Psoriasis: Targets and Therapy

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ORIGINAL RESEARCH

Tobacco Smoking Interacted with Alcohol Drinking Could Increase the Failure of $PASI_{75}$ Achievement at Week 8 Among Patients with Psoriasis: Findings Based on a Psoriasis Cohort

Fanlingzi Shen[1,2,*], Yu Song[3,*], Yan Qiang[1,*], Xiangjin Gao[1], Siyuan Li[2], Rui Zhang[1], Zhongzhi Gao[1], Bin Li[1], Wencheng Jiang[4], Ruiping Wang[1,2]

[1]Clinical Research Center, Shanghai Skin Diseases Hospital, School of Medicine, Tongji University, Shanghai, People's Republic of China; [2]School of Public Health, Shanghai University of Traditional Chinese Medicine, Shanghai, People's Republic of China; [3]Department of Dermatology, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, People's Republic of China; [4]Department of Traditional Chinese Medicine, Shanghai Skin Diseases Hospital, School of Medicine, Tongji University, Shanghai, People's Republic of China

*These authors contributed equally to this work

Correspondence: Wencheng Jiang, Department of Traditional Chinese Medicine, Shanghai Skin Diseases Hospital, Medical School, Tongji University, 1278 Baode Road, Shanghai, 200443, People's Republic of China, Email drjiangwencheng@163.com; Ruiping Wang, Clinical Research & Innovation Transformation Center, Shanghai Skin Diseases Hospital, Medical School, Tongji University, 1278 Baode Road, Shanghai, 200443, People's Republic of China, Email w19830901@126.com

Purpose: Tobacco smoking and alcohol drinking are positively associated with psoriasis prevalence and disease severity. Researches focusing on the influence of smoking and drinking on the treatment efficacy of psoriasis are still limited, especially their interaction effect. This study aims to explore the interactive effects of smoking and drinking on the treatment efficacy in psoriasis patients.

Patients and Methods: From 2021 to 2022, we recruited 560 patients with psoriasis from Shanghai Skin Diseases Hospital. Demographic and clinical features as well as treatment efficacy were collected through questionnaire interview and physical examination during patient's hospital visit at week 0, week 4 and week 8. Logistic regression model was used to explore the influence of smoking and drinking on the treatment efficacy in psoriasis patients, and multiplicative and additive interaction models were used to verify the interaction effect of smoking and drinking on the treatment efficacy.

Results: The prevalence of smoking and drinking among psoriasis patients was respectively 43.8% and 25.4%, and 19.6% of them with both smoking and drinking. Logistic regression analysis showed that patients with smoking (OR=7.78, 95% CI: 5.26~11.49) and drinking (OR=5.21, 95% CI: 3.29~8.27) had higher risk of experiencing the failure to achieve $PASI_{75}$ at week 8, even with the adjustment of confounders. Moreover, multiplicative as well as additive model showed that tobacco smoking interacted with alcohol drinking which influenced the treatment efficacy more severely (OR=12.74, 95% CI: 7.16~22.67). The proportion of $PASI_{75}$ achievement in female patients (OR=19.54) and patients with methotrexate (OR=28.31) and biologics (OR=21.61) were more likely being affected by smoking and drinking.

Conclusion: Tobacco smoking and alcohol drinking could increase the failure of $PASI_{75}$ achievement in patients with psoriasis, individually and interactively. We recommend that dermatologists should educate patients to pay attention to the negative effects of smoking and drinking, encourage them to quit, and thus improve the treatment efficacy.

Keywords: psoriasis, tobacco smoking, alcohol drinking, interaction, additive model, multiplicative model

Introduction

Psoriasis is a common chronic inflammatory skin disease that occurs in cases worldwide, with adult prevalence estimates ranging from 0.91% to 8.5%.[1,2] Psoriasis not only affects the skin of patients, causing scaly erythema or plaques, but also

Received: 10 August 2024
Accepted: 18 September 2024
Published: 23 September 2024

can induce complications outside of the skin, such as arthritis, cardiovascular disease, and metabolic diseases.[3] It seriously affects the patient's health and quality of life, and imposes a great burden to the patient and society.

Clinical treatment choice for psoriasis patients usually depends on the severity of diseases, patients' personal option, and goal of treatment. Oral retinoids, methotrexate, cyclosporine and phototherapy are common conventional treatments. In recent years, the increase of emerging therapies such as small molecules and biologics has significantly improved the safety and efficacy of psoriasis treatment; however, some patients only achieved poor efficacy.[4] Factors that affecting the therapeutic effect of psoriasis patients are manifold, including gender, age, comorbidities, environment, and therapies, all of which influence the efficacy of treatment.[5–9]

In recent years, the influence of lifestyle factors has attracted more and more attention. Tobacco smoking and alcohol drinking are widely viewed as negative factors affecting health. The World Health Organization's report showed that more than 8 million people die from tobacco use, and alcohol drinking contributes to 3 million deaths worldwide each year.[10,11] Tobacco smoking and alcohol drinking are among the top 10 risk factors for disability-adjusted life years globally and are also the top risk factors in China.[12,13] Previous studies have shown that tobacco smoking and alcohol drinking are closely related to the prevalence and severity of psoriasis and are controllable risk factors of concern.[14,15] Richer et al[16] reported that there was a significant correlation between tobacco smoking and psoriasis, and the severity of psoriasis increased with heavier intensity and more year of tobacco smoking. A systematic literature review by Brenaut et al[17] indicated that psoriasis patients had higher alcohol consumption than the general population, and several case–control studies have also reported alcohol as a risk factor for psoriasis. In addition, tobacco smoking and alcohol drinking can also reduce the treatment response of patients with psoriasis.[5,18]

