Original Investigation

Hypertension, Antihypertensive Medication Use, and Risk of Psoriasis

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IMPORTANCE Individuals with psoriasis have an elevated risk of hypertension, and antihypertensive medications, especially β-blockers, have been linked to psoriasis development. However, the association of prior existing hypertension and antihypertensive medications with risk of incident psoriasis has not been assessed using prospective data.

OBJECTIVE To evaluate the association of hypertension and antihypertensive medications with risk of psoriasis.

DESIGN, SETTING, AND PARTICIPANTS We performed a prospective cohort study (June 1, 1996, to June 1, 2008) of 77 728 US women from the Nurses' Health Study who provided biennially updated data on hypertension and antihypertensive medications.

MAIN OUTCOMES AND MEASURES Physician-diagnosed psoriasis.

RESULTS A total of 843 incident psoriasis cases were documented during 1 066 339 person-years of follow-up. Compared with normotensive women, women with a hypertension duration of 6 years or more were at a higher risk of developing psoriasis (hazard ratio [HR], 1.27; 95% CI, 1.03-1.57). In stratified analysis, the risk of psoriasis was higher among hypertensive women without medication use (HR, 1.49; 95% CI, 1.15-1.92) and among hypertensive women with current medication use (HR, 1.31; 95% CI, 1.10-1.55) when compared with normotensive participants without medication use. Compared with women who never used β-blockers, the multivariate HRs for psoriasis for women who regularly used β-blockers were 1.11 (95% CI, 0.82-1.51) for 1 to 2 years of use, 1.06 (95% CI, 0.79-1.40) for 3 to 5 years of use, and 1.39 (95% CI, 1.11-1.73) for 6 years or more of use (*P* for trend = .009). No association was found between use of other individual antihypertensive drugs and risk of psoriasis.

CONCLUSIONS AND RELEVANCE Long-term hypertensive status is associated with an increased risk of psoriasis. Long-term regular use of β-blockers may also increase the risk of psoriasis.

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Psoriasis is an immune-mediated chronic systemic disease that affects approximately 3% of the US population and more than 125 million individuals worldwide.[1-4] Psoriasis has been associated with significant morbidity and substantial economic costs to patients and the health care system.[5] Previous studies have reported that psoriasis is associated with an increased risk of cardiovascular disease,[6-8] and individuals with psoriasis are also at an increased risk of hypertension, a well-known risk factor of cardiovascular disease.[9-15] However, most previous studies are cross-sectional or case-control studies and thus limit clear investigation on the temporal association between psoriasis and hypertension. On the basis of the evidence that psoriasis and hypertension may increase the risk of cardiovascular disease and previous reports that individuals with psoriasis are more likely to have concurrent hypertension, it is reasonable to infer that hypertension may also be associated with the development of psoriasis. To our knowledge, no prospective data on the risk of incident psoriasis associated with hypertension are currently available.

In addition, medications for treating some comorbidities have been frequently reported to induce or exacerbate psoriasis, among which antihypertensive medications, especially β-blockers, have received increasing attention.[16-21] However, findings from a previous large case-control study[16] did not find a substantially altered risk of psoriasis for several widely used antihypertensive drugs (eg, diuretics, β-blockers, calcium channel blockers, and angiotensin-converting enzyme [ACE] inhibitors). Currently, prospective data on the association between antihypertensive medications and risk of psoriasis are limited, and whether there is a casual association between these drugs and psoriasis incidence needs fur-

ther examination. To address the hypothesis that a history of hypertension and related antihypertensive medication use may increase the risk of psoriasis, we investigated these associations based on prospective data from a large cohort of US women from the Nurses' Health Study.

Methods

Study Population

The institutional review board of Partners Health Care System approved this study. The return of completed self-administered questionnaires was considered as written informed consent. The Nurses' Health Study was established in 1976 when 121 701 married, female registered nurses aged 30 to 55 years who were residing in the United States at the time of enrollment responded to a baseline questionnaire that included questions about their medical history and lifestyle risk factors. Information on risk factors and health data was updated every 2 years by mailed questionnaires. The overall follow-up rate reached 96% during the study.

