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Impact of IL-17A Inhibitors on Serum Uric Acid Levels in Psoriatic Patients with Hyperuricemia: A Prospective Observational Study

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Purpose: This prospective observational study investigated whether interleukin (IL)-17A inhibitors could reduce serum uric acid (SUA) levels in psoriatic patients with hyperuricemia. It also explored the risk factors for hyperuricemia in psoriatic patients and the effectiveness of IL-17A inhibitors for the skin lesions of psoriatic patients with hyperuricemia.

Methods: Patients aged ≥18 years with moderate to severe plaque psoriasis along with concomitant hyperuricemia (defined as an SUA level >416 μmol/L in men and >357 μmol/L in women) at baseline were treated with either secukinumab or ixekizumab. SUA levels were longitudinally assessed over 1 year. We evaluated the changes in SUA level and factors associated with SUA changes. Binary logistic regression was conducted to identify risk factors for hyperuricemia in psoriatic patients. Additionally, we examined effectiveness of IL-17A inhibitors for patients with psoriasis and hyperuricemia including Psoriasis Area Severity Index (PASI) 75, 90, and 100 response rates at 1 year.

Results: Our study included 196 individuals diagnosed with psoriasis and hyperuricemia. The mean SUA levels were 481±68 μmol/L at baseline and 442±78 μmol/L after 1 year of treatment with IL-17A inhibitors ($p<0.001$). Subgroup analysis revealed a consistent and significant decrease in SUA levels across different genders, age groups (30–39, 40–49, ≥50 years), BMI categories, baseline PASI scores, PASI improvement rates, and among patients treated with different IL-17A inhibitors. Patients aged ≥50 years and with a BMI <24 exhibited a higher SUA reduction rate. Male gender, age under 40 years, obesity, hypertension, hypertriglyceridemia, and a PASI score of ≥20 were independent risk factors for hyperuricemia in patients with psoriasis. The PASI 75, 90, and 100 response rates in psoriatic patients with hyperuricemia were 88.3%, 60.2%, and 28.6%, respectively, after 1 year of treatment with IL-17A inhibitors.

Conclusion: Our findings suggest that SUA levels decrease significantly under IL-17A inhibitors treatment in psoriatic patients with hyperuricemia. Patients aged ≥50 years and with a BMI <24 had greater benefits. This study provides a theoretical basis for the selection of biologics to treat psoriatic patients with hyperuricemia.

Keywords: psoriasis, uric acid, hyperuricemia, IL-17A inhibitor

Introduction

Psoriasis, an immune-mediated chronic inflammatory multisystem disease affecting 1%–2% of the population,[1] is characterized by keratinocyte hyperproliferation and elevated levels of type 1 T helper cell (Th1) and type 17 T helper cell (Th17) cytokines.[2] Genetic susceptibility, environmental factors, and complex immunological mechanisms, including the activation of dendritic cells, keratinocytes, and various cytokines, contribute to the development of psoriasis.[3] In addition to skin lesions, psoriasis may manifest as psoriatic arthritis with various systemic inflammation-related comorbidities, such as cardiovascular diseases, metabolic syndrome, obesity, dyslipidemia, diabetes, inflammatory bowel disease, psychiatric conditions, and non-alcoholic fatty liver disease.[4–8]

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Hyperuricemia, an abnormal increase in fasting serum uric acid (SUA) levels caused by purine metabolism disorder, was historically known as "the disease of kings and the king of diseases." The numerous factors associated with hyperuricemia risk include gender, age, ethnicity, overweight or obesity status, smoking, lifestyle, and environmental conditions.[9,10] Uric acid is a key signal involved in activation of the NLR family pyrin domain containing 3 (NLRP3) inflammasome, which mediates pro-inflammatory effects by triggering the release of cytokines such as interleukin (IL)-1β.[11]

Recent studies have frequently linked psoriasis with elevated SUA levels.[12–17] A hospital-based cross-sectional study revealed that psoriatic patients had higher SUA levels and a significantly greater prevalence of hyperuricemia compared with non-psoriatic patients.[15] Furthermore, hyperuricemia has been detected in 13.0% to 40.7% of psoriatic patients.[18] Increased uric acid synthesis, caused by keratinocyte hyperproliferation, has been implicated in the onset of elevated SUA levels in psoriatic patients. There is some evidence that psoriatic patients with hyperuricemia experience substantial improvement in psoriasis during treatment for hyperuricemia.[19]

Although the relationship between SUA and psoriasis has been explored, the impact of systemic psoriasis treatments on SUA levels in psoriatic patients has received limited attention.[20] It has been suggested that treatment with biologic agents can decrease the risk of systemic comorbidities in psoriatic patients. Biologics targeting IL-17A, such as secukinumab and ixekizumab, have demonstrated clinically significant therapeutic effects and safety in patients with moderate to severe plaque psoriasis.[21] Nowadays, IL-17A inhibitors are the most widely used biologics in China. In our previous use, we found by chance that SUA levels decreased in some psoriatic patients after treatment with IL-17A inhibitors after a period of time. A few studies have examined the impacts of tumor necrosis factor (TNF)-α inhibitors, IL-12/23 or IL-23 inhibitors on SUA. Thus far, limited data are available concerning the impact of IL-17A inhibitors on SUA levels, and they are retrospective, short-term, and the findings have been inconsistent. Thus, we investigated the impact of IL-17A inhibitors on SUA levels in psoriatic patients with hyperuricemia in this study. We also explored factors affecting the rate of change in SUA levels before and after treatment with IL-17A inhibitors. Additionally, we explored the risk factors for hyperuricemia in patients with psoriasis and the effectiveness of IL-17A inhibitors in treating psoriatic patients with hyperuricemia.

Methods

Study Design and Patients

This prospective observational study was conducted at Peking Union Medical College Hospital, Beijing, from April 2021 to September 2023. We enrolled adults with moderate to severe plaque psoriasis concurrent with hyperuricemia. The control group was adults with moderate to severe plaque psoriasis with normal serum uric acid level at baseline. Participants received IL-17A inhibitors and were followed up for one year. The primary endpoint was the change in SUA levels after one year of treatment. Secondary endpoints included the risk factors for hyperuricemia in patients with psoriasis and the effectiveness of IL-17A inhibitors in treating psoriatic patients with hyperuricemia.