Previous researches have shown that smoking and drinking are highly correlated behaviors, with tobacco smokers tending to show a higher propensity to drink alcohol.[19] It was estimated that the prevalence of co-users of tobacco and alcohol in China was 14.1%, which was at a high level.[20] Notably, there was a significant increase in health risks for those both with tobacco smoking and alcohol drinking.[21] A study pointed out that the risk of all-cause mortality and premature mortality of people who smoked and drank at the same time was 75% and 112% higher than that of non-smokers and non-drinkers.[22] Although the harmful effects of tobacco smoking and alcohol drinking on health were reported widely, current researches focusing on the influence of tobacco smoking and alcohol drinking on the treatment efficacy of psoriasis patients is still relatively limited, especially their interaction effect. This study aims to evaluate the effects of tobacco smoking, alcohol drinking and their interaction on the treatment efficacy of psoriasis, so as to provide a basis for improving the treatment efficacy and quality of life of patients with psoriasis.

Materials and Methods

Study Population

This observational study was based on a cohort of psoriasis patients established at the Shanghai Skin Diseases Hospital from 2021 to 2022. A previous survey showed that the prevalence of tobacco smoking and alcohol drinking in patients with psoriasis in Shanghai was 25.83% and 16.94%, respectively.[23] In this study, we applied the sample size calculation formula $n=[\mu_{\alpha}^2 \times p(1-p)]/\delta^2$ and set p=30%, α=0.05, δ=15% of p, and a non-response rate of 10%, the sample size calculation indicated that at least 445 psoriasis patients should be recruited. 560 patients with psoriasis were eventually recruited and analyzed. This study was reviewed and approved by the Institutional Review Boards of Shanghai Skin Disease Hospital (2021–44), and was then registered in the Chinese Clinical Trial Registry (ChiCTR2200066403). This study strictly adhered to the Declaration of Helsinki.

Data Collection

In this study, data were collected through a self-designed questionnaire. The questionnaire includes: (1) demographic characteristics: age, gender, education, etc; (2) lifestyle habits: tobacco smoking, alcohol drinking, etc; (3) information on psoriasis family history, medical history of non-communicable disease (NCD), psoriasis severity at the baseline, including body surface area (BSA), psoriasis area and severity index (PASI), physician global assessment (PGA); and (4) therapy and PASI score evaluation at week 4 and week 8, respectively, and records of adverse events. Information on

demographic characteristics, lifestyle habits, and family history was self-reported by patients; information on psoriasis severity, clinical therapies and efficacy, and adverse effects was evaluated and recorded by the dermatologists.

Diagnosis and Treatment Efficacy Evaluation of Psoriasis

In this study, the diagnosis of psoriasis was based on the Chinese Clinical Dermatology, which is in line with the global guidelines for psoriasis diagnosis and treatment.[24] PASI was used to assess the severity of the psoriasis lesions. The treatment efficacy was evaluated by the changes of PASI. The $PASI_{75}$ is defined as patients achieving ≥75% improvement in PASI score and calculated by the formula [(PASI at baseline – PASI at week t)/PASI at baseline] ×100%. The proportion of patients with $PASI_{75}$ achievement at week 8 was set as the main efficacy indicator and the failure to reach $PASI_{75}$ at week 8 was defined as poor efficacy.

Definition of Tobacco Smoking, Alcohol Drinking and Classification of Other Covariates

In this study, a smoker was defined as a person who had smoked at least 100 cigarettes in his or her lifetime. A drinker was defined as a person who drank alcohol at least twice a week for at least six months. Age was stratified into <50 years and ≥50 years. Education was recorded as years of schooling completed and categorized as 0~9 years (junior high school and lower), 10~12 years (senior high school), and >12 years (college and above). Individual monthly income was categorized as ≤5000, 5001~10000, and >10000 (Chinese Yuan, CNY). Marital status was categorized as married and unmarried. Body mass index (BMI) was calculated as weight/height^2 (kg/m$^{2)}$ and categorized as underweight (<18.5), normal weight (18.5~23.9), overweight (24.0~27.9), and obese (≥28.0). Psoriasis family history was defined as having at least one first-degree relative (parents, siblings, and children) with psoriasis. Medical history of NCD meant that the patient suffers from at least one of diabetes mellitus, hypertension, hyperlipidemia, hyperuricemia, coronary atherosclerotic heart disease, nonalcoholic fatty liver disease, tumors, and chronic renal insufficiency. The therapy covered five options, acitretin group (25~50mg daily), methotrexate group (MTX, 15~20mg per week, with folic acid supplementation), narrow band ultraviolet (NB-UVB) (2~4 times weekly), benvitimod group (2 times each day) and biologics group (ustekinumab, risankizumab, secukinumab, etc).