Case Ascertainment

In 2008, Nurses' Health Study participants responded to an item on the questionnaire that inquired about any history of physician-diagnosed psoriasis and the date of diagnosis (1997 or before, 1998-2001, 2002-2005, 2006-2007, or 2008). A total of 2477 participants reported having been diagnosed as having psoriasis, and 888 of those diagnoses occurred after 1997. We confirmed a subset of participants with self-reported psoriasis using the Psoriasis Screening Tool questionnaire,[22] which inquires about the type of clinicians making the diagnosis and phenotypes. A pilot study[22] using the Psoriasis Screening Tool questionnaire had 99% sensitivity and 94% specificity for psoriasis screening. The confirmation rate of self-reports was 92%.

Assessment of Hypertension

History of physician-diagnosed hypertension was assessed at cohort inception (1976) and updated every 2 years using biennial questionnaires. Once a participant reported physician-diagnosed hypertension, she was considered to have a positive history of hypertension until the end of the follow-up. Self-reported hypertension has a high accuracy in the cohort participants, with 100% self-reports confirmed by medical records.[23]

Assessment of Antihypertensive Medications

Regular antihypertensive medication use during the past 2 years was assessed in the biennial questionnaires. Individual drugs included in the follow-up questionnaires were thiazide diuretics (1980, 1982, 1988, 1994, 1996, 1998, 2000, 2002, 2004, and 2006); β-blockers, calcium channel blockers, or other antihypertensive drugs (1988, 1994, 1996, 1998, 2000, 2002, 2004, and 2006); and ACE inhibitors (1988, 1996, 1998, 2000, 2002, 2004, and 2006).

Covariates

Information on weight, smoking, cardiovascular disease (including myocardial infarction and stroke), type 2 diabetes mellitus, hypercholesterolemia, menopausal status, postmenopausal hormone use, nonsteroidal anti-inflammatory drug (NSAID) use, and multivitamin supplement use was collected biennially throughout the follow-up. Height was assessed in 1976. Body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) was assessed every 2 years during the follow-up (note that we collected information on weight biennially). Alcohol intake was available in 1994, 1998, 2002, and 2006. Physical activity was assessed in 1996, 1998, 2000, and 2004.

Statistical Analysis

Women who reported a baseline history of psoriasis were excluded from the analysis. Person-years of follow-up for each participant were calculated from the return date of the baseline questionnaire to the date of diagnosis of psoriasis, date of death, time of loss to follow-up, or end of follow-up, whichever came first. Means (SDs) for continuous characteristics and proportions for categorical characteristics were calculated by history of hypertension at baseline.

Cox proportional hazards regression model analyses stratified by age and 2-year follow-up intervals were used to estimate the age- and multivariate-adjusted hazard ratios (HRs) and 95% CIs of incident psoriasis associated with hypertension and antihypertensive medications. Selection of covariates in multivariate analyses was based on current knowledge of risk factors of psoriasis. Multivariate HRs were calculated after adjusting for age, BMI (<24.9, 25-29.9, 30-34.9, and ≥35), alcohol intake (0, <5, 5-9.9, or ≥10 g/d), physical activity (<3, 3-8.9, 9-17.9, 18-26.9, and ≥27 metabolic equivalent hours per week), smoking (never, past, and current smoking with 1-14, 15-24, or ≥25 cigarettes per day), cardiovascular disease, type 2 diabetes, hypercholesterolemia, postmenopausal hormone use, NSAID use, and multivitamin supplement use. Analyses for regular antihypertensive medication use or hypertension were additionally adjusted for hypertension or antihypertension medication use in fully adjusted models, respectively. All variables were coded as time-varying variables to account for potential changes during the follow-up. To differentiate the effect of hypertension from those of antihypertensive medications, we stratified the analysis for hypertension by status of regular antihypertensive medication use. We further evaluated the effects of duration of hypertension and antihypertensive medications (1-2 years, 3-5 years, and ≥6 years). We selected the duration of 6 years as the cutoff because we have a follow-up of 12 years (June 1, 1996, to June 1, 2008). All statistical analyses were conducted using SAS statistical software, version 9.2 (SAS Institute Inc). All statistical tests were 2-tailed, and the significance level was set at $P < .05$.

Results

We documented 843 incident psoriasis cases among 77 728 participants during 1 066 339 person-years of follow-up. **Table 1** provides the baseline characteristics of the study population. Women with hypertension tended to be older; had higher BMIs; had proportionately higher prevalence rates of cardiovascu-

lar disease, type 2 diabetes, and hypercholesterolemia; and were less physically active than those without hypertension.

