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Meniere's Disease and Statins: Is There an Association? A Single Institution Study

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Abstract

Meniere's disease (MD) is a complex inner ear disease related to endolymphatic hydrops and with multiple other etiologies suggested including autoimmunity and vascular insufficiency. Statins are lipid-lowering medications with additional effects including reduction of oxidative stress and inflammation. We performed a cross-sectional study comparing patients with MD on statins to those not on statins to see if there is any difference in disease activity (major vertigo spells) and hearing stage utilizing linear and logistic regression. Our analysis showed no difference in the average number of major vertigo spells per month ($\beta = .07$, $P = .9$) between statin users and nonusers; however, statin users were found to have lower odds of worse hearing (odds ratio = 0.46, $P = .047$). Further studies are needed to confirm our results.

Keywords

Meniere's disease, statin

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Meniere's disease (MD) is an inner ear disorder, with an estimated prevalence of 190 per 100,000 in the United States, that causes vertigo, fluctuating hearing loss (HL), tinnitus, aural fullness, and other symptoms[1,2] significantly impairing patients' quality of life.[3] MD is a complex, multifactorial disease, related to endolymphatic hydrops possibly due to autoimmunity but other theories such as vascular insult to stria vascularis and head and neck venous stasis have been suggested.[4,5]

Due to possible contribution of autoimmunity and vascular deficiency in MD, the role of statins (hydroxymethylglutaryl-coenzyme A reductase inhibitors) in therapeutic strategies for prevention of inner ear conditions is of interest.[6,7] Statins are some of the most commonly prescribed cholesterol-lowering medications.[8] Their benefits may however surpass lowering lipid levels and include: (1) improving vascular microcirculation, (2) reducing oxidative stress, and (3) decreasing inflammation.[6] Furthermore, the protective effect of statins against noise-induced HL and gentamicin ototoxicity have been demonstrated in animal models, and its use in humans may be associated with a reduced amount of HL and tinnitus.[9,10]

To our knowledge, the only clinical study investigating the role of statins in MD is a Korean database study which showed no association between prior statin use and MD, but did show a lower odds of MD among middle-aged lipophilic statin users.[7] The aim of our study is to examine the association between statins and MD.

Methods

This is a single institution, cross-sectional study. The Institutional Review Board of West Virginia University Hospital approved retrospective data acquisition. The institutional registry was queried for adult patients with MD who were followed in our clinic between October 2019 and October 2021. The diagnosis of definitive or probable MD and hearing stage (A-D) were based on American Academy of Otolaryngology–Head and Neck Surgery clinical guidelines on MD.[11] Statin use was then determined by review of patient charts. Additional data collected included baseline demographics, comorbidities (diabetes, hypertension, hyperlipidemia, and coronary artery disease), frequency of major spells in the last month, hearing stage, and treatment. Univariable analysis was then performed using t test for continuous variables and χ^2 for categorical variables. Multivariable linear regression was used to compare difference in major spells while multivariable logistic regression was used to compare difference in hearing among statin groups, controlling for confounders. The hearing stage was dichotomized by combining normal with mild HL and

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Table 1. Baseline Characteristics for Statin Groups

	No statin (N = 113)	Statin (N = 94)	*P* value
Age (mean ± SE)[a]	56.8 ± 13.7	63.3 ± 11.4	<.001
Age of MD onset (mean ± SE)	47.4 ± 14.9	54.0 ± 13.2	.0009
Sex[a]			
Female	75 (66.4%)	45 (47.9%)	.007
Male	38 (33.6%)	49 (52.1%)	
DM[a]			
No	103 (91.2%)	58 (61.7%)	<.001
Yes	10 (8.8%)	36 (38.3%)	
CAD[a]			
No	110 (97.3%)	76 (80.9%)	<.001
Yes	3 (2.7%)	18 (19.1%)	
HLD[a]			
No	85 (75.2%)	21 (22.3%)	<.001
Yes	28 (24.8%)	73 (77.7%)	
HTN[a]			
No	63 (55.8%)	31 (33.0%)	.001
Yes	50 (44.2%)	63 (67.0%)	
Migraine Disease			
No	53 (46.9%)	52 (55.3%)	.23
Yes	60 (53.1%)	42 (44.7%)	
Smoker			
No	102 (90.3%)	81 (86.2%)	.36
Yes	11 (9.7%)	13 (13.8%)	
Diuretic			
No	34 (30.1%)	29 (30.9%)	.91
Yes	79 (69.9%)	65 (69.1%)	
Betahistine			
No	92 (81.4%)	82 (87.2%)	.25
Yes	21 (18.6%)	12 (12.8%)	
Lipoflavonoid			
No	111 (98.2%)	93 (100.0%)	.20
Yes	2 (1.8%)	0 (0.0%)	
Low salt diet			
No	17 (15.0%)	19 (20.2%)	.33
Yes	96 (85.0%)	75 (79.8%)	
Prior IT			
No	78 (69.0%)	52 (55.9%)	.098
Gentamicin	4 (3.5%)	3 (3.2%)	
Steroid	29 (25.7%)	31 (33.3%)	
Both	2 (1.8%)	7 (7.5%)	
MD diagnosis			
Definitive	99 (87.6%)	83 (88.3%)	.88
Probable	14 (12.4%)	11 (11.7%)	
MD duration, mo (mean ± SE)	115 (100)	128 (118)	.4
Hearing stage			
A	29 (25.9%)	27 (28.7%)	.81
B	24 (21.4%)	18 (19.1%)	
C	15 (13.4%)	16 (17.0%)	
D	44 (39.3%)	33 (35.1%)	
Major vertigo spells (mean ± SE)	1.8 ± 3.9	2.4 ± 5.1	.43