Statistical Analysis

In this study, data were analyzed by using SPSS 26.0 (SPSS Inc., Chicago, Illinois, United States). Quantitative variables were expressed as mean and standard deviation (SD) if they conformed to normal distribution, and t-tests were used for comparisons between groups. Quantitative variables were expressed as median and interquartile range (IQR) if they conformed to skewed distribution, and non-parametric rank sum tests were used for comparisons between groups. Qualitative variables were expressed as frequency counts (n) and percentage (%), and chi-squared test was used for comparison between groups. The logistic regression model analysis was used to calculate the odds ratios (OR) and 95% confidence intervals (CI) to illustrate the association between tobacco smoking, alcohol drinking and treatment efficacy in patients with psoriasis, respectively. In this study, we divided patients with psoriasis into group A (non-smoker and non-drinker), group B (non-smoker but drinker), group C (smoker but non-drinker) and group D (smoker and drinker), and the OR_{00}, OR_{01}, OR_{10} and OR_{11} were used to represent the association between tobacco smoking, alcohol drinking and the treatment efficacy at week 8 in patients with psoriasis in group A, group B, group C and group D, respectively. And the additive interaction model ($OR_{11}+OR_{00}\neq OR_{01}+OR_{10}$) and the multiplicative interaction model ($OR_{11}\times OR_{00}\neq OR_{01}\times OR_{10}$) were then calculated to identify and evaluate the interaction effect between tobacco smoking and alcohol drinking on the treatment efficacy at week 8 in patients with psoriasis. In this study, a p-value of <0.05 (two-tailed) was considered statistically significant.

Results

Demographic Characteristics of Psoriasis Patients

A total of 560 patients with psoriasis were recruited and analyzed in this study, of which 408 (72.9%) were males and the median age was 47 years (IQR: 36.0~61.0). Approximately 48% of patients had an education of college and above, and 39% of them had individual income less than 5000 CNY per month, and 80% of them were married. In this study, 43.8%

of psoriasis patients were tobacco smokers and 25.4% were alcohol drinkers, and over half of them had NCDs. The prevalence of tobacco smoking, alcohol drinking and NCDs between male and female patients with psoriasis were all statistically significant (P<0.05), Table 1.

In this study, the proportion of patients with psoriasis in Group A, Group B, Group C and Group D were 50.5%, 5.7% 24.1% and 19.6%, respectively. Data in Table 2 indicated that patients with tobacco smoking and alcohol drinking had a higher percentage of ≥50 years old, lower proportion of college and above education, and higher prevalence of NCDs, the differences were all statistically significant (P < 0.05). Table 2.

The Clinical Features and $PASI_{75}$ Achievement

In this study, the median PASI score at baseline among 560 psoriasis patients was 11.1 (IQR: 7.9~16.6). Data in Table 3 indicated that differences in PASI and BSA at baseline, and therapy options between Group A, Group B, Group C and Group D were not statistically significant (P>0.05). Patients with psoriasis in Group A had lower PASI and BSA score at week 4 and week 8 than those in Group B, Group C and Group D, and the achievement of $PASI_{75}$ was statistically higher in

Table 1 Basic Characteristics of Psoriasis Patients

Variables	Total Patients (n=560)	Male Patients (n=408)	Female Patients (n=152)	*P*
Age (years), median (IQR)	47.0 (36.0, 61.0)	48.0 (36.0, 62.0)	47.0 (35.0, 57.0)	0.28
Age (years), *n* (%)				0.57
<50	306 (54.6)	220 (53.9)	86 (56.6)	
≥50	254 (45.4)	188 (46.1)	66 (43.4)	
Education, *n* (%)				0.15
Junior high and lower	159 (28.4)	110 (27.0)	49 (32.2)	
Senior high	134 (23.9)	106 (26.0)	28 (18.4)	
College and above	267 (47.7)	192 (47.0)	75 (49.4)	
Monthly income (CNY), *n* (%)				0.46
≤5000	216 (38.6)	153 (37.5)	63 (41.4)	
5001–10,000	218 (38.9)	158 (38.7)	60 (39.5)	
>10,000	126 (22.5)	97 (23.8)	29 (19.1)	
Marital status, *n* (%)				
Married	448 (80.0)	326 (79.9)	122 (80.3)	0.92
Unmarried/others	112 (20.0)	82 (20.1)	30 (19.7)	
BMI (kg/m^2), *n* (%)				<0.01
<18.5	22 (3.9)	11 (2.7)	11 (7.2)	
18.5–23.9	205 (36.6)	131 (32.1)	74 (48.7)	
24.0–27.9	217 (38.8)	174 (42.6)	43 (28.3)	
≥28.0	116 (20.7)	92 (22.5)	24 (15.8)	
Psoriasis family history, *n* (%)				0.76
Yes	124 (22.1)	89 (21.8)	35 (23.0)	
No	436 (77.9)	319 (78.2)	117 (77.0)	
NCD, *n* (%)				<0.01
Yes	302 (53.9)	240 (58.8)	62 (40.8)	
No	258 (46.1)	168 (41.2)	90 (59.2)	
Tobacco smoking				<0.01
Yes	245 (43.8)	226 (55.4)	19 (12.5)	
No	315 (56.2)	182 (44.6)	133 (87.5)	
Alcohol drinking				<0.01
Yes	142 (25.4)	130 (31.9)	12 (7.9)	
No	418 (74.6)	278 (68.1)	140 (92.1)	
PASI at week 0, median (IQR)	11.1 (7.9, 16.6)	12.0 (8.5, 18.0)	9.7 (6.9, 13.6)	<0.01

Abbreviations: IQR, interquartile range; CNY, Chinese Yuan; BMI, body mass index; NCD, non-communicable diseases; PASI, psoriasis area and severity index.