Hypertension was associated with an elevated risk of psoriasis in multivariate-adjusted models (HR, 1.21; 95% CI, 1.04-1.40) (**Table 2**). This association became insignificant with additional adjustment for antihypertensive medication use (HR, 1.13; 95% CI, 0.93-1.37). However, there was a higher risk of psoriasis among women with hypertension duration of 6 years or more in the fully adjusted model (HR, 1.27; 95% CI, 1.03-1.57) compared with normotensive women (*P* for trend = .03). In stratified analysis, we found a higher risk of psoriasis among hypertensive women without medication use (HR, 1.49; 95% CI, 1.15-1.92) and among hypertensive women with current medication use (HR, 1.31; 95% CI, 1.10-1.55) when compared with normotensive women without medication use (**Table 3**).

Analyses for antihypertensive medications suggest an association between regular antihypertensive medication use and risk of psoriasis in the multivariate-adjusted model (HR, 1.19; 95% CI, 1.03-1.37), which became insignificant with additional adjustment for hypertension in the fully adjusted model (HR, 1.10; 95% CI, 0.92-1.32) (**Table 4**). Among individual antihypertensive drugs, a marginal association was found between the regular use of β-blockers and risk of psoriasis in the multivariate-adjusted model (HR, 1.18; 95% CI, 0.99-1.40), which also became null with additional adjustment for hypertension in the fully adjusted model (HR, 1.12; 95% CI, 0.93-1.34). Of interest, this association persisted in a duration-dependent manner, with a higher risk of psoriasis found among regular users of β-blockers with a duration of use of 6 years or more (HR, 1.39; 95% CI, 1.11-1.73; *P* for trend = .009) (**Table 5**). In contrast, no association was found between other individual antihypertensive drugs and risk of psoriasis. Sensitivity analyses were performed among women without baseline cardiovascular disease and type 2 diabetes, and results were essentially unchanged (see eTables 1-3 in the Supplement).

Table 1. Baseline Characteristics of the Study Population by History of Hypertension[a]

Characteristic[b]	No Hypertension (n=47 897)	Hypertension (n=29 831)[c]
Age, mean (SD), y	60.1 (6.8)	62.6 (6.7)
White race	46 604 (97.3)	28 488 (95.5)
Body mass index, mean (SD)[d]	25.5 (4.5)	28.5 (5.8)
Alcohol intake, mean (SD), g/d	5.1 (8.6)	4.8 (9.2)
Physical activity, mean (SD), metabolic equivalent h/wk	19.6 (23.2)	16.4 (21.0)
Current smoking	5772 (11.8)	2574 (9.2)
Cardiovascular disease	405 (0.9)	866 (2.6)
Type 2 diabetes mellitus	1066 (2.2)	2665 (8.9)
Hypercholesterolemia	21 477 (45.9)	19 458 (63.9)
Postmenopausal hormone use	19 039 (43.0)	12 039 (43.6)
NSAID use	23 711 (52.8)	16 205 (59.7)
Multivitamin supplement use	22 630 (52.8)	13 883 (51.5)

Abbreviation: NSAID, nonsteroidal anti-inflammatory drug.

[a] Data are presented as number (percentage) of participants with available data unless otherwise indicated.

[b] All variables other than age have been standardized to the age distribution of the study population.

[c] Median hypertension duration was 11 years.

[d] Body mass index is calculated as weight in kilograms divided by height in meters squared.

Discussion

Our study examined the association among hypertension, antihypertensive medication use, and risk of incident psoriasis using prospective data from a large cohort of US women. After

Table 2. Hazard Ratios of Psoriasis According to Hypertension Status

Hypertension Status	No. of Cases	No. of Person-years	Adjusted Hazard Ratio (95% CI)		
			Age	Multivariate[a]	Multivariate[b]
Hypertension					
No	366	540 694	1 [Reference]	1 [Reference]	1 [Reference]
Yes	477	525 645	1.34 (1.17-1.54)	1.21 (1.04-1.40)	1.13 (0.93-1.37)
Hypertension duration, y					
0	366	540 694	1 [Reference]	1 [Reference]	1 [Reference]
1-2	39	58 959	0.97 (0.70-1.35)	0.91 (0.65-1.27)	0.93 (0.65-1.33)
3-5	61	85 435	1.06 (0.80-1.39)	0.97 (0.74-1.28)	0.97 (0.71-1.31)
≥6	377	381 251	1.47 (1.27-1.71)	1.32 (1.13-1.54)	1.27 (1.03-1.57)
P value for trend			<.001	<.001	.03

[a] Simultaneously adjusted for age, body mass index, alcohol intake, physical activity, smoking status, cardiovascular disease, type 2 diabetes mellitus, hypercholesterolemia, postmenopausal hormone use, nonsteroidal anti-inflammatory drug use, and multivitamin supplement use.

[b] Additionally adjusted for antihypertensive medication use.

Table 3. Hazard Ratios of Psoriasis According to Hypertension Stratified by Status of Antihypertensive Medication Use

Antihypertensive Medication Use Status	No. of Cases	No. of Person-years	Adjusted Hazard Ratio (95% CI)	
			Age	Multivariate[a]
No hypertension and no medication	282	445 705	1 [Reference]	1 [Reference]
Hypertension with no medication	77	78 445	1.57 (1.22-2.02)	1.49 (1.15-1.92)
Hypertension with past medication	38	55 883	1.10 (0.78-1.54)	0.97 (0.69-1.37)
Hypertension with current medication	359	386 026	1.49 (1.27-1.75)	1.31 (1.10-1.55)

[a] Simultaneously adjusted for age, body mass index, alcohol intake, physical activity, smoking status, cardiovascular disease, type 2 diabetes mellitus, hypercholesterolemia, postmenopausal hormone use, nonsteroidal anti-inflammatory drug use, and multivitamin supplement use.

Table 4. Hazard Ratios of Psoriasis According to Status of Regular Antihypertensive Medication Use

Antihypertensive Medication Use Status	No. of Cases	No. of Person-years	Adjusted Hazard Ratio (95% CI)		
			Age	Multivariate[a]	Multivariate[b]
Overall antihypertensive medication use					
Nonregular users	442	632 210	1 [Reference]	1 [Reference]	1 [Reference]
Regular users	401	434 129	1.32 (1.15-1.52)	1.19 (1.03-1.37)	1.10 (0.92-1.32)
Thiazide diuretic use					
Nonregular users	710	923 449	1 [Reference]	1 [Reference]	1 [Reference]
Regular users	133	142 890	1.21 (1.00-1.45)	1.09 (0.90-1.32)	1.02 (0.83-1.24)
β-Blocker use					
Nonregular users	684	900 025	1 [Reference]	1 [Reference]	1 [Reference]
Regular users	159	166 314	1.25 (1.05-1.49)	1.18 (0.99-1.40)	1.12 (0.93-1.34)
Calcium channel blocker use					
Nonregular users	747	968 410	1 [Reference]	1 [Reference]	1 [Reference]
Regular users	96	97 929	1.26 (1.01-1.56)	1.15 (0.93-1.43)	1.09 (0.87-1.35)
ACE inhibitor use					
Nonregular users	733	953 227	1 [Reference]	1 [Reference]	1 [Reference]
Regular users	110	113 112	1.26 (1.03-1.54)	1.16 (0.94-1.42)	1.08 (0.87-1.33)

Abbreviation: ACE, angiotensin-converting enzyme.

[a] Simultaneously adjusted for age, body mass index, alcohol intake, physical activity, smoking status, cardiovascular disease, type 2 diabetes mellitus, hypercholesterolemia, postmenopausal hormone use, nonsteroidal anti-inflammatory drug use, and multivitamin supplement use.

[b] Additionally adjusted for hypertension.

adjusting for a number of potential confounders, we found that a prior history of hypertension was associated with an increased risk of psoriasis among women with a hypertension duration of 6 years or more. Specifically, hypertensive women without medication use and with current medication use were more likely to develop psoriasis compared with normotensive women without medication use. Among the individual antihypertensive drugs, only β-blockers were associated with an increased risk of psoriasis after regular use for 6 years or more. In sensitivity analyses among women without baseline cardiovascular disease and type 2 diabetes, most findings as stated above were only slightly attenuated and remained statistically significant.

