Effects of adalimumab and secukinumab on comorbidities associated with metabolism in patients with plaque psoriasis

Si Zhang[1], Lin Cai[1], Heng Zhang[1], Zheng Zhao[1,2], Xiaoyang Liu[1], Yan Zhao[1], Jianzhong Zhang[1]

[1]Department of Dermatology, Peking University People's Hospital, Beijing 100044, China;
[2]Department of Dermatology, Peking University International Hospital, Beijing 102206, China.

To the Editor: Psoriasis is often associated with comorbidities such as cardiovascular diseases, obesity, and metabolic syndrome (MS). However, the prevalence of abovementioned diseases in Chinese patients with plaque psoriasis is still unknown. Recently, biologics such as tumor necrosis alpha inhibitors, interleukin-17A inhibitors have been successfully used in the treatment of plaque psoriasis. However, the effects of biological treatment on comorbidities associated with metabolism are still controversial. Study on the relationship between the comorbidities associated with metabolism and plaque psoriasis and the effects of biologics are necessary.

The study protocol was approved by the Ethics Committee of Peking University People's Hospital (No. 2021PHB045). In this retrospective cohort study, the sample size was first calculated using PASS software version 15.0.5 (Power Analysis and Sample Size, NCSS, Kaysville, UT, USA). Using a two-sided significance (alpha) of 0.05, a 1:1 group allocation ratio was performed and the non-response rate was 20%. A total of 348 participants (174 patients and 174 controls) were needed for a 90% power to reject the null hypothesis using a two-sample unequal-variance *t* test. The clinical records of 191 healthy Chinese adults and 189 adult patients with plaque psoriasis consulted from January 2019 to December 2020 were then evaluated.

Patients did not take drugs that regulate blood pressure, blood lipids, and blood sugar within 12 weeks. Patients undergoing systemic therapy within 12 weeks, including hormones, actinides, cyclosporine, methotrexate, and others, including phototherapy, photochemotherapy, biological agents, and so on, dyslipidemia, hyperglycemia, and hypertension caused by other reasons, including serious endocrine system diseases, such as hypothyroidism and Cushing syndrome were excluded. Clinical information including demographic characteristics, disease duration, history of comorbidities, physical examination, and blood biochemistry analysis was performed at the first visit. The 189 patients with plaque psoriasis were divided into three groups, receiving adalimumab, secukinumab or conventional treatment, respectively. Physical examination and blood biochemistry analysis were performed at baseline, 24, and 48 weeks, respectively.

In this study, all statistical analyses were performed using SPSS 24.0 (IBM Corp, Armonk, NY, USA). Continuous variables with normal distribution were expressed as mean ± standard deviation. Categorical variables were summarized as counts (percentages). The independent-sample *t* test was used to compare the psoriasis group and the control group, mild-to-moderate psoriasis and severe psoriasis, and the relationship between psoriasis and multiple variables. The paired-sample *t* test was used to compare the changes of MS and related indicators at baseline, weeks 24 and week 48 of biological treatment. Missing data were filled by the last observation carried forward (LOCF) method. P value < 0.05 was considered statistically significant.

The subjects in our study included a total of 189 patients (mean age 40.20 ± 11.87 years) with plaque psoriasis (64 with mild/moderate (body surface area [BSA] < 10%), and 125 with severe psoriasis (BSA ≥ 10%) and 191 healthy (mean age 40.81 ± 10.14 years) controls). Sixty-four patients with severe psoriasis were treated with adalimumab, and 58 patients with severe psoriasis were treated with secukinumab.

By comparing the case group with the control group, we found the relationship between psoriasis and comorbidities associated with metabolism. The prevalence of MS in 16.9% of patients with psoriasis was significantly higher compared to controls (6.8%, $P = 0.002$). A significant difference in the prevalence of overweight/obesity was observed between psoriasis and control groups (55.6% and 40.3%, $P = 0.003$). A significant difference in the

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Correspondence to: Prof. Lin Cai, Department of Dermatology, Peking University People's Hospital, No. 11. Xizhimen South St, Beijing 100044, China
E-Mail: scailin66@hotmail.com

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prevalence of hypertension was observed between psoriasis and control groups (22.2% and 11.5%, $P = 0.005$). A significant difference in the prevalence of diabetes was observed between psoriasis and control groups (15.3% and 6.3%, $P = 0.001$). Lastly, a significant difference in the prevalence of low–high-density lipoprotein cholesterol (HDL-C) was observed between psoriasis and control groups (18.5% and 9.9%, $P = 0.017$). The results were not related to the severity of psoriasis (Supplementary Table 1, http://links.lww.com/CM9/B45).