Table 2 Demographic Features of the Different Groups of the Psoriasis Patients

Variables	Group A (n=283)	Group B (n=32)	Group C (n=135)	Group D (n=110)	*P*
Age (years), median (IQR)	43.0 (35.0, 57.0)	44.0 (33.5, 56.0)	50.0 (36.0, 62.0)	55.0 (40.0, 65.0)	<0.01
Age (years), *n* (%)					<0.01
<50	177 (62.5)	20 (62.5)	66 (48.9)	43 (39.1)	
≥50	106 (37.5)	12 (37.5)	69 (51.1)	67 (60.9)	
Gender, *n* (%)					<0.01
Male	153 (54.1)	29 (90.6)	125 (92.6)	101 (91.8)	
Female	130 (45.9)	3 (9.4)	10 (7.4)	9 (8.2)	
Education, *n* (%)					<0.01
Junior high and lower	72 (25.4)	9 (28.1)	44 (32.6)	34 (30.9)	
Senior high	51 (18.0)	6 (18.8)	36 (26.7)	41 (37.3)	
College and above	160 (56.5)	17 (53.1)	55 (40.7)	35 (31.8)	
Monthly income (CNY), *n* (%)					0.11
≤5000	101 (35.7)	15 (46.9)	51 (37.8)	49 (44.5)	
5001–10,000	107 (37.8)	11 (34.4)	63 (46.7)	37 (33.6)	
>10,000	75 (26.5)	6 (18.8)	21 (15.6)	24 (21.8)	
Marital status, *n* (%)					0.48
Married	221 (78.1)	24 (75.0)	111 (82.2)	92 (83.6)	
Unmarried/others	62 (21.9)	8 (25.0)	24 (17.8)	18 (16.4)	
BMI (kg/m^2), *n* (%)					0.78
<18.5	11 (3.9)	0 (0.0)	5 (3.7)	6 (5.5)	
18.5–23.9	112 (39.6)	10 (31.3)	48 (35.6)	35 (31.8)	
24.0–27.9	107 (37.8)	14 (43.8)	50 (37.0)	46 (41.8)	
≥28.0	53 (18.7)	8 (25.0)	32 (23.7)	23 (20.9)	
Psoriasis family history, *n* (%)					0.93
Yes	61 (21.6)	7 (21.9)	29 (21.5)	27 (24.5)	
No	222 (78.4)	25 (78.1)	106 (78.5)	83 (75.5)	
NCD, *n* (%)					0.01
Yes	132 (46.6)	19 (59.4)	81 (60.0)	70 (63.6)	
No	151 (53.4)	13 (40.6)	54 (40.0)	40 (36.4)	

Notes: Group A (non-smoker and non-drinker), Group B (non-smoker but drinker), Group C (smoker but non-drinker) and Group D (smoker and drinker).

Abbreviations: IQR, interquartile range; CNY, Chinese Yuan; BMI, body mass index; NCD, non-communicable diseases.

Group A than those in Group B, Group C and Group D, the difference was statistically significant (P<0.05), Table 1 and Table 3.

Association Between Smoking, Drinking and Treatment Efficacy in Psoriasis Patients

In this study, logistic regression indicated that psoriasis patients with tobacco smoking had higher proportion of poor treatment efficacy (without $PASI_{75}$ achievement) at week 8 than those without tobacco smoking (OR=7.78, 95% CI: 5.26~11.49), the findings were consistent even with the adjustment of potential confounding factors in Model 1 (OR=8.25, 95% CI: 5.33–12.78), Model 2 (OR=13.18, 95% CI: 7.76–22.38) and Model 3 (OR=10.65, 95% CI: 6.18–18.34). Similarly, psoriasis patients with drinking also had higher proportion of poor treatment efficacy at week 8 than those without drinking (OR=5.21, 95% CI: 3.29–8.27), the findings were consistent even with the adjustment of potential confounding factors in Model 1 (OR=4.60, 95% CI: 2.86–7.40), Model 2 (OR=4.79, 95% CI: 2.86–8.02) and Model 3 (OR=2.62, 95% CI: 1.47–4.65). Table 4.

Table 3 Clinical Features of Different Groups of the Psoriasis Patients

Variables	Group A (n=283)	Group B (n=32)	Group C (n=135)	Group D (n=110)	*P*
PASI, median (IQR)					
Week 0	10.8 (7.9, 15.6)	12.4 (9.6, 17.1)	11.2 (8.0, 17.3)	11.2 (8.1, 17.8)	0.32
Week 4	5.4 (3.3, 9.0)	7.4 (4.3, 10.8)	6.5 (3.4, 10.5)	7.5 (4.6, 11.2)	<0.01
Week 8	1.8 (0.8, 3.6)	5.0 (2.3, 7.5)	4.6 (2.3, 8.1)	5.9 (2.8, 9.0)	<0.01
BSA, median (IQR)					
Week 0	15.0 (9.8, 29.0)	16.0 (11.8, 34.0)	14.0 (9.0, 26.0)	16.7 (11.5, 28.5)	0.47
Week 4	9.5 (5.0, 17.0)	10.0 (7.5, 16.5)	9.0 (4.7, 17.0)	12.0 (7.0, 22.0)	0.04
Week 8	4.0 (1.0, 8.0)	6.0 (2.4, 13.5)	5.0 (2.0, 12.0)	8.5 (3.0, 15.0)	<0.01
Therapy, *n* (%)					0.46
Acitretin	29 (10.2)	8 (25.0)	17 (12.6)	20 (18.2)	
Methotrexate	58 (20.5)	5 (15.6)	21 (15.6)	23 (20.9)	
NB-UVB	50 (17.7)	5 (15.6)	20 (14.8)	18 (16.4)	
Benvitimod	13 (4.6)	1 (3.1)	8 (5.9)	5 (4.5)	
Biologics	133 (47.0)	13 (40.6)	69 (51.1)	44 (40.0)	
Treatment efficacy, *n* (%)					<0.01
Achieve $PASI_{75}$	198 (70.0)	10 (31.2)	32 (23.7)	17 (15.5)	
Not achieve $PASI_{75}$	85 (30.0)	22 (68.8)	103 (76.3)	93 (84.5)	

Notes: Group A (non-smoker and non-drinker), Group B (non-smoker but drinker), Group C (smoker but non-drinker) and Group D (smoker and drinker).