Eligibility criteria included adults aged ≥18 years with moderate to severe plaque psoriasis (defined as affected body surface area [BSA] ≥3%) and a history of plaque psoriasis for at least 6 months prior to study inclusion, along with concomitant hyperuricemia (defined as an SUA level >416 μmol/L in men and >357 μmol/L in women) at baseline. Eligibility criteria of the control group included adults aged ≥18 years with moderate to severe plaque psoriasis and a history of plaque psoriasis for at least 6 months prior to study inclusion, along with normal serum uric acid level at baseline. Participants were excluded if they were currently receiving treatment with uric acid-lowering or uric acid-elevating medications, including allopurinol, febuxostat, ethambutol, and acitretin. Additionally, individuals with active infections, malignancies, inflammatory bowel diseases, or women who were pregnant or breastfeeding were also excluded from the study.

This study protocol was approved by the Peking Union Medical College Hospital Ethics Committee (ZS-2850, I-22PJ559), and the study was registered with the Chinese Clinical Trial Registry (ChiCTR2100045823). Informed consent was obtained from all participants. This study complied with the Declaration of Helsinki.

Data Collection and Outcome Definitions

Baseline characteristics were recorded, including demographic data (gender, age, weight, and BMI), psoriasis duration, nail involvement, Psoriasis Area and Severity Index (PASI), BSA, static Physician Global Assessment, previous psoriasis treatment history, comorbidities (hypertension and diabetes), and social history (alcohol consumption and smoking). Baseline assessments included a complete blood cell count; blood biochemistry; an infectious panel covering hepatitis B and C, human immunodeficiency virus, and T-SPOT.TB; and a chest X-ray. Patients then received either secukinumab (300 mg weekly for 5 weeks, followed by a monthly subcutaneous injection of 300 mg) or ixekizumab (160 mg at week 0, then 80 mg every other week for 12 weeks, followed by a monthly subcutaneous injection of 80 mg). Follow-up visits were scheduled at 1, 2, and 3 months, then quarterly for 1 year. Complete blood cell count and blood biochemistry were conducted biannually. Patients were required to fast for more than 12 hours before each biochemical test.

BMI was calculated as weight in kilograms divided by height in meters squared (kg/m2). Normal weight was defined as BMI ≥18.5 to <24 kg/m^2, overweight was defined as BMI ≥24 to <28 kg/m^2, and obesity was defined as BMI ≥28 kg/m^2. Hypertension was defined as blood pressure ≥140/90 mmHg and/or the receipt of treatment for hypertension. Hyperglycemia was defined as fasting blood glucose ≥6.1 mmol/L and/or the receipt of treatment for diabetes mellitus. Hypercholesterolemia was defined as total cholesterol ≥5.7 mmol/L and hypertriglyceridemia was defined as triglycerides ≥1.7 mmol/L. Alcohol use was defined as weekly intake of >150 mL of alcohol for at least 6 months, and smoking was defined as continuous daily tobacco use for at least 6 months.

The primary outcome was the changes in SUA level in psoriatic patients with hyperuricemia after 1 year of treatment with IL-17A inhibitors. The SUA reduction rate was defined as (baseline SUA – SUA after 1 year of treatment)/baseline SUA. Factors associated with SUA reduction rate were explored. Secondary outcomes included: 1) risk factors for hyperuricemia in psoriatic patients. For the analysis of hyperuricemia risk factors, a cohort of psoriatic patients undergoing IL-17A inhibitors with normal baseline SUA levels from our center was included. 2) effectiveness of IL-17A inhibitors for patients with psoriasis and hyperuricemia including PASI 75, 90, and 100 response rates at 1 year.

Statistical Analysis

For normally distributed continuous variables, means ± standard deviations were calculated, and intergroup differences were analyzed using two-tailed *t*-tests. Non-normally distributed continuous variables were summarized using medians (25th and 75th percentiles); intergroup differences were assessed using the Mann–Whitney *U*-test. Categorical variables were expressed as numbers (percentages), and intergroup differences were analyzed with the chi-squared test or Fisher's exact test. To compare changes in SUA levels before and after treatment, paired samples *t*-tests or the Wilcoxon signed-rank test were applied as appropriate. Missing data were limited to the 12-month SUA measurements for patients who discontinued after the 6-month follow-up. For these patients, their 6-month SUA measurements were carried forward to the 12-month time point using the last observation carried forward method. There were no missing values for other variables as complete baseline data collection was required for study enrollment. A sensitivity analysis excluding patients with missing data was performed to assess the robustness of our findings. Multiple linear regression analysis was utilized to explore factors affecting the SUA reduction rate. After excluding one outlier, we employed the enter method (also known as forced entry or simultaneous entry method) for variable inclusion in the multiple linear regression analysis. This method involves simultaneously entering all independent variables into the model without stepwise selection. To validate our findings regarding factors affecting SUA reduction rate, we conducted an additional sensitivity analysis including only patients who showed decreased SUA levels after treatment. Binary logistic regression was conducted to identify risk factors for hyperuricemia in psoriatic patients. Variables with statistical significance in univariate analyses and variables considered clinically meaningful were entered into the regression analysis. All data were analyzed using SPSS 26.0 software (SPSS Inc., Chicago, IL, USA). The threshold for statistical significance was set to $p<0.05$.

Results

Patient Disposition and Baseline Characteristics

Between April 2021 and September 2023, our study included 196 individuals diagnosed with psoriasis and hyperuricemia. Among them, 191 (97.4%) completed the one-year follow up, while 5 (2.6%) discontinued after the 6-month

follow-up for various reasons: 3 were lost to follow-up, 1 withdrew informed consent, and 1 switched to the IL-23 inhibitor.