A total of 64 patients were treated with adalimumab, the prevalence of hypercholesterolemia was 3.1% at baseline, 10.9% at week 24, and 12.5% at week 48, which was statistically significant compared with baseline ($P = 0.024$ and $P = 0.033$). The prevalence of hypertriglyceridemia was 28.1% at baseline, and 42.2% at week 48, which was statistically different compared with baseline ($P = 0.028$). Furthermore, adalimumab had no significant effect on body mass index (BMI), blood glucose, and blood pressure of patients with psoriasis [Table 1]. A total of 58 patients received secukinumab, the prevalence of hypertriglyceridemia was 31.0% in patients with psoriasis at baseline, 44.8% at week 24, and 53.4% at week 48, which was statistically different compared with baseline ($P = 0.010$ and $P = 0.001$). Secukinumab had no significant effect on BMI, blood glucose, and blood pressure of patients with psoriasis [Table 1].

Approximately 20% to 30% of adults suffer from MS, one of the leading causes of death worldwide.[1] In 2018, it was reported that the prevalence of MS in Chinese adults was 9.82%. Data showed that the prevalence of MS was higher in patients with psoriasis compared to the general population. The correlation between MS and the severity of psoriasis was controversial. According to previous reports, MS, obesity, hypertriglyceridemia, and hyperglycemia were more prevalent in patients with severe psoriasis. Our study did not show this association, which might be due to differences in gender, age, race, genetic background, and lifestyle.

Zhang *et al*[2] reported that the prevalence of being overweight and obesity in Chinese adults was 28.1% and 5.2%, respectively ($N = 441,306$). In our study, the prevalence of overweight/obesity in patients with plaque psoriasis was higher than that of the general population, which was consistent with the results of reported studies. However, it was reported that patients who underwent bariatric surgery had a significantly lower risk for psoriasis and psoriatic arthritis.

In an epidemiological survey, it was shown that the prevalence of hypertension was 23.2% in Chinese adults. In our study, the prevalence of hypertension in the general population was 11.5%, which was significantly higher in patients with psoriasis (22.2%). We demonstrated that hypertension was not associated with the severity of psoriasis, which reflected previous findings. Previous studies showed a paradoxical association between hypertension and psoriasis.

It has been reported that diabetes was more prevalent in psoriatic patients. Zhang *et al*[3] reported that the prevalence of diabetes in Chinese adults was 6.3%. In our study, the prevalence of diabetes in patients with psoriasis was higher than that in the general population (15.3% *vs*. 6.3%); the underlying mechanism is still unknown. Do Vale Moreira *et al*[4] showed that hyperglycemia and insulin resistance caused chronic damage to the cardiovascular system. Therefore, controlling glucose levels in patients with psoriasis is important for preventing cardiovascular events.

Table 1: Clinical characteristics before and after treatment with adalimumab and Secukinumab.

	Adalimumab					Secukinumab				
Variables	**Baseline**	**Week 24**	**Week 48**	***P* 1**	***P* 2**	**Baseline**	**Week 24**	**Week 48**	***P* 1**	***P* 2**
Patients, *n* (M/F)	64 (41/23)	58 (39/19)	44 (30/14)	–	–	58 (48/10)	58 (48/10)	53 (45/8)		
BMI (kg/m^2), mean ± SD	25.93 ± 5.12	26.01 ± 5.08	26.15 ± 4.68	0.659	0.766	25.28 ± 3.57	26.10 ± 3.51	26.36 ± 2.62	0.710	0.883
Overweight/obesity, *n* (%)	35 (54.7)	35 (54.7)	37 (57.8)	1.000	0.658	33 (56.9)	34 (58.6)	39 (67.2)	0.473	0.172
Hypertension, *n* (%)	14 (21.9)	6 (9.4)	12 (18.8)	0.031	0.531	8 (13.8)	5 (8.6)	14 (24.1)	0.182	0.083
Blood glucose (mg/L), mean ± SD	5.68 ± 2.35	5.93 ± 3.13	5.62 ± 2.47	0.243	0.658	5.66 ± 1.82	5.79 ± 1.75	5.67 ± 1.92	0.171	0.917
Diabetes, *n* (%)	10 (15.6)	10 (15.6)	9 (14.1)	1.000	0.568	10 (17.2)	12 (20.7)	10 (17.2)	0.322	1.000
TC (mg/L), mean ± SD	4.76 ± 0.74	4.86 ± 0.91	4.85 ± 0.99	0.193	0.290	4.64 ± 0.86	4.65 ± 0.80	4.79 ± 0.98	0.913	0.069
Hypercholesterolemia, *n* (%)	2 (3.1)	7 (10.9)	8 (12.5)	0.024	0.033	3 (5.2)	3 (5.2)	6 (10.3)	1.000	0.182
TG (mg/L), mean ± SD	1.59 ± 1.26	1.98 ± 2.03	2.38 ± 5.20	0.014	0.158	1.60 ± 0.76	1.97 ± 1.17	2.08 ± 1.23	<0.001	<0.001
Hypertriglyceridemia, *n* (%)	18 (28.1)	21 (32.8)	27 (42.2)	0.443	0.028	18 (31)	26 (44.8)	31 (53.4)	0.010	0.001
HDL-C (mg/L), mean ± SD	1.19 ± 0.37	1.17 ± 0.25	1.19 ± 0.25	0.687	0.931	1.12 ± 0.32	1.16 ± 0.27	1.13 ± 0.25	0.124	0.579
Low HDL-C, *n* (%)	10 (15.6)	10 (15.6)	6 (9.4)	1.000	0.251	15 (25.9)	12 (20.7)	14 (24.1)	0.260	0.766
LDL-C (mg/L), mean ± SD	3.09 ± 0.63	3.09 ± 0.66	3.14 ± 0.76	0.981	0.494	2.89 ± 0.71	2.78 ± 0.69	2.85 ± 0.77	0.105	0.612
High LDL-C, *n* (%)	5 (7.8)	4 (6.3)	6 (9.4)	0.658	0.709	5 (8.6)	2 (3.4)	4 (6.9)	0.260	0.234
MS, *n* (%)	12 (19)	6 (9)	8 (13)	0.057	0.208	5 (8.6)	10 (17.2)	11 (19)	0.246	0.202