Abbreviations: IQR, interquartile range; PASI, psoriasis area and severity index; BSA, body surface area; $PASI_{75}$, at least 75% PASI reduction at week 8 compared with the PASI at baseline.

Table 4 The Association of Treatment Efficacy and Tobacco Smoking and Alcohol Drinking Among Psoriasis Patients Without the Achievement of $PASI_{75}$ at Week 8 in Shanghai

Variables	The Risk of Poor Treatment Efficacy [OR (95% CI)]			
	Crude	Model 1	Model 2	Model 3
Tobacco smoking				
Yes	7.78 (5.26–11.49)	8.25 (5.33–12.78)	13.18 (7.76–22.38)	10.65 (6.18–18.34)
No	1.00	1.00	1.00	1.00
Alcohol drinking				
Yes	5.21 (3.29–8.27)	4.60 (2.86–7.40)	4.79 (2.86–8.02)	2.62 (1.47–4.65)
No	1.00	1.00	1.00	1.00

Notes: Model 1: adjusted age, gender, marital status, education, individual monthly income. Model 2: adjusted age, gender, marital status, education, individual monthly income, BMI, psoriasis family history, NCD and therapy. Model 3: adjusted age, gender, marital status, education, individual monthly income, BMI, psoriasis family history, NCD, therapy, tobacco smoking and alcohol drinking.

Abbreviations: OR, odds ratio; CI, confidence interval.

Interaction Effect of Smoking and Drinking on the Treatment Efficacy in Psoriasis Patients

Logistic regression was applied to explore the association between tobacco smoking as well as alcohol drinking and the achievement of $PASI_{75}$ at week 8 among psoriasis patients in different groups which setting Group A as the reference (OR_{00}=1.00). Figure 1 indicates that patients with alcohol drinking (OR_{01}=5.12, 95% CI: 2.33~11.29), tobacco smoking (OR_{10}=7.50, 95% CI: 4.68~12.01) and those both with smoking and drinking (OR_{11}=12.74, 95% CI: 7.16~22.67) had higher proportion of achieving poor treatment efficacy (without $PASI_{75}$ achievement). Both of the additive model ($OR_{11}+OR_{00}\neq OR_{01}+OR_{10}$) and the multiplicative model ($OR_{11}\times OR_{00}\neq OR_{01}\times OR_{10}$) indicated that tobacco smoking interacted with alcohol drinking which influencing the treatment efficacy at a more severe level among patients with psoriasis. The interaction effect between smoking and drinking on treatment efficacy in patients with psoriasis was consistent even with the adjustment of age, gender, education, marital status, monthly income and other factors (Figure 1).