Psoriasis is a disease characterized by T-cell–mediated hyperproliferation of keratinocytes and inflammatory processes[3] and is classified as a T_H1 disease.[24] Hypertension is also characterized by increased oxidative stress and inflammation,[25] and immune mechanisms are reported to be involved in the development of hypertension, with different helper T cells (eg, T_H1 and T_H2 lymphocytes and T-regulatory cells) participating as pro- and anti-inflammatory cells.[26] Population-based studies[27,28] have found that chronic inflammation is associated with an increased risk of hypertension. Therefore, hypertension may be associated with psoriasis development because of the shared inflammatory pathways. In the current study, we found that women with a hypertension duration of 6 years or more were more likely to develop psoriasis, whereas the risk was not apparent among women with a hypertension duration of less than 6 years. This finding is consistent with the existing concept that psoriasis is associated with a chronic inflammatory state.[1] Hypertensive participants with longer disease durations may have a greater possibility of developing psoriasis later because of the long-lasting increased levels of systemic oxidative stress and inflammation.[25,26]

In addition, overall hypertension was associated with an increased risk of psoriasis in the multivariate model, and this association attenuated and became insignificant after additionally adjusting for antihypertensive medication use (Table 2). Of interest, overall antihypertension medication use was also associated with an increased risk of psoriasis in the multivariate model, and this association attenuated and became insignificant after additionally adjusting for hypertension (Table 4). The results suggest that hypertension and antihypertensive medication use may be associated with the development of psoriasis, although neither was associated with the risk individually. Stratified analyses provided a better overview of the association among hypertension, antihypertensive medication use, and risk of psoriasis. The risk of psoriasis associated with hypertension appeared to be specific to women with hypertension without medication use and with current medication use and appeared to be specific to women with long-term duration of hypertension or duration of antihypertensive medication use of 6 years or more. Therefore, special attention on psoriasis screening may be needed for patients with long-term duration of hypertension and related antihypertensive medication use in clinical practices.

A number of previous studies,[16-21,29] including case reports and case-control analyses, have reported a possible association between induction or exacerbation of psoriasis and exposure to drugs, such as β-blockers, calcium channel blockers, ACE inhibitors, lithium, and NSAIDs. However, prospective data from population-based studies have not been available to date. Our detailed analyses on individual antihypertensive drugs revealed that only β-blockers were associated with an increased risk of psoriasis after regular use for 6 years or more. Therefore, it is likely that the association between hypertension and psoriasis among women with current medication use was driven by β-blockers. Previous case-control and case-crossover studies have found evidence of the association between β-blockers and psoriasis,[17,20] although inconsistent results also exist.[16] Association of β-blockers with risk of psoriasis has biological plausibility. β-Blockers can block β-adrenergic receptors in the skin, preventing β-agonists from binding to the receptors. This process subsequently leads to a decrease in cellular levels of cyclic adenosine monophosphate, an intracellular messenger in a path-

Table 5. Hazard Ratios of Psoriasis According to Duration of Regular Antihypertensive Medication Use