Overweight and obesity were defined as BMI ≥ 25 kg/m^2 and 30 kg/m^2, respectively. Hypertension was defined as SBP/DBP ≥ 140 mmHg/90 mmHg based on the Chinese Guidelines for the Management of Hypertension in 2010. Diabetes was defined as FPG ≥ 6.1 mmol/L and/or2hPG ≥ 7.8 mmol/L based on the 1999 WHO diagnostic criteria. Dyslipidemia was defined as TG ≥ 1.7 mmol/L, TC ≥ 6.2 mmol/L, LDL-C ≥ 4.1 mmol/L, or HDL-C < 0.9 mmol/L (male) or <1.0 mmol/L (female) based on the Chinese Guideline for the Management of Dyslipidemia in Adults in 2016. MS was defined as the CDS in 2004, meeting the following three items or more: overweight and/or obesity, diabetes, hypertension, dyslipidemia. *P* 1: week 24 *vs*. baseline; *P* 2: week 48 *vs*. baseline. Missing data are filled by the LOCF method. Statistical significance defined as a *P* value < 0.05. 2hPG: 2h postprandial blood glucose; BMI: Body mass index; CDS: Chinese Diabetes Society; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HDL-C: High-density lipoprotein cholesterol; LOCF: Last observation carried forward; LDL-C: Low-density lipoprotein cholesterol; M/F: Male : Female; MS: Metabolic syndrome; SD: Standard deviation; SBP: Systolic blood pressure; TC: Total cholesterol; TG: Triglycerides.

Increased levels of serum cholesterol, triglyceride, and low-density lipoprotein cholesterol (LDL-C), and decreased HDL-C levels are associated with psoriasis. The prevalence of hypercholesterolemia, hypertriglyceridemia, low HDL-C, and high LDL-C levels in Chinese adults was 9.01%, 27.02%, 14.36%, and 10.23%, respectively. However, our study population had a lower prevalence of hypercholesterolemia and higher LDL-C compared to that study.

Similar to previous reports, we found that psoriatic patients who received adalimumab or secukinumab have a significant change in lipid profile.[5,6] It was speculated that the effect of tumor necrosis factor (TNF)-α on the lipid profile was associated with the induction of free fatty acids, liver cell activation, promotion of free fatty acid to triglycerides (TG), and degradation of HDL-C by binding to Gi (inhibitory adenylate cyclase g protein) receptors.[7] Moreover, TNF-α can reduce serum TG and HDL-C by interfering with LDL receptors, apolipoproteins a and b.[7] The mechanisms for these changes in patients treated with IL-17A are poorly understood. TNF-α inhibitors (adalimumab) and IL-17 inhibitors (secukinumab) had no significant effect on BMI, blood glucose, and blood pressure. Although the efficacy and safety of adalimumab and secukinumab in Chinese patients with psoriasis have been reported, attention should be paid to their effects on lipid metabolism.

Limitations of our study include its retrospective nature, single-center, and the short-term observation period. Therefore, a large sample, multicenter, long-term prospective study should be carried out to prove the correlation between psoriasis and lipid profile.

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Conflicts of interest

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