Baseline characteristics of the patients are detailed in Table 1. In summary, 164 (83.7%) participants were men; the mean age was 41±12 years, with the majority being under 50 years of age (150 cases, 76.5%). The mean duration of

Table 1 Baseline Characteristics of the Participants

	Psoriatic Patients with Hyperuricemia at Baseline (n=196)	**Psoriatic Patients with Normal Serum Uric Acid Level at Baseline (n=171)**	***P* value**
Demographic data			
Sex, male	164 (83.7%)	111 (64.9%)	<0.001
Age, years	41±12	43±13	0.212
18–29	31 (15.8%)	23 (13.5%)	0.755
30–39	77 (39.3%)	64 (37.4%)	
40–49	42 (21.4%)	36 (21.1%)	
≥ 50	46 (23.5%)	48 (28.1%)	
Weight, kg	82.7±14.2	73.0±14.0	<0.001
BMI, kg/m^2	27.5±4.0	25.3±3.8	<0.001
Laboratory test results			
SUA, μmol/L	481±68	310±66	<0.001
TC, mmol/L	5.09±1.04	4.84±1.05	0.020
HDL-C, mmol/L	1.09±0.21	1.18±0.30	0.016
LDL-C, mmol/L	3.12±0.83	2.97±0.90	0.094
TG, mmol/L	1.96 (1.12, 2.91)	1.25 (0.86, 1.89)	<0.001
Psoriasis			
Psoriasis duration, years	13.9±10.0	15.6±9.7	0.102
PASI	17.0 (10.8, 25.0)	13.8 (9.0, 20.4)	0.003
BSA, %	17.5 (10.0, 30.0)	15.0 (10.0, 30.0)	0.110
sPGA (0–4)	3.4 (3.0, 4.0)	3.0 (3.0, 4.0)	0.103
Types of psoriasis			
Plaque psoriasis	191 (97.4%)	163 (95.3%)	0.426
Plaque with PsA	4 (2.0%)	8 (4.7%)	
Plaque with PPP	1 (0.5%)	0	
Nail involved	108 (63.2%)	87 (54.0%)	0.092
Family history of psoriasis	65 (33.2%)	59 (34.5%)	0.787
Previous psoriasis treatment history			
Traditional systemic therapy	66 (33.7%)	59 (34.5%)	0.867

(*Continued*)

Table 1 (Continued).

	Psoriatic Patients with Hyperuricemia at Baseline (n=196)	Psoriatic Patients with Normal Serum Uric Acid Level at Baseline (n=171)	*P* value
Acitretin	58 (29.6%)	51 (29.8%)	0.961
MTX	13 (6.6%)	16 (9.4%)	0.335
Cyclosporine	2 (1.0%)	2 (1.2%)	1.000
Phototherapy	61 (31.1%)	59 (34.5%)	0.491
Biologic agents	51 (26.0%)	31 (18.1%)	0.070
TNF-α inhibitors	50 (25.5%)	29 (17.0%)	0.047
IL-17 inhibitors	1 (0.5%)	1 (0.6%)	1.000
IL-12/23 inhibitors	0	1 (0.6%)	0.945
Comorbidity and social history			
Hypertension	50 (25.5%)	24 (14.0%)	0.006
Hyperglycemia	40 (20.4%)	31 (18.1%)	0.581
Alcohol consumption	32 (16.3%)	13 (7.6%)	0.011
Smoking	72 (36.7%)	57 (33.3%)	0.496
Therapy			
Secukinumab	175 (89.3%)	147 (86.0%)	0.355
Ixekizumab	21 (10.7%)	24 (14.0%)	0.333

Notes: Data are presented as mean ± standard deviation, median (25th, 75th percentile), or number (percentage) as appropriate. Differences between groups were analyzed using independent samples *t*-test for normally distributed continuous variables, Mann–Whitney *U*-test for non-normally distributed continuous variables, and chi-square test or Fisher's exact test for categorical variables.

Abbreviations: BMI, body mass index; BSA, body surface area; IL, interleukin; MTX, methotrexate; PASI, Psoriasis Area and Severity Index; PPP, palmoplantar pustular psoriasis; PsA, psoriatic arthritis; sPGA, static Physician Global Assessment; SUA, serum uric acid; TC, total cholesterol; TG, triglycerides; TNF-α, tumor necrosis factor-α.

psoriasis was 13.9±10.0 years, and median PASI was 17.0 (10.8, 25.0), Furthermore, 65 of these patients (33.2%) had a family history of psoriasis; 66 (33.7%) had used traditional systemic therapy, 61 (31.1%) had received phototherapy, and 51 (26.0%) had been treated with biologic agents, primarily TNF-α inhibitors. Hypertension was present in 50 patients (25.5%), and hyperglycemia was present in 40 patients (20.4%); 32 patients (16.3%) reported alcohol consumption, and 72 patients (36.7%) were smokers. In terms of treatment, 175 patients (89.3%) received secukinumab, whereas 21 patients (10.7%) received ixekizumab. The mean SUA levels at baseline were 481±68 μmol/L.

Primary Outcome

Changes in SUA Levels Before and After Treatment

After 1 year of IL-17A inhibitor treatment, SUA levels decreased in 139 patients (70.9%) and increased in 57 patients (29.1%). The mean SUA levels in the psoriatic patients with hyperuricemia were 481±68 μmol/L at baseline and 442 ±78 μmol/L after 1 year of treatment ($p<0.001$). Subgroup analysis revealed a consistent and significant decrease in SUA levels across different genders, age groups (30–39, 40–49, ≥50 years), BMI categories (normal, overweight, obese), baseline PASI scores (<10, 10–19.9, ≥20), PASI improvement rates (<75%, 75%-90%, ≥90%), and among patients treated with different IL-17A inhibitors (secukinumab, ixekizumab). However, the reduction in SUA levels in the 18–29