Antihypertensive Medical Use States	No. of Cases	No. of Person-years	Adjusted Hazard Ratio (95% CI)		
			Age	Multivariate[a]	Multivariate[b]
Overall antihypertensive medication use, y					
0	359	524 150	1 [Reference]	1 [Reference]	1 [Reference]
1-2	52	73 920	1.03 (0.77-1.38)	0.94 (0.70-1.27)	0.87 (0.63-1.19)
3-5	87	104 463	1.21 (0.96-1.54)	1.10 (0.87-1.40)	1.02 (0.78-1.32)
≥6	286	293 094	1.43 (1.22-1.68)	1.26 (1.06-1.49)	1.15 (0.93-1.41)
P value for trend			<.001	.01	.16
Thiazide diuretic use, y					
0	551	758 389	1 [Reference]	1 [Reference]	1 [Reference]
1-2	49	49 682	1.37 (1.02-1.84)	1.23 (0.92-1.66)	1.16 (0.85-1.57)
3-5	57	68 332	1.14 (0.87-1.50)	1.03 (0.78-1.35)	0.98 (0.74-1.29)
≥6	154	149 931	1.41 (1.18-1.69)	1.23 (1.02-1.49)	1.16 (0.95-1.41)
P value for trend			<.001	.05	.24
β-Blocker use, y					
0	592	799 129	1 [Reference]	1 [Reference]	1 [Reference]
1-2	48	52 453	1.24 (0.92-1.67)	1.17 (0.87-1.57)	1.11 (0.82-1.51)
3-5	55	62 679	1.18 (0.90-1.56)	1.11 (0.84-1.46)	1.06 (0.79-1.40)
≥6	105	91 251	1.56 (1.26-1.92)	1.46 (1.18-1.81)	1.39 (1.11-1.73)
P value for trend			<.001	.001	.009
Calcium channel blocker use, y					
0	670	877 735	1 [Reference]	1 [Reference]	1 [Reference]
1-2	34	35 865	1.23 (0.87-1.74)	1.14 (0.81-1.61)	1.07 (0.75-1.52)
3-5	58	48 415	1.55 (1.18-2.03)	1.43 (1.09-1.87)	1.34 (1.02-1.77)
≥6	51	53 360	1.25 (0.94-1.67)	1.13 (0.85-1.52)	1.08 (0.80-1.45)
P value for trend			.002	.03	.10
ACE inhibitor use, y					
0	680	866 002	1 [Reference]	1 [Reference]	1 [Reference]
1-2	42	41 808	1.29 (0.94-1.77)	1.20 (0.87-1.65)	1.11 (0.80-1.53)
3-5	42	44 844	1.18 (0.86-1.61)	1.09 (0.80-1.49)	1.00 (0.72-1.37)
≥6	53	54 590	1.23 (0.93-1.64)	1.12 (0.84-1.49)	1.03 (0.77-1.38)
P value for trend			.03	.23	.64

Abbreviation: ACE, angiotensin-converting enzyme.

[a] Simultaneously adjusted for age, body mass index, alcohol intake, physical activity, smoking status, cardiovascular disease, type 2 diabetes mellitus, hypercholesterolemia, postmenopausal hormone use, nonsteroidal anti-inflammatory drug use, and multivitamin supplement use.

[b] Additionally adjusted for hypertension.

way that stimulates proteins responsible for differentiation and inhibition of proliferation.[29] A decrease of cyclic adenosine monophosphate further leads to a decrease in intracellular calcium and consequently increased cellular proliferation and lack of differentiation as seen in psoriasis.[30] In addition, it has been reported that β-blockers increase phosphorylation in T cells in psoriasis, which may be relevant to intracellular levels of calcium.[31] The results of blockade are marked by excessive release of enzymes from lymphocytes, neutrophils, and macrophages, which is believed to be responsible for the presence of hyperproliferation and psoriasiform change.[32] The blockade of β-adrenergic receptors has been implicated in the pathogenesis of β-blocker–provoked psoriasis.[29]

Other widely used antihypertensive drugs, including thiazide diuretics, calcium channel blockers, and ACE inhibitors, were not associated with risk of psoriasis in the current study. Although analyses according to duration of regular medication use suggest trends toward increasing risk of psoriasis with use of these drugs, the risk estimates were largely insignificant. Therefore, these antihypertensive drugs may not be able to alter an individual's risk of developing psoriasis on the basis of existing hypertensive status. It is also possible that the previous findings on the induction or exacerbation of psoriasis associated with certain antihypertensive drugs were actually contributed by existing hypertensive status in part.

Our study has several strengths. First, we collected detailed, updated information on hypertension and antihypertensive medication use through the cohort follow-up and thus avoided the potential recall bias of case-control studies that collected exposure data after incidence of psoriasis. Second, we were able to examine the effects of several widely used antihypertensive drugs (including thiazide diuretics, β-blockers, calcium channel blockers, and ACE inhibitors) separately during the cohort follow-up. Third, our participants were all registered nurses, and the accuracy of self-reported hypertension and antihypertensive medication use is likely to be high as demonstrated previously.[23] Fourth, we were able to control for a number of potential confounders that may have affected the association of interest based on detailed follow-up information.

Several study limitations should be noted when interpreting the results. First, survivorship bias would be a major concern on the selection of participants given that the psoriasis

question was asked in 2008. We cannot obtain information from participants with psoriasis who died before the inquiry of outcome disease. However, the health care–related professional background of our participants was reassuring, and the relatively higher accuracy of their reports would have tended to cause nondifferential misclassification of psoriasis, resulting in a conservative estimate of HRs.

In addition, we compared the baseline characteristics of women who responded to the 2008 psoriasis question with those who did not respond and found that their main characteristics (eg, age and BMI) were similar.[33] Therefore, it is unlikely that our results would change greatly because of response bias. Second, we only assessed regular antihypertensive medication use during the follow-up but did not have the drug dosage information, which may be critical in determining the extent of disease risk. Third, our study participants were mostly white older women and thus may limit generalizing the results to men and other ethnicities.

Conclusions

Our study provides evidence that a prior history of long-term hypertension of 6 years or more was associated with an increased risk of psoriasis. Among the individual antihypertensive drugs investigated in the study, only β-blockers were associated with an increased risk of psoriasis after long-term regular use for 6 years or more. These findings provide novel insights into the association among hypertension, antihypertensive medications, and psoriasis. However, further work is necessary to confirm our findings and clarify the biological mechanisms that underlie these associations.

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Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Wu.
Critical revision of the manuscript for important intellectual content: All authors.
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Invited Commentary

PRACTICE GAPS

Psoriasis Provoked or Exacerbated by Medications
Identifying Culprit Drugs

April W. Armstrong, MD, MPH

A critical practice gap exists in identifying the causes of psoriasis flares, especially medication-related causes. Some physicians may not consistently examine medications for their contribution to psoriasis flares. However, a careful consideration of the role of medications in psoriasis exacerbation may improve long-term psoriasis control.

Several factors are important in evaluating the role of medications in psoriasis flares: (1) medications can exacerbate preexisting psoriasis and/or induce psoriasis on clinically uninvolved skin in patients with psoriasis (the incidence of psoriasis exacerbation is generally greater than that of psoriasis induction); (2) the strength of evidence linking different medications with psoriasis flares varies considerably; and (3) the latency period between drug ingestion and psoriasis flares varies among medications and can be much lengthier for certain medications.

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Although many medications have been implicated in psoriasis flares, strong evidence exists linking β-blockers, lithium, antimalarials, and interferons. Medications with a possible link to psoriasis exacerbation include angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, nonsteroidal antiinflammatory drugs, and tumor necrosis factor inhibitors.

β-Blockers are categorized into cardioselective or noncardioselective types, and both have been involved in psoriasis induction and exacerbation. The latency period from ingestion of β-blockers to psoriasis flares varies from several days to 12 months in patients with psoriasis.[1] In patients without a history of psoriasis, regular use of β-blockers for 6 years or longer is associated with the development of psoriasis.[2]

Lithium has been more commonly associated with psoriasis exacerbation than induction. The mean latency period is 20 weeks for psoriasis exacerbation and 48 weeks for psoriasis induction.

Antimalarials are associated with psoriasis exacerbation. Exacerbations are more frequently seen in patients treated with chloroquine than hydroxychloroquine. The latency period for antimalarial-exacerbated psoriasis is 4 to 12 weeks.

Solutions to narrow gaps in identifying medication-related psoriasis flares include a careful review of a patient's medication list with special attention to medications with strong evidence of contributing to psoriasis exacerbation. Furthermore, it is important for dermatologists to recognize medications with latency periods beyond the typical 2 to 4 weeks and to inquire about historical use of these medications with known long latency periods. More important, dermatologists need to critically evaluate the true probability that the medication contributes to the psoriasis exacerbation in the context of maturity of evidence and other non–medication-related causes of psoriasis exacerbation. Thus, hasty discontinuation of use of medications that have a low probability of contributing to psoriasis flares may be more aggressive than necessary.

Barriers to change include a lack of recognition of medication-related psoriasis exacerbations by health care professionals. Additional barriers may include the inability and/or unwillingness to identify alternative therapies to the offending agent. For example, when a β-blocker is identified as highly probable in contributing to psoriasis exacerbation, selecting an alterative antihypertensive drug may deviate from guideline-based care. Thus, when dermatologists recommend discontinuation of use of a medication, they need to coordinate care with other health care professionals to ensure that the patient is offered appropriate alternative treatments for substitution. Narrowing this practice gap will help reduce medication-related psoriasis flares and significantly improve long-term outcomes in patients with psoriasis.

ARTICLE INFORMATION

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