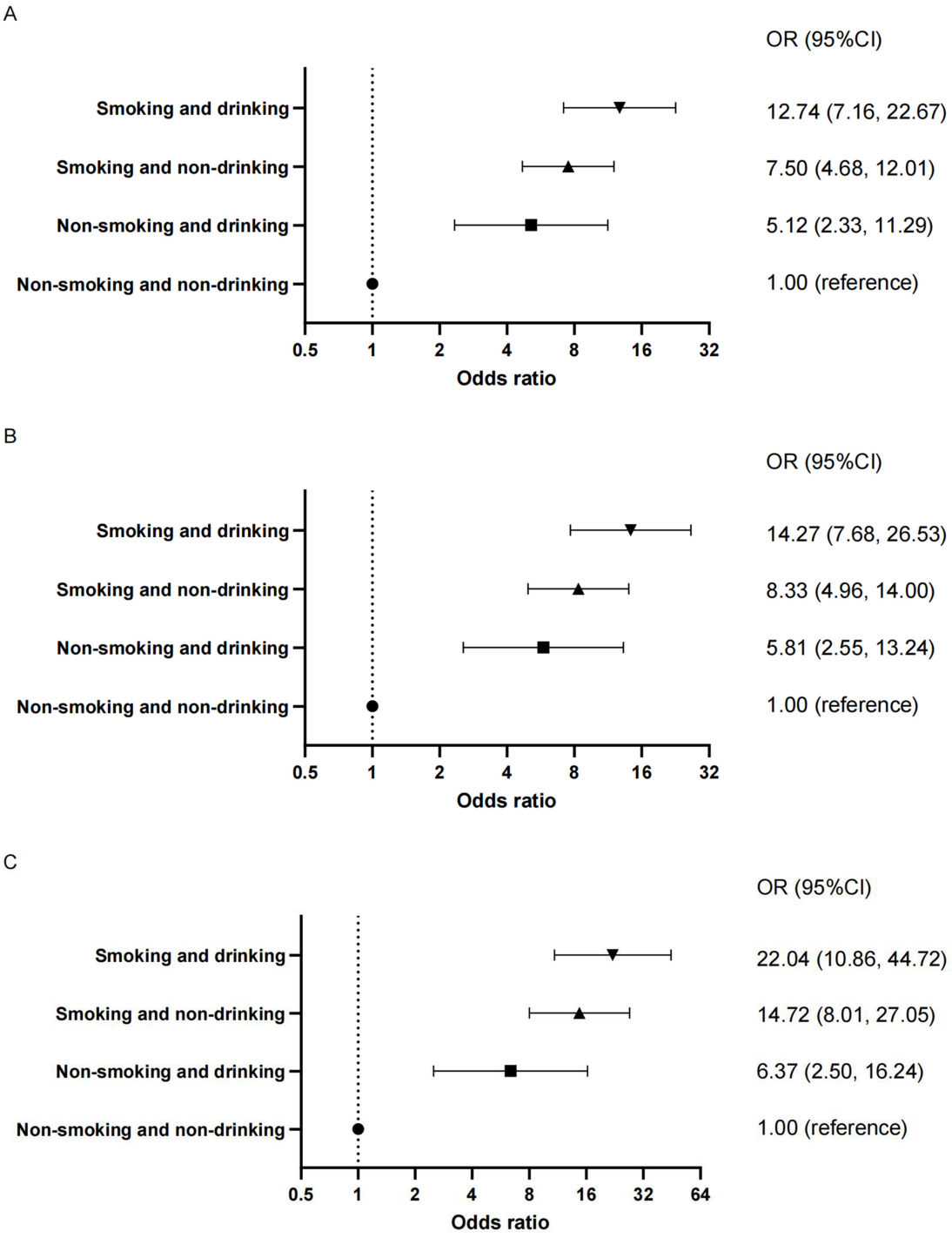

Figure 1 Interaction of tobacco smoking and alcohol drinking influence the treatment efficacy in patients with psoriasis. ((**A**) the crude OR for the association between smoking and drinking and the proportion of patients without $PASI_{75}$ achievement. (**B**) the adjusted OR for association between smoking and drinking and without $PASI_{75}$ achievement with the adjustment of age, gender, marital status, education and individual monthly income. (**C**) the adjusted OR for association between smoking and drinking and without $PASI_{75}$ achievement with the adjustment of age, gender, marital status, education, individual monthly income, BMI, psoriasis family history, NCD and therapy.).

Sensitivity Analysis of the Interaction Effect by Sex and Treatment Options

In this study, subgroup analyses showed that there was an interaction effect between tobacco smoking and alcohol drinking on the achievement of $PASI_{75}$ at week 8 both in male and female patients. Male psoriasis patients both with smoking and drinking had 12.24 times (OR=12.24, 95% CI: 6.53~22.94) higher risk of experiencing a failure in the

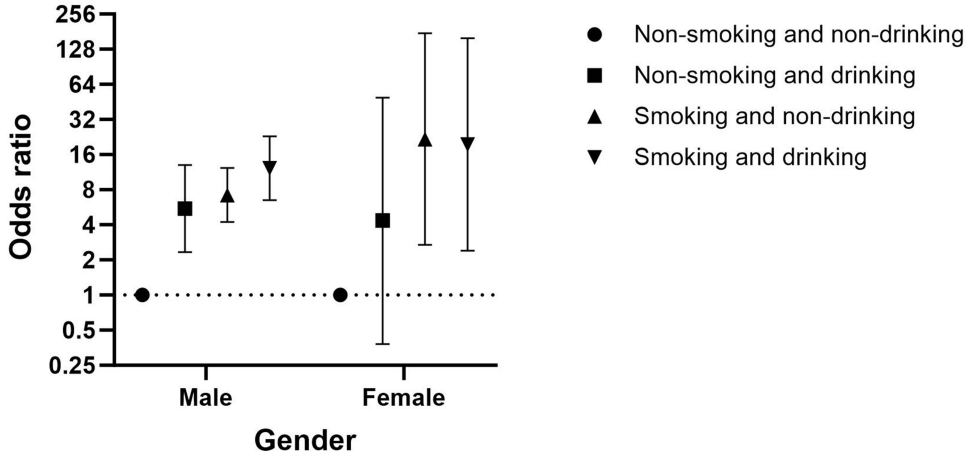

Figure 2 The association between smoking and drinking and the proportion of patients without $PASI_{75}$ achievement by gender.

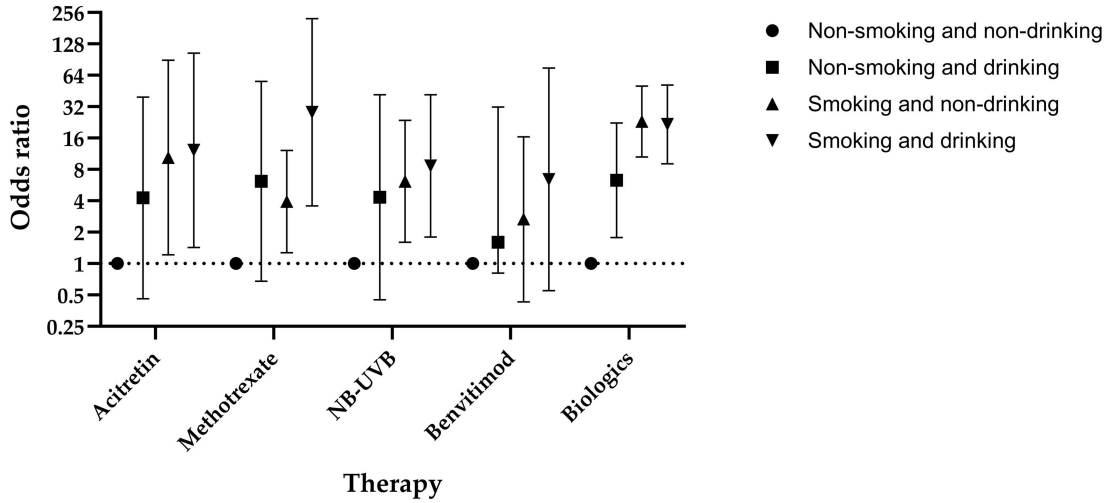

Figure 3 The association between smoking and drinking and the proportion of patients without $PASI_{75}$ achievement by different treatment options.

achievement of $PASI_{75}$ at week 8 after receiving treatment, and the risk was 19.54 (OR=19.54, 95% CI: 2.40~159.36) in female patients with psoriasis, Figure 2.

For psoriasis patients receiving different therapies, tobacco smoking and alcohol drinking also had an interaction effect on the achievement of $PASI_{75}$ at week 8. Patients with both smoking and drinking had a higher risk of experiencing the failure of $PASI_{75}$ achievement than patients without smoking and drinking, the findings were consistent in acitretin treatment group (OR=12.22, 95% CI: 1.43~104.29), methotrexate treatment group (OR=28.31, 95% CI: 3.58~223.87), NB-UVB treatment group (OR=8.67, 95% CI: 1.80~41.71), benvitimod treatment group (OR=6.40, 95% CI: 0.55~74.89) and biologics treatment group (OR=21.61, 95% CI: 9.07~51.50) (Figure 3).

Discussion

In our previous studies based on this psoriasis patient cohort, we have observed a negative correlation between tobacco smoking and the $PASI_{75}$ achievement in patients with psoriasis.[25] Additionally, we have also identified a detrimental impact of alcohol drinking on the treatment efficacy.[26] In this study, we focused to explore the interactive impact of tobacco smoking and alcohol drinking on the treatment efficacy among patients with psoriasis for the first time in China. The findings indicated that the prevalence of tobacco smoking and alcohol drinking was 43.8% and 25.4% in psoriasis patients, and 19.6% of them were both of tobacco smoker and alcohol drinker. Logistic regression indicated that patients

with drinking (OR_{01}=5.12, 95% CI: 2.33~11.29), smoking (OR_{10}=7.50, 95% CI: 4.68~12.01) and those both with smoking and drinking (OR_{11}=12.74, 95% CI: 7.16~22.67) had higher risk of experiencing the failure of $PASI_{75}$ achievement at week 8 than those without smoking and drinking. Moreover, both of the additive model and the multiplicative model indicated that tobacco smoking interacted with alcohol drinking which inhibited the achievement of $PASI_{75}$ at a more severe level among patients with psoriasis. Therefore, dermatologists should advise psoriasis patients to quit tobacco smoking and alcohol drinking to achieve better psoriasis treatment efficacy and improve their quality of life.

The effect of tobacco smoking on patients with psoriasis is multifaceted. Previous studies have shown that tobacco smokers have higher risk of psoriasis, and the risk and severity of psoriasis are positively correlated with the intensity and cumulative exposure to tobacco.[27–29] Although growing studies have reported the negative effect of tobacco smoking on the treatment efficacy of patients with psoriasis, the evidence is still limited.[30] In this study, the findings support tobacco smoking is associated with poor efficacy in patients with psoriasis, and tobacco smokers have 7.78 times higher risk of experiencing the unachieved $PASI_{75}$ at week 8 after the treatment. The mechanism of tobacco smoking affects the occurrence, development and prognosis of psoriasis is unclear. Current research suggests that oxidative damage and inflammatory reactions caused by nicotine in tobacco and other harmful substances produced by combustion adversely affect the condition, thereby aggravating the symptom and poor prognosis of psoriasis.[31,32]

Alcohol was one of the first identified environmental risk factors for psoriasis, and it is now believed that increased alcohol drinking is associated with the psoriasis severity, and excessive alcohol drinking can lead to the decrease of treatment efficacy in patients with psoriasis.[33,34] Michalski et al[15] pointed out that the severity of skin lesions in patients with psoriasis was related to the drinking pattern, and the PASI and BSA scores increased significantly with the increase of alcohol consumption and drinking frequency. Iskandar et al[35] reported that alcohol abuse was associated with poor response to systemic treatment. In this study, we also found that alcohol drinking increased the risk of poor response to treatment in patients with psoriasis even with the adjustment of other potential confounders. The possible reason for the adverse effect of alcohol on the progression and efficacy of psoriasis is that alcohol can induce immune dysfunction, trigger and aggravate the inflammatory response, which is not conducive to treatment.[18] In addition, alcohol abusers have limited treatment options which might also increase the difficulty of treatment and lead to the poor response among patients with psoriasis.[36]

This study explored the interaction effects of tobacco smoking and alcohol drinking on the efficacy of psoriasis patients. Findings showed that there was an interaction between tobacco smoking and alcohol drinking based on the additive model, and psoriasis patients with tobacco smoking and alcohol drinking had excessive higher risk of experiencing the failure of $PASI_{75}$ achievement at week 8 (OR=12.74) than those only with tobacco smoking (OR=7.50) and those only with alcohol drinking (OR=5.12) as well. The interactive effects of tobacco smoking and alcohol drinking on the treatment efficacy of patients with psoriasis are complex and interrelated, there maybe a common mechanism for their negative impact on the disease progression of psoriasis. Both of tobacco smoking and alcohol drinking are closely associated with psoriasis through affecting the expression of certain immune molecules, inducing an inflammatory response, and causing enhanced activation of T-cells, and the impact of tobacco smoking and alcohol drinking might be mutually intensified with their concurrent exposure.[32]

