Participants in the aforementioned studies generally had lower baseline TG and FPG levels than those in our cohort (TG: 2.08 mmol/L; FPG: 5.90 mmol/L). Differences in follow-up durations may also have contributed to the inconsistent findings. If metabolic improvements occur predominantly during the early stage of treatment and subsequently plateau, a longer follow-up might obscure early changes due to a “plateau phase”. In addition, some previous studies included patients receiving different biologic agents or employed cross-sectional designs, which may have limited their ability to detect metabolic changes specifically associated with IL-17A inhibition.

Nevertheless, favorable metabolic trends have been reported in some studies. Corrao et al. suggested in their review of immunometabolism, that IL-17 and IL-23 inhibitors may modulate metabolic status by reducing adipose tissue inflammation, with potentially greater effects in patients with a higher metabolic burden [22]. A randomized controlled trial involving 120 patients reported that IL-17 and IL-23 inhibitors exerted greater improvements in blood glucose, TG, and HDL-C levels than cyclosporine [23]. A study of older patients with psoriasis found that IL-17/IL-23 inhibitors maintained long-term PASI response similar to those observed in younger patients [24]. In addition, Wang et al. found that the baseline TG/HDL-C ratio independently predicted the durability of the response to secukinumab at 52 weeks [25].

However, in the univariate analysis, baseline TG and HDL-C only met the prespecified criterion for entry in to the multivariate model (P = 0.069 and 0.086, respectively) but were not independently associated with the PASI 75 response in the multivariable model. Therefore, we further examined the relationship between dynamic changes in metabolic indices during treatment and lesion improvement. Changes in TG and HDL-C were significantly correlated with the percentage improvement in PASI (r = -0.35 and 0.44, respectively; both P < 0.01), suggesting moderate associations between changes in these metabolic indices and clinical improvement. A retrospective cohort study suggested that the lipid effects of IL-17A inhibitors may vary according to patients' baseline metabolic profiles. Patients with mixed dyslipidaemia experienced reductions in TC, TG, and LDL-C after treatment, whereas those with normal baseline lipid levels showed slight increases in TG and LDL-C [26]. In this study, TC and LDL-C levels did not change significantly after secukinumab treatment, which is consistent with the largely neutral effects on lipid profiles reported by previous studies [27, 28]. These findings suggest that short-term IL-17A inhibition may preferentially affect triglyceride-rich lipoprotein metabolism and pathways related to insulin sensitivity more readily than cholesterol homeostasis.

The relatively elevated baseline TG levels (mean 2.08 mmol/L) and relatively low HDL-C levels (mean 1.04 mmol/L) in this study may indicate a population with a greater potential for metabolic improvement, which may partially explain the significant decreases in FPG, TG, and HDL-C observed in this study. From a clinical perspective, the absolute reduction - 0.3-0.5 mmol/L in FPG and 0.2-0.3 mmol/L in TG over 12 weeks - were modest. Whether changes of this magnitude translate into a clinically meaningful reduction in long-term cardiovascular risk remains uncertain. Therefore, these findings should be regarded as preliminary signals of early metabolic changes rather than established clinical benefits, and their long-term significance requires confirmation through studies with extended follow-up. Multivariate logistic regression indicated that secukinumab therapy was independently associated with a higher likelihood of achieving a PASI 75 response (OR = 13.66), and each one-point increase in baseline PASI score was associated with an approximately 9% reduction in the odds of achieving PASI 75 (OR = 0.91), indicating that patients with more severe baseline disease were less likely to achieve PASI75 even with highly efficacious treatment.