Abbreviations: CAD, coronary artery disease; DM, diabetes mellitus; HLD, hyperlipidemia; HTN, hypertension; IT, intratympanic injection; MD, Meniere's disease1.

[a]Statistically significant.

Table 2. Baseline Characteristics of Statin Users by Solubility (Hydrophilic vs Lipophilic)

	Hydrophilic statin (N = 37)	Lipophilic statin (N = 76)	*P* value
Age (mean ± SE)[a]	58.0 ± 11.1	66.8 ± 10.3	<.001
Sex[a]			
Female	23 (62%)	22 (39%)	.025
Male	14 (38%)	35 (61%)	
DM			
No	19 (51%)	39 (68%)	.096
Yes	18 (49%)	18 (32%)	
CAD			
No	30 (81%)	46 (81%)	.96
Yes	7 (19%)	11 (19%)	
HLD			
No	10 (27%)	11 (19%)	.38
Yes	27 (73%)	46 (81%)	
HTN			
No	13 (35%)	18 (32%)	.72
Yes	24 (65%)	39 (68%)	
Smoker			
No	31 (84%)	50 (88%)	.59
Yes	6 (16%)	7 (12%)	
Diuretic			
No	15 (41%)	14 (25%)	.10
Yes	22 (59%)	43 (75%)	
Betahistine			
No	31 (84%)	51 (89%)	.42
Yes	6 (16%)	6 (11%)	
Lipoflavonoid			
No	37 (100%)	56 (100%)	
Yes			
Low salt diet			
No	10 (27%)	9 (16%)	.19
Yes	27 (73%)	48 (84%)	
Prior IT[a]			
No	20 (56%)	32 (56%)	.76
Gentamicin	1 (3%)	2 (4%)	
Steroid	11 (31%)	20 (35%)	
Both	4 (11%)	3 (5%)	
MD diagnosis			
Definitive	32 (86%)	51 (89%)	.66
Probable	5 (14%)	6 (11%)	
Hearing stage[a]			
A	15 (41%)	12 (21%)	.012
B	10 (27%)	8 (14%)	
C	2 (5%)	14 (25%)	
D	10 (27%)	23 (40%)	
Major vertigo spells (mean ± SE)	3.0 ± 6.0	2.0 ± 4.6	.41
Migraine			
No	32 (55%)	19 (54%)	.93
Yes	26 (45%)	16 (46%)	

Abbreviations: CAD, coronary artery disease; DM, diabetes mellitus; HLD, hyperlipidemia; HTN, hypertension; IT, intratympanic injection; MD, Meniere's disease.

[a]Statistically significant.