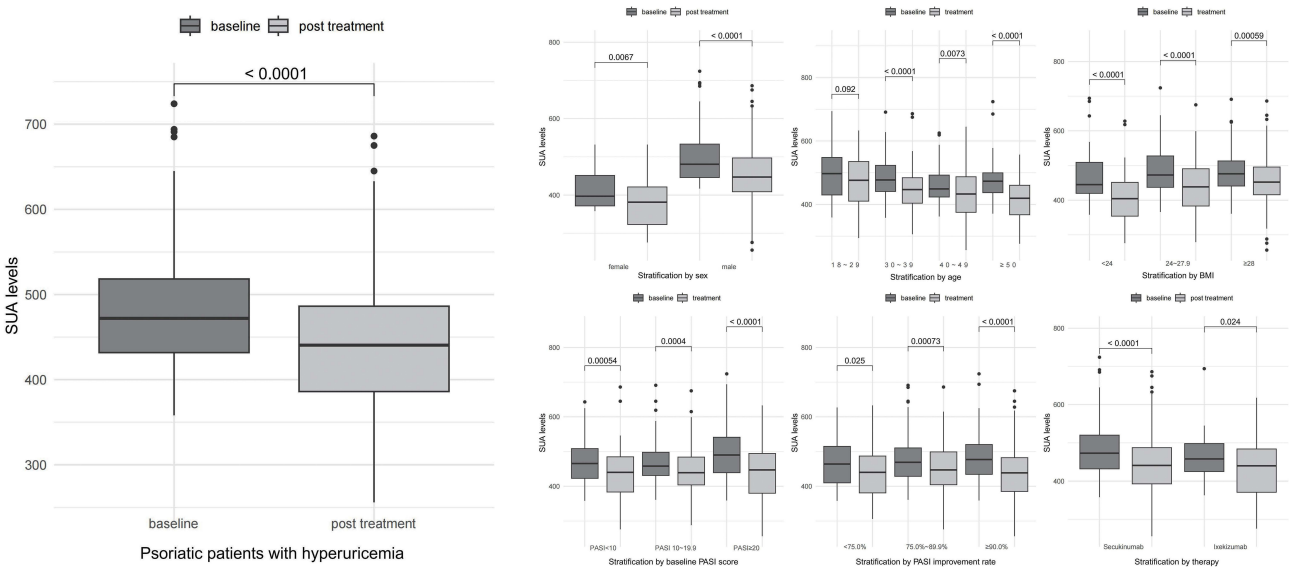

Figure 1 Impact of IL-17A inhibitors on SUA levels in psoriatic patients with hyperuricemia. Bar graphs showing mean serum uric acid levels (μmol/L) at baseline and after 1 year of IL-17A inhibitor treatment, stratified by sex, age, BMI, baseline PASI score, PASI improvement rate, and type of IL-17A inhibitor. BMI categories were defined according to Chinese criteria: normal (<24 kg/m²), overweight (24–27.9 kg/m²), and obesity (≥28 kg/m²). PASI improvement rate was calculated as [(baseline PASI - PASI after 1 year of treatment)/baseline PASI] × 100%. Error bars represent standard deviations. P values were calculated using paired samples *t*-test.
Abbreviations: BMI, body mass index; PASI, Psoriasis Area and Severity Index; SUA, serum uric acid.

years subgroup did not reach statistical significance post-treatment (494 vs 475, p=0.092). Detailed results are provided in Figure 1 and Table 2.

To assess the robustness of our findings, we performed a sensitivity analysis including only the 191 patients with complete 12-month SUA levels, excluding the 5 patients with missing data. The results from this complete-case analysis

Table 2 Impact of IL-17A Inhibitors on SUA Levels in Psoriatic Patients with Hyperuricemia

	SUA Level at Baseline (μmol/L)	SUA Level After 1 Year of Treatment (μmol/L)	SUA Reduction (μmol/L)	95% CI	*P* value
All patients (N=196)	481±68	442±78	39±70	29–49	<0.001
Sex					
Female (N=32)	413±51	382±62	31±60	9–52	0.007
Male (N=164)	494±63	453±75	41±72	30–52	<0.001
Age (years)					
18–29 (N=31)	494±87	475±93	20±63	−3–43	0.092
30–39 (N=77)	484±63	450±71	34±58	21–47	<0.001
40–49 (N=42)	465±61	434±72	32±73	9–55	0.007
≥50 (N=46)	481±69	413±73	68±83	43–92	<0.001
BMI (kg/m²)					
<24 (N=36)	471±86	411±82	59±75	34–85	<0.001
24–27.9 (N=76)	485±67	441±74	44±69	28–60	<0.001
≥28 (N=84)	482±61	456±75	26±67	12–41	<0.001

(*Continued*)

Table 2 (Continued).

	SUA Level at Baseline (μmol/L)	SUA Level After 1 Year of Treatment (μmol/L)	SUA Reduction (μmol/L)	95% CI	*P* value
Baseline PASI score					
<10 (N=36)	472±71	438±86	35±55	16–53	<0.001
10–19.9 (N=77)	472±60	444±69	27±66	13–43	<0.001
≥20 (N=83)	493±73	441±81	52±78	35–69	<0.001
PASI improvement rate (%)					
<75.0% (N=15)	467±74	438±92	29±44	4–53	0.025
75.0%–89.9% (N=63)	481±77	452±79	30±66	13–46	<0.001
≥90.0% (N=118)	482±63	437±75	45±74	32–59	<0.001
IL-17A inhibitors					
Secukinumab (N=175)	482±69	443±78	39±70	29–50	<0.001
Ixekizumab (N=21)	473±68	434±78	39±73	6–72	0.024

Notes: Data are presented as mean ± standard deviation. Changes in SUA levels were analyzed using paired samples *t*-test. BMI categories were defined according to Chinese criteria: normal (<24 kg/m²), overweight (24–27.9 kg/m²), and obesity (≥28 kg/m²). PASI improvement rate was calculated as [(baseline PASI - PASI after 1 year of treatment)/baseline PASI] × 100%.

Abbreviations: BMI, body mass index; CI, confidence interval; PASI, Psoriasis Area and Severity Index; SUA, serum uric acid.

were highly consistent with our primary analysis. In males (n=161), mean SUA levels decreased from 493±62 μmol/L at baseline to 452±74 μmol/L at 12 months (p<0.001). In females (n=30), mean SUA levels decreased from 408±47 μmol/L at baseline to 375±55 μmol/L at 12 months (p=0.006). Details are provided in Supplementary Table 1.

Given that male patients constituted the majority of our cohort (83.7%), we conducted a separate analysis focusing on male patients. As shown in Supplementary Table 2, the pattern of SUA reduction in male patients was consistent with our primary analysis. Male patients showed significant SUA reduction from 494±63 μmol/L at baseline to 453±75 μmol/L after one year of treatment (mean difference: 41±72 μmol/L, 95% CI: 30–52, p<0.001). Similar to the overall cohort, the SUA-lowering effect was most pronounced in male patients aged ≥50 years (mean difference: 72±88 μmol/L, p<0.001) and those with BMI <24 kg/m² (mean difference: 62±83 μmol/L, p<0.001).

A subgroup of 53 patients (27.0%) completed SUA measurements at all scheduled time points (baseline, 6 months, and 12 months). Repeated measures ANOVA, after confirming normal distribution (Shapiro–Wilk test), no outliers (box plot), and sphericity (Mauchly's test: $\chi 2=1.776$, P=0.411), showed significant changes in SUA levels over time (F=12.711, P<0.001). The mean±SD SUA levels decreased from 490±83 μmol/L at baseline to 449±80 μmol/L at 6 months (mean difference: 41 μmol/L, p<0.001) and 445±82 μmol/L at 12 months (mean difference: 45 μmol/L, p<0.001 vs baseline), while the change between 6 and 12 months was minimal (mean difference: 4 μmol/L, p=1.000). This pattern, as illustrated in Supplementary Figure 1, indicates that the major SUA-lowering effect occurs within the first 6 months and then stabilizes.

Factors Affecting the SUA Reduction Rate

To further investigate which patients experienced the most notable reductions in SUA levels, multiple linear regression analysis was employed. The dependent variable was the SUA reduction rate, with the independent variables including gender, age (referencing 18–29 years), BMI (referencing ≥28), and PASI improvement rates (referencing <75%). The analysis confirmed the absence of multicollinearity among the independent variables, independence of observations, normally distributed residuals with homogeneity of variance, and no high leverage or influential points. After excluding one outlier, we employed the enter method for variable inclusion. The final model was statistically significant, with an

F-value of 3.578, p=0.001, R^2 of 0.118, and an adjusted R^2 of 0.085. Age and BMI emerged as statistically significant predictors. Specifically, patients aged ≥50 years exhibited a 10% higher SUA reduction rate compared to the 18–29 years reference group (95% CI 0.04–0.16, *p*=0.001). Additionally, those with a BMI <24 demonstrated an 8% higher SUA reduction rate than obese patients (95% CI 0.02–0.13, *p*=0.004). Gender and PASI improvement rates did not reach statistical significance. Details are provided in Table 3.

To validate these findings, we conducted an additional sensitivity analysis including only the 139 patients who showed decreased SUA levels after treatment. After excluding one outlier, the results remained consistent: age ≥50 years (B=0.08, 95% CI: 0.03–0.14, p=0.003) and BMI <24 (B=0.06, 95% CI: 0.02–0.11, p=0.008) remained significant predictors, with the model's R^2 increasing to 0.147 (adjusted R^2=0.101). Details are provided in Supplementary Table 3.

Secondary Outcomes

Risk Factors for Hyperuricemia in Psoriatic Patients

From April 2021 to September 2023, our center also enrolled 171 patients diagnosed with plaque psoriasis for IL-17A inhibitor therapy, all of whom exhibited normal baseline SUA levels. Univariate analysis showed that male gender, hypertension, and alcohol consumption were significantly more prevalent in patients with hyperuricemia compared to those with normal SUA levels. Additionally, body weight, BMI, SUA level, blood triglycerides level, and PASI were significantly higher among patients with hyperuricemia than among patients with normal SUA levels. Key baseline population characteristics are detailed in Table 1.

Binary logistic regression analysis was used to explore risk factors for hyperuricemia in psoriatic patients. The model included ten independent variables: gender, age (with ≥50 years as the reference), BMI (with <24 as the reference),

Table 3 Factors Affecting Uric Acid Reduction Rate Before and After IL-17A Inhibitor Treatment

Independent Variables	Unstandardized Coefficients			Standardized Coefficients (Beta)	*P* value
	B	Standard Error	95% CI for B		
Sex, male	0.02	0.03	−0.03–0.07	0.05	0.502
Age, years					
18–29	Ref				
30–39	0.04	0.03	−0.01–0.10	0.16	0.117
40–49	0.03	0.03	−0.04–0.09	0.08	0.407
≥50	0.10	0.03	0.04–0.16	0.32	<0.001
BMI					
≥28.0	Ref				
<24.0	0.08	0.03	0.02–0.13	0.22	0.005
24.0–27.9	0.04	0.02	−0.002–0.08	0.14	0.063
PASI improvement rate					
<75.0%	Ref				
75.0%–89.9%	−0.02	0.04	−0.10–0.05	−0.08	0.520
≥90.0%	0.01	0.04	−0.07–0.08	0.02	0.897

Notes: Multiple linear regression analysis was performed with serum uric acid (SUA) reduction rate as the dependent variable. SUA reduction rate was defined as (baseline SUA - SUA after 1 year of treatment)/baseline SUA. Reference categories: female for sex, age 18–29 years, BMI ≥28.0, and PASI improvement <90%. BMI categories were defined according to Chinese criteria: normal (<24 kg/m²), overweight (24–27.9 kg/m²), and obesity (≥28 kg/m²). PASI improvement rate was calculated as [(baseline PASI - PASI after 1 year of treatment)/baseline PASI] × 100%. The model was statistically significant (F=3.578, p=0.001) with R^2=0.118 and adjusted R^2=0.085.

Abbreviations: BMI, body mass index; CI, confidence interval; PASI, Psoriasis Area and Severity Index.

baseline PASI score (with <10 as the reference), hypertriglyceridemia (with triglycerides <1.7 mmol/L as the reference), hypercholesterolemia (with total cholesterol <5.7 mmol/L as the reference), hypertension, diabetes, smoking, and alcohol consumption. Employing a forward stepwise (likelihood ratio) approach, the final logistic model was statistically significant, with a chi-square value of 73.00 (p<0.001). This model identified male gender, age under 40 years, obesity, hypertension, hypertriglyceridemia, and a PASI score of ≥20 as independent factors associated with increased odds of hyperuricemia in patients with psoriasis. Specifically, male patients had a 1.88 times higher odds of hyperuricemia compared to female patients (95% CI: 1.09–3.25, p=0.024). Patients aged 18–29 years had a 3.62 times higher odds compared to those aged ≥50 years (95% CI: 1.51–8.70, p=0.004), and those aged 30–39 had a 2.24 times higher odds (95% CI: 1.06–4.71, p=0.034). Obese patients had a 2.54 times higher odds compared to those with a normal BMI (95% CI: 1.32–4.88, p=0.005). Patients with hypertension had a 3.36 times higher odds than those without (95% CI: 1.55–7.30, p=0.002), and those with hypertriglyceridemia had a 2.38 times higher odds compared to those with normal triglyceride levels (95% CI: 1.47–3.85, p<0.001). Patients with a PASI score of ≥20 had a 2.60 times higher odds than those with a PASI score of <10 (95% CI: 1.41–4.80, p=0.002). Smoking, alcohol consumption, hyperglycemia and hypercholesterolemia were not identified as statistically significant risk factors. Further details are included in Figure 2.

Among 171 psoriatic patients with normal baseline SUA levels receiving IL-17A inhibitor treatment, 136 (79.5%) completed one-year SUA measurements. The paired t-test results showed no significant changes in SUA levels after one year of IL-17A inhibitor treatment in either male patients (baseline: 345±61 μmol/L vs one year: 351±75 μmol/L, p=0.210) or female patients (baseline: 285±44 μmol/L vs one year: 292±59 μmol/L, p=0.347). Details are presented in Supplementary Table 4.

Effectiveness of IL-17A Inhibitors for Psoriatic Patients with Hyperuricemia

The PASI 75, 90, and 100 response rates in psoriatic patients with hyperuricemia were 88.3%, 60.2%, and 28.6%, respectively, after 1 year of treatment with IL-17A inhibitors. While the PASI 75, 90, and 100 response rates in psoriatic patients with

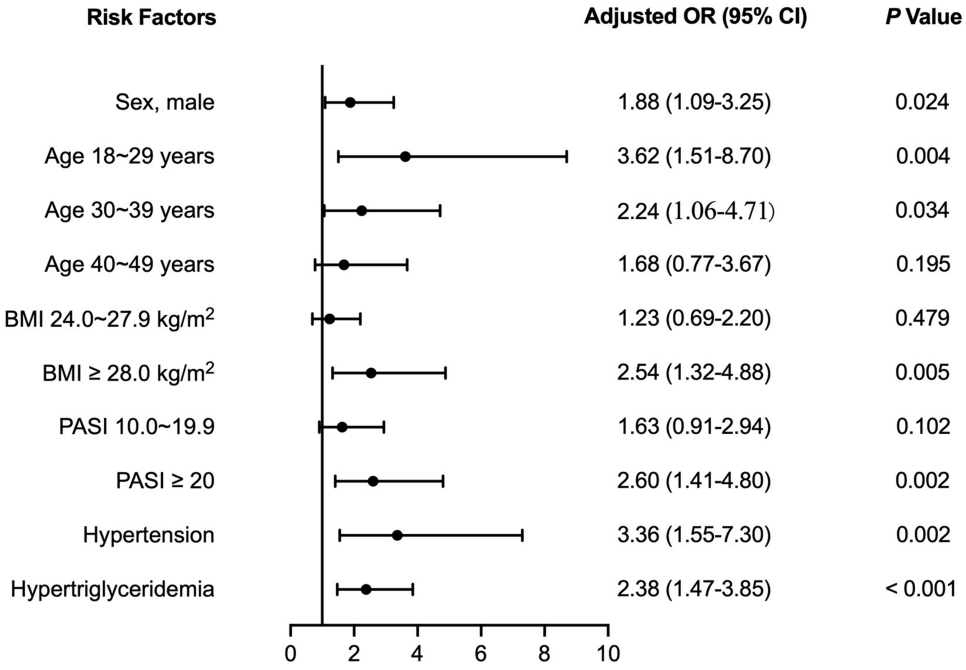

Figure 2 Risk factors for hyperuricemia in psoriatic patients. Forest plot showing odds ratios (OR) and 95% confidence intervals (CI) from binary logistic regression analysis. The initial model included 10 independent variables: sex, age (reference: ≥50 years), BMI (reference: <24 kg/m²), baseline PASI score (reference: <10), hypertriglyceridemia (reference: triglycerides <1.7 mmol/L), hypercholesterolemia (reference: total cholesterol <5.72 mmol/L), hypertension, diabetes, smoking, and alcohol consumption. BMI categories were defined according to Chinese criteria: normal (<24 kg/m²), overweight (24–27.9 kg/m²), and obesity (≥28 kg/m²). Using forward stepwise (likelihood ratio) method, the final model identified six significant predictors and was statistically significant (chi-square=73.00, p<0.001).
Abbreviations: BMI, body mass index; PASI, Psoriasis Area and Severity Index.

normal SUA level at baseline were 87.1%, 58.5%, and 32.2%, respectively, after 1 year of treatment with IL-17A inhibitors. There was no significant difference in the response rates between the two groups (p=0.402, 0.503, 0.194, respectively).

Discussion

This study revealed a significant decrease in SUA levels among psoriatic patients with hyperuricemia after 1 year of IL-17A inhibitor treatment. This finding was consistent regardless of gender, age, BMI, baseline PASI, and PASI improvement rate. Moreover, we found that age and BMI emerged as statistically significant predictors. Specifically, patients aged ≥50 years and with a BMI <24 exhibited a higher SUA reduction rate. Male gender, age under 40 years, obesity, hypertension, hypertriglyceridemia, and a PASI score of ≥20 were identified as independent factors associated with increased odds of hyperuricemia in patients with psoriasis. Notably, there was no significant difference in PASI response rates between patients with normal SUA levels and patients with hyperuricemia who received IL-17A inhibitors for 1 year, indicating that hyperuricemia did not impact the treatment efficacy.

Elevated SUA levels and hyperuricemia have frequently been observed in psoriatic patients.[14,22] A meta-analysis of 27 studies revealed that SUA levels and hyperuricemia frequency were significantly higher in the psoriasis group than in the control group, regardless of stratification by region, gender, and metabolic disease status. Additionally, SUA levels were higher in patients with erythrodermic or arthritic psoriasis than in the control group.[23] Merola et al[13] reported that psoriasis was associated with an increased risk of gout in a prospective cohort study of 27,751 men and 71,059 women in the United States. In a case-control study of 119 psoriatic patients, Gisondi et al[24] demonstrated that psoriasis was a strong predictor of hyperuricemia, despite adjustments for age, gender, and metabolic syndrome status. Finally, Tsuruta et al[25] suggested that elevated SUA levels constituted an independent risk factor for psoriatic arthritis.