Our cytokine analysis showed that secukinumab administration was accompanied by significant decreases in IL-17A, IL-22, and TNF-α levels, and an increase in the anti-inflammatory factor IL-10. The change in IL-17A was strongly correlated with the degree of PASI improvement (r = 0.69), which is consistent with the established role of IL-17A inhibition in the therapeutic mechanism of secukinumab [7]. However, baseline IL-17A was not retained in the final multivariable regression analysis. One possible explanation is that baseline IL-17A levels were somewhat associated with treatment assignment - the secukinumab group had slightly higher baseline IL-17A levels than the calcipotriol group - and treatment group itself was the strongest predictor of PASI75 response, with possible overlapping effects between the two variables, and the forward stepwise regression method preferentially retained the variable with greater contribution. Baseline IL-17A may also have been correlated with baseline PASI or other covariates, thereby reducing its independent contribution after multivariable adjustment. Overall, univariable findings suggest that baseline IL-17A may have predictive value, but its utility as an independent biomarker of therapeutic response warrants further validation in larger, appropriately stratified cohorts.

The concomitant decreases in IL-22 and TNF-α suggest broader modulation of the inflammatory network following IL-17A inhibition, whereas the increase in IL-10 may reflect a shift toward a less inflammatory immune environment. Although IL-17 inhibitors suppress the Th17 axis, they might trigger a compensatory transition toward Th2/Th22, and cases of paradoxical eczema after secukinumab therapy have been reported [29, 30]. A meta-analysis reported a 2.2%-12.1% occurrence rate of eczematous adverse events among patients receiving anti-IL-17A treatment [31]. This study did not specifically assess those events. Future studies with longer follow-up should prospectively monitor eczematous reactions and related immunological changes, including alterations in IL-22 levels [32].

Although our findings may have clinical relevance, several limitations should be acknowledged. First, the retrospective design was inherently susceptible to selection and information bias. Although no significant differences were observed in measured baseline characteristics between groups, undetected confounders could not be excluded [33, 34]. Second, the sample size was relatively limited (n = 147). Although significant between-group differences were detected in the primary efficacy outcomes, it had limited ability to support reliable subgroup analyses, particularly analyses stratified by baseline metabolic characteristics. Consequently, the differential effects of secukinumab among patients with varying metabolic burdens could not be adequately evaluated. Future prospective studies should incorporate prespecified stratification based on baseline metabolic characteristics to identify patients who may be more likely to experience favorable metabolic changes [35]. Third, the observation window of this study was limited to 12 weeks. Although this period was sufficient to capture short-term skin responses, it was inadequate to determine whether the improvements in glucolipid metabolism would persist, diminish, or plateau over time. It also precluded a comprehensive evaluation of long-term metabolic safety outcome, such as new-onset hyperlipidemia or abnormal glycemic fluctuations. Therefore, the metabolic and safety findings of this study should be regarded as preliminary. Their long-term trends and clinical significance should be evaluated in studies with follow-up of ≥ 24 weeks and prespecified, standardized metabolic and safety endpoints. Fourth, the PASI 75 response rate in the calcipotriol cohort was 42.1%, which is relatively high for topical treatment in patients with moderate-to-severe psoriasis. This finding may partly reflect the inclusion of patients at the less severe end of the eligibility range. Therefore, caution is required when interpreting the observed between-group differences, and prospective studies using clinically comparable treatment groups are warranted.

Conclusion

This study compared the effects of secukinumab versus calcipotriol ointment in patients with moderate-to-severe plaque psoriasis. Secukinumab treatment was associated with greater skin lesion clearance and quality-of-life improvement than calcipotriol ointment. Secukinumab was also associated with reductions in FPG and TG levels and increases in HDL-C levels, and changes in these metabolic indices demonstrated moderate correlations with the degree of lesion improvement. However, baseline TG and HDL-C were not independently associated with treatment response. These findings indicate that for patients with moderate-to-severe psoriasis complicated by metabolic abnormalities, secukinumab may offer concurrent metabolic regulatory trends while effectively clearing skin lesions; nevertheless, the causal relationship and long-term sustainability of these effects require further validation through prospective studies with extended follow-up.

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Disclosure of conflict of interest

None.

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