Subgroup analysis in this study showed that the additive interaction of smoking and drinking on the efficacy of treatment among psoriasis patients was more significant in women. Previous literature has reported a higher risk of death in female tobacco smokers and/or alcohol drinkers compared to males and attributed the possible underlying mechanism for this gender disparity to biological differences or behavioral differences.[22] In this study, the reason for gender difference in interaction of smoking and drinking on the efficacy of treatment among psoriasis patients is not clear. It maybe caused by the differences in the levels of sex hormones in males and females,[37,38] female psoriasis patients with both of smoking and drinking tend to be more sensitive to the nicotine and other harmful substances produced by combustion and alcohol-induced harms, which adversely affect the response to treatment in a severe and extensive level. Among patients receiving different therapies, the additive interaction of tobacco smoking and alcohol drinking had a greater impact on patients with the treatment of methotrexate and biologics, making the treatment complex and challenging, and biological mechanisms of which need to be explored in more in-depth studies.

Tobacco smoking and alcohol drinking are two important controllable risk factors for psoriasis. Our study emphasizes the detrimental effects of tobacco smoking, alcohol drinking and their interactions on the treatment as well as the necessity of quitting smoking and drinking. Lifestyle interventions for psoriasis patients who smoke and drink alcohol are highly cost-effective. Therefore, during the treatment process, dermatologists should educate patients to pay attention to the negative effects of smoking and drinking on disease development and prognosis, encourage patients to quit smoking and drinking, and provide corresponding support and guidance to help patients change their unhealthy lifestyles, thus improving the treatment efficacy.

A strength of this study was that a longitudinal design was used for data collection, and the 8-week follow-up ensured 100% adherence by patients with psoriasis. Meanwhile, clinical data on patients with psoriasis were extracted directly from the Health Information System (HIS), avoiding recall bias and resulting in higher quality data. Furthermore, we used two interaction models to verify and emphasize the impact of tobacco smoking and alcohol drinking on the treatment efficacy of patients with psoriasis, which has obvious public health value.

This study has some limitations. First, all psoriasis patients are enrolled in one hospital, which ensures the high internal authenticity, but the generalization of the findings is limited. Second, information on the lifestyle habits of psoriasis patients was obtained through questionnaires, and there may be information bias. Third, the time point for treatment efficacy assessment is set as in week 8, but week 12 is more commonly used for treatment efficacy assessment, especially for the treatment of biologics, so the rate of $PASI_{75}$ achievement in week 8 in this study has limited comparability with other studies, and the incorporation of more assessment time points should be considered. Fourth, there are many factors affecting the treatment efficacy of psoriasis patients. In this study, we only assessed smoking and drinking habits, and more factors need to be considered in the future, such as dietary, exercise, and so on. Fifth, this study explored statistical interactions, the biological mechanisms of which need to be further validated to gain a deeper understanding of the relationship between tobacco smoking, alcohol drinking and psoriasis. Sixth, the proportion of males in Group A is significantly lower than that in Groups B-D, which may lead to bias in the interpretation of the research results.

Conclusion

This study indicated that both of tobacco smoking and alcohol drinking could increase the risk of experiencing the failure of $PASI_{75}$ achievement in patients with psoriasis, and the multiplicative model as well as the additive model verified the interaction effect of tobacco smoking and alcohol drinking on the poor treatment response among psoriasis patients. So, we recommended that dermatologists should educate patients to pay attention to the negative effects of smoking and drinking, encourage them to quit and provide corresponding support and guidance to assist them to change unhealthy lifestyles, thus improving the treatment efficacy.

Abbreviations

BMI, Body Mass Index; BSA, Body Surface Area; CI, Confidence Interval; CNY, Chinese Yuan; HIS, Health Information System; IQR, Interquartile Range; MTX, Methotrexate; NB-UVB, Narrow; Band Ultraviolet B; NCD, Non-communicable Disease; OR, Odds Ratio; PASI, Psoriasis Area and; Severity Index; PGA, Physician Global Assessment; SD, Standard Deviation.

Data Sharing Statement

The data for this study are available upon request from the corresponding author. The request should state the title and aim of the research for which the data are requested.

Ethics Approval and Informed Consent

This study was approved by the Institutional Review Boards of Shanghai Skin Diseases Hospital, Shanghai, China (2021-44). Informed consent was obtained before starting the study, and the study was strictly performed in accordance with the Declaration of Helsinki.

Acknowledgments

We would like to thank the dermatologists in Shanghai Skin Disease Hospital for data collection in this study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was supported by the Clinical Research Three Year Plan of SHDC (SHDC2022CRS053, SHDC2024CRX032), the Clinical Research Program of Shanghai Municipal Health Commission (202240371), Intelligence Fund of Shanghai Skin Diseases Hospital (2021KYQD01), China YMIOO Program (LCIIT2022-09), Shanghai Talent Development Fund (2021073). These funders had no role in the study design, data collection and analysis, decision to publish, or manuscript preparation.

Disclosure

The authors report no conflicts of interest in this work.

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