Previous studies have explored factors that may affect SUA levels in psoriatic patients. The present study showed that male gender, age under 40 years, obesity, hypertension, hypertriglyceridemia, and a PASI score of ≥20 were identified as independent factors associated with increased odds of hyperuricemia in patients with psoriasis. These results support previous findings that elevated SUA levels and hyperuricemia were positively associated with obesity and hypertriglyceridemia.[14,24,26–28] Although the specific mechanism of hypertriglyceridemia and hyperuricemia has not been elucidated. Some scholars have suggested that it may be due to the disorder of free fatty acids metabolism caused by triglyceride, as the increase of triglyceride leads to increased free fatty acid production. Accelerating the decomposition of adenosine triphosphate, which leads to an increase in uric acid, the end product of purine metabolism. Some studies have shown that the synthesis of fatty acids in the liver is linked to the synthesis of the de novo purine and the accelerated production of urea. The effects of triglyceride metabolic disorder on hyperuricemia remain to be further elucidated. Similarly, Lai et al reported that SUA levels were positively correlated with BMI (p<0.001); overweight status exhibited the strongest correlation with hyperuricemia among patients with psoriatic arthritis (p<0.001).[29] In contrast, Gisondi et al found no associations between SUA levels and age, gender, or PASI among patients with psoriatic arthritis.[29,30] The relationship of SUA with psoriasis severity remains a topic of debate. Notably, many studies have shown a positive association between PASI values and SUA levels or hyperuricaemia.[1,16,23,24,31–34] For example, in a case-control study of 119 psoriatic patients, Gisondi et al found that psoriatic patients with PASI values ≥10 had significantly higher SUA levels compared with psoriatic patients who had PASI values <10.[24] In the present study, we found that a PASI score of ≥20 was associated with increased odds of hyperuricemia in patients with psoriasis. Patients with a PASI score of ≥20 had a 2.60 times higher odds than those with a PASI score of <10. However, some published studies have shown no relationship between SUA levels and PASI values.[1,14,18,22]

Other factors potentially affecting SUA levels in psoriatic patients include age, ethnicity, regional characteristics, and alcohol consumption. Older age, male gender, and Black ethnicity are recognized risk factors for hyperuricemia.[35,36] In contrast, Kwon et al[16] found that SUA levels in psoriatic patients were not significantly correlated with age, age at psoriasis onset, or family history of psoriasis. Zhang et al[23] revealed that patients with moderate to severe psoriasis from European and American regions, as well as Southeast Asia, were more likely to exhibit hyperuricemia. Moreover, Choi et al reported that SUA levels increased with increasing alcohol intake, presumably because alcohol raises SUA levels by enhancing uric acid production and reducing urinary excretion.[37] Intriguingly, we identified hypertension as a factor

associated with increased odds of hyperuricemia in psoriatic patients; to our knowledge, this relationship has not been reported in previous literature.

In the present study, we found that SUA levels decreased significantly among psoriatic patients with hyperuricemia after 1 year of treatment with IL-17A inhibitors. Subgroup analysis showed consistent and significant reductions in SUA levels regardless of gender, age, BMI, baseline PASI, and PASI improvement rate. Our results are consistent with findings by Tamer et al,[20] who detected a statistically significant decrease in SUA levels among patients treated with ixekizumab and secukinumab for 3 months. However, their study was retrospective and short-term, with a small sample size. Similarly, Zhao et al[22] observed that SUA levels decreased among patients with plaque psoriasis who received secukinumab for 48 weeks. Moreover, Gerdes et al[2] reported that SUA levels decreased in patients with plaque psoriasis during 52 weeks of treatment with secukinumab; this finding was present in the overall population and in patients with elevated baseline SUA levels. However, there have been conflicting results. For example, Karataş et al[38] found no significant change in SUA levels between 0 and 6 months among patients receiving secukinumab, and Hagino et al[32] noted that SUA levels did not significantly change after treatment with IL-17 inhibitors.

To our knowledge, relatively few studies have examined the impacts of IL-12/23 or IL-23 inhibitors on SUA. One study revealed that SUA levels were lower among psoriatic patients after 3 months of treatment with ustekinumab ($p<0.001$). However, there were no significant changes in SUA levels after 3 months of treatment with risankizumab ($p<0.182$) or guselkumab ($p<0.786$).[20] Hagino et al[32] also reported no significant change in SUA levels after treatment with ustekinumab, guselkumab, and risankizumab. Importantly, studies regarding the effects of TNF-α inhibitors on SUA have revealed greater variation. Hagino et al[32] reported that SUA levels were decreased after 12 weeks of treatment with adalimumab and after 52 weeks of treatment with all TNF-α inhibitors (eg, adalimumab, infliximab, and certolizumab pegol). The variability in these findings could be partially attributed to small sample sizes and uneven distribution among the treatments—infliximab, adalimumab, and certolizumab pegol were administered to 28, 17, and 11 patients, respectively. Similarly, Tamer et al[20] found that SUA levels were decreased in psoriatic patients after 3 months of treatment with adalimumab ($p<0.001$) or infliximab ($p<0.002$). In contrast, Zhao et al[22] reported no significant change in SUA levels among patients with plaque psoriasis who received adalimumab for 48 weeks.

The mechanism contributing to hyperuricemia susceptibility in psoriatic patients remains unclear. Goldman[19] speculated that the accelerated replacement rate of keratinocytes in psoriatic patients leads to increased DNA formation and purine synthesis, causing excessive uric acid production and elevated SUA levels. Furthermore, urate crystals (a type of alarmin) activate innate immunity through NALP inflammasomes, enhancing the production of cytokines such as IL-1 and IL-8. Uratsuji et al[39] confirmed that epidermal keratinocytes cultured with uric acid crystals form NALP inflammasomes and produce large amounts of TNF-α, IL-1a, IL-8/chemokine (CXC motif) ligand 8, and IL-6. These cytokines play important roles in the pathogenesis of psoriasis. Elevated SUA levels are positively correlated with several pro-inflammatory markers, such as white blood cell count and the levels of CRP, IL-17, IL-6, and TNF-α.[40] These findings suggest that psoriasis increases SUA levels, and urate crystals may further promote psoriasis development. There is some evidence that psoriatic patients with hyperuricemia experience substantial psoriasis improvement during treatment for hyperuricemia.[19]