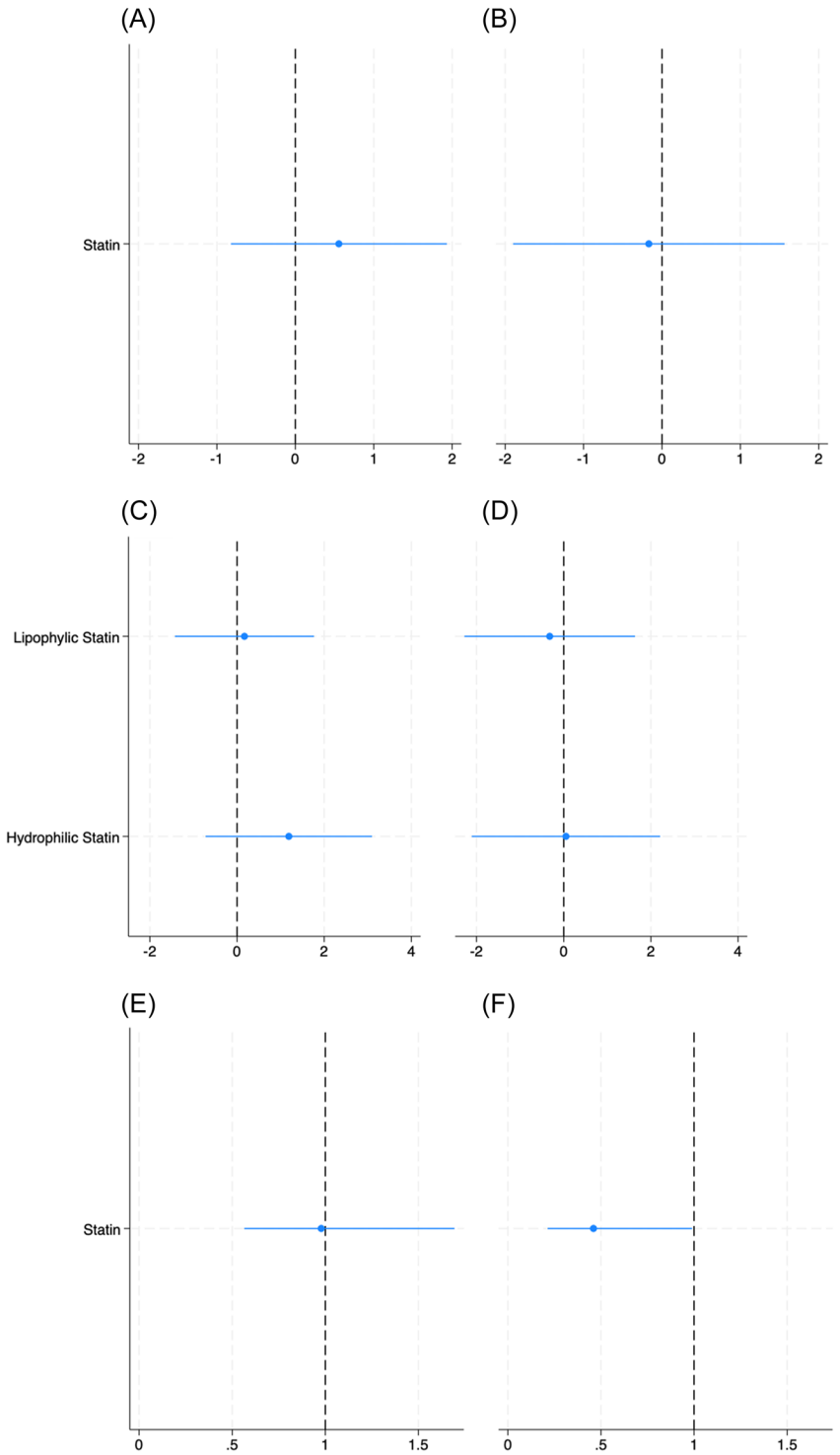

Figure 1. Univariable (A) and multivariable (B) linear regression comparing major spells in statin versus no statin groups. The statin group showed higher frequency of major spells per month compared to no statin group on univariable analysis (higher by 0.56 spells on average, $P = 0.4$) but a lower frequency of major spells (lower by 0.17 spells on average, $P = 0.9$). Both were not significant as evident by the horizontal lines crossing the 0 mark and indicating no difference between groups. Univariable (C) and multivariable (D) linear regression comparing major spells in hydrophilic and lipophilic statin groups versus no statin group. The difference in major spells between hydrophilic statin (higher by an average of 1.19 spells on univariable and 0.05 spells on multivariable analysis) and no statin groups as well as between lipophilic statin (higher by an average of 0.17 spells on univariable and lower by an average of 0.32 spells on multivariable analysis) and no statin group is very close to 0 and the confidence intervals cross 0, making the difference in major spells not significant both on univariable and multivariable analysis. Univariable (E) logistic regression comparing hearing stage in statin versus no statin groups showed no difference in hearing stage on univariable analysis (odds ratio = 0.98 and confidence interval crosses 1). However, on multivariable (F) analysis, the odds of worse hearing (stage C or D) were almost half in the statin group compared to no statins (0.46 and confidence interval does not cross 1). Please note that multivariable regression controlled for age, sex, diabetes, hyperlipidemia, hypertension, coronary artery disease, and intratympanic injections.

moderate with severe. Stata 13 was used for analyses (StataCorp LP).

Results

A total of 207 patients were included in our study (94 on statins). Univariable analysis showed significant difference in age, sex, and comorbidities only between statin (older, higher male proportion and more comorbidities) and no statin groups (**Table 1**). When looking within the statin group only, there was a significant difference in age, sex, and hearing stage among the patients on lipophilic (older, higher male proportion and worse hