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Effect of statin use on incidence of eczema and atopic dermatitis: A retrospective cohort study

To the Editor: Statins are widely prescribed because of their efficacy in primary and secondary prevention of myocardial infarction via alterations in cholesterol metabolism.[1] Numerous statin-induced dermatologic complications have been reported but with less attention to eczema/atopic dermatitis (Table I).[2,3] We sought to determine the relationship between statin use and incidence of eczema.

We designed a retrospective cohort study using TriNetX, a global federated health research network providing access to statistics on electronic medical records (diagnoses, medications, laboratory values) from approximately 1 million patients admitted to the University of Iowa Hospitals and Clinics. TriNetX is an autogenerated, deidentified database with a waiver from the Western Institutional Review Board. Patients were selected based on a history of coronary artery disease to ensure robust statin use. A cohort taking a statin before January 1, 2012, was compared to a statin-naive population in terms of eczema (*International Classification of Diseases*, 10th revision, L20-L30) development over a 6-year period to January 1, 2018. Individuals using nonstatin antilipemic medications, such as ezetimibe, were excluded. We further stratified results by demographic factors and particular statin use (atorvastatin vs simvastatin). Comparisons were made using multivariate logistic regression models (SAS, version 9.4; SAS Institute, Cary, NC) for each stratum and for differences within strata groups.

We identified 9678 patients with heart disease, 5803 of whom had received a statin. The study population was composed of more men than women (63.0% vs 37.0%) and primarily older adults (82.6% with age > 60 y). Age and sex were similar between statin and statin-naive groups. The 6-year incidence rate (IR) of eczema in individuals taking statins was 6.77% compared to 1.68% in those not taking a statin, resulting in a risk ratio of 4.04 (95% confidence interval, 3.12-5.23; $P < .001$) (Table II). Age older than 60 years (risk ratio, 6.21) was the age group at greatest relative risk for eczema ($P < .001$). Individuals taking atorvastatin (IR, 9.09%) trended toward a marginally higher incidence of eczema than those taking simvastatin (IR, 7.78%) ($P = .0749$).

This study showed a strong association between statin use and incidence of eczema, which was largely unchanged by further stratification. Older adults, who composed a majority of the study population, had the greatest risk. Moreover, the difference between atorvastatin (higher-intensity statin) and simvastatin reflected a class effect and raises the possibility of a dose-response relationship. However, this study was limited by data availability in TriNetX, including lack of timing of disease onset. Additionally, our criteria included unspecified dermatitis, a potential confounder that may not necessarily represent eczema. Of note, our cohort had a lower prevalence of statin use compared to the typical 75% to 80%, likely because those who also used nonstatin antilipemic agents were excluded.

Statins should decrease cholesterol in the skin given their mechanism of action. However, statins have also been shown to have immunomodulating effects.[4] In older adults, who have higher risk for xerosis, eczema development may be more driven

Table I. Reported dermatologic adverse effects from statin therapy[3]

Statin medication	Reported dermatologic adverse effects
Atorvastatin	Face edema, photosensitivity reaction, cheilitis, pruritus, contact dermatitis, dry skin, acne, sweating, urticaria, eczema, seborrhea, skin ulceration, bullous dermatosis
Cerivastatin*	Hypersensitivity reaction
Fluvastatin	Rash, allergic reaction
Lovastatin	Pruritus, rash, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, dry skin and mucous membranes, hair and nail changes, alopecia, skin discoloration, lupus erythematosus–like syndrome
Pravastatin	Rash
Simvastatin	Lichenoid eruption, lupus erythematosus–like syndrome, dermatomyositis, photosensitivity rash, eczematous changes, cheilitis

*Withdrawn from the market because of risk of severe rhabdomyolysis.

Table II. Stratified incidence and risk ratios for eczema

Variable	Sample size, n (%)	Incidence rate of eczema, % (95% CI)		Risk ratio (95% CI)	*P* value	*P* value between strata
		Taking statin	Not taking statin			
Total population	9678 (100)	6.77 (6.13 to 7.42)	1.68 (1.27 to 2.08)	4.04 (3.12 to 5.23)	**<.001**	—
Male sex	6097 (63.0)	6.31 (5.54 to 7.09)	1.22 (0.77 to 1.67)	5.18 (3.51 to 7.63)	**<.001**	**.0943**
Female sex	3581 (37.0)	7.64 (6.48 to 8.81)	2.34 (1.60 to 3.09)	3.26 (2.29 to 4.64)	**<.001**	
Age 20-51 y	415 (4.3)	3.53 (−11.24 to 18.29)	4.90 (−7.31 to 17.11)	0.72 (0.27 to 1.88)	.5036	**<.001**
Age 51-60 y	1241 (12.8)	5.98 (4.35 to 7.60)	3.56 (1.79 to 5.33)	1.68 (0.95 to 2.95)	.735	
Age >60 y	7996 (82.6)	7.02 (6.30 to 7.74)	1.13 (0.76 to 1.50)	6.21 (4.42 to 8.73)	**<.001**	
White race	8479 (87.6)	6.62 (5.95 to 7.28)	1.89 (1.42 to 2.37)	3.49 (2.66 to 4.59)	**<.001**	**.5066**
Non-white race	724 (7.5)	10.40 (7.49 to 13.31)	2.33 (0.62 to 4.03)	4.47 (2.04 to 9.79)	**<.001**	
Weight 45-67 kg*	990 (10.2)	6.87 (5.29 to 8.44)	2.63 (1.52 to 3.73)	2.62 (1.62 to 4.23)	**<.001**	**.3216**
Weight 68-90 kg*	2285 (23.6)	7.22 (6.15 to 8.28)	1.80 (1.10 to 2.50)	4.01 (2.65 to 6.08)	**<.001**	
Weight 91-113 kg*	1625 (16.8)	5.97 (4.82 to 7.12)	1.12 (0.39 to 1.85)	5.33 (2.71 to 10.50)	**<.001**	
Weight >113 kg*	831 (8.6)	7.10 (5.35 to 8.85)	2.39 (0.85 to 3.94)	2.97 (1.49 to 5.92)	**<.001**	
Rural living†	6793 (70.2)	7.66 (6.44 to 8.89)	1.50 (0.77 to 2.23)	5.10 (3.06 to 8.51)	**<.001**	**.2589**
Urban living†	2879 (29.7)	6.37 (5.62 to 7.13)	1.74 (1.26 to 2.23)	3.65 (2.70 to 4.94)	**<.001**	
Atorvastatin only‡	1870	9.09 (10.39 to 7.79)	—	—	—	**.0749**
Simvastatin only‡	5270	7.78 (7.06 to 8.50)	—	—	—	

CI, Confidence interval.
Bold indicates significant *P* values.
*Weight class in kilograms. Weight class was chosen over body mass index because of limited data for body mass index.
†Rural versus urban living was determined by zip code by using US government consensus data.
‡As part of a follow-up comparison in a separate study and analysis with the same methods.

by the dry-skin mechanism than immune overdrive.[5] These findings warrant further investigation, including assessment for predisposing conditions and dose-response rates, in an effort to better understand this relationship and develop strategies for preventing drug-induced eczema. Replicating this study across other databases may also improve the validity of the findings.

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