IL-17A inhibitor treatment leads to a decrease in SUA levels through an unclear mechanism. IL-17, a pro-inflammatory cytokine mainly produced by Th17 cells and type 3 innate lymphoid cells upon stimulation by cytokines such as IL-6 or IL-1, promotes the production of other cytokines and chemokines that enhance inflammation. IL-17 plays a key role in the development of psoriasis, and serum IL-17 levels decrease after psoriasis treatment.[40] Recently, a novel IL-17 signaling pathway was identified downstream of uric acid in a hyperuricemic rat model. In particular, long-term injection of uric acid induced robust IL-17 production and Th17 cell recruitment. Administration of an anti-IL-17 monoclonal antibody attenuated uric acid-induced kidney injury in experimental rats through a mechanism involving nuclear factor-κB inactivation.[41] However, it is unclear whether urinary UA excretion increases after IL-17 inhibitor treatment. A recent randomized, double-blind, placebo-controlled pilot study showed positive correlations of SUA levels with IL-6, IL-17, and TNF-α.[42] Based on the above theoretical considerations and experimental data, we hypothesize that there are two main reasons why IL-17A inhibitors can reduce SUA levels. First, IL-17A inhibitors substantially alleviate psoriasis severity, normalize the rate of keratinocyte replacement, and decrease the purine decomposition that contributes to uric acid production, leading to lower SUA levels. Second, IL-17A inhibitors significantly reduce the serum levels of

pro-inflammatory cytokines such as IL-17, IL-6, and TNF-α, leading to decreased levels of alarmins (eg, urate crystals) and lower SUA levels. Some of the alarmins are derived from keratinocytes with enhanced turn-over. Other possible factors include changes in body weight and metabolic status after treatment with IL-17A inhibitors.

There were no significant differences in PASI 75, 90, and 100 response rates between psoriatic patients with and without hyperuricemia after 1 year of treatment with IL-17A inhibitors, indicating that SUA levels did not impact treatment efficacy. Similarly, Hagino et al[32] found no significant correlations between percentage changes in SUA and percentage reductions in PASI after treatment with TNF-α inhibitors or IL-17 inhibitors. These results indicate that the effects of TNF-α inhibitors and IL-17 inhibitors on SUA may not directly correspond to their effects on psoriatic lesions.

This study had some notable strengths. First, it was a single-center prospective observational study with a large sample size, which provided sufficient power for binary logistic regression analysis and multiple linear regression analysis. Second, we identified age and BMI as significant predictors affecting the SUA reduction rate before and after treatment with IL-17A inhibitors, which is a novel finding. For psoriatic patients with concurrent hyperuricemia, IL-17A inhibitors might be particularly beneficial, especially in those aged ≥50 years or with BMI <24, due to their enhanced SUA-lowering effect. Regular monitoring of SUA levels during treatment may help track this additional benefit and guide overall patient management. Nevertheless, this study also had some limitations. First, we could not eliminate the confounding effects of medications for other comorbid conditions, such as insulin, because some patients were taking these medications when they received biologic treatments. Second, there was a selection bias towards greater disease severity because the study was conducted in a tertiary medical center. Third, we acknowledge that our analysis of factors associated with hyperuricemia has limitations in terms of generalizability. Since our study population was restricted to patients with moderate to severe plaque psoriasis (defined as affected body surface area ≥3%) who were candidates for IL-17A inhibitor therapy, the identified factors may not be representative of the broader psoriasis population, including those with mild disease or other types of psoriasis. Future studies including patients across all severity levels and various types of psoriasis would be valuable to establish a more comprehensive understanding of hyperuricemia in the general psoriasis population. Fourth, our study was limited by the lack of complete intermediate time point data for SUA measurements. The well-established safety profile of IL-17A inhibitors, which typically do not require frequent biochemical monitoring, contributed to reduced adherence to the study protocol's scheduled laboratory tests. Analysis of patients with complete data showed that the SUA-lowering effect mainly occurred in the first 6 months and then stabilized. Future studies with more frequent and systematic SUA measurements would be valuable to confirm this temporal pattern in a larger population. Finally, the effects of IL-17A inhibitors on SUA metabolism may be variable and susceptible to disruption by other factors, such as diet, alcohol consumption, medications, and other comorbid conditions. Therefore, a comprehensive, multicenter, long-term (eg, 5 years) prospective study is warranted to examine the relationship between psoriasis and SUA levels.

This study highlighted the impact of IL-17A inhibitors on SUA levels in psoriatic patients with hyperuricemia. The present results support several recommendations. First, treatment with IL-17A inhibitors may be a useful treatment option for psoriatic patients with hyperuricemia. Our results indicated that patients aged ≥50 years and with a BMI <24 experienced greater reductions in SUA levels and increased benefits during IL-17A inhibitor treatment. Second, considering that elevated SUA levels independently predict the risk of cardiovascular disease events and mortality,[24,43] early detection of hyperuricemia is important in psoriasis management. We recommend that all psoriatic patients routinely undergo SUA screening, with increased frequency for patients with factors identified in this study that are associated with increased odds of hyperuricemia: male gender, age under 40 years, obesity, hypertension, hypertriglyceridemia, and a PASI score of ≥20. Third, to reduce the risk of hyperuricemia, psoriatic patients (especially men) should be advised to carefully manage their diet and weight. Education regarding a low-purine diet is essential for psoriatic patients. Long-term dietary exposure to alcohol, red meat, seafood, and sugar-sweetened beverages can increase the likelihood of hyperuricemia.[44,45]

Conclusion

In this single-center prospective observational study, we found that SUA levels were significantly decreased in psoriatic patients with hyperuricemia after 1 year of IL-17A inhibitor treatment. Additionally, we noted that patients aged ≥50

years and with a BMI <24 experienced greater reductions in SUA levels during IL-17A inhibitor treatment. Our findings provide a theoretical basis to support the selection of biologic treatments for psoriatic patients with hyperuricemia; large-scale interventional clinical trials are needed to confirm the long-term efficacy of IL-17 inhibitor treatment in such patients. Considering that elevated SUA levels have been associated with increased risks of cardiovascular disease, metabolic syndrome, and adverse cardiovascular outcomes, hyperuricemia monitoring should be a key aspect of psoriasis management. Future research should aim to establish a comprehensive understanding of the connections between psoriasis comorbidities and hyperuricemia or SUA levels, with the goals of preventing additional comorbidities and disease progression.

Data Sharing Statement

No additional unpublished data are available.

Ethics Statement

This study protocol was approved by the Peking Union Medical College Hospital Ethics Committee (ZS-2850, I-22PJ559), and the study was registered with the Chinese Clinical Trial Registry (ChiCTR2100045823). Informed consent was obtained from all participants.

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Disclosure

The authors report no conflicts of interest in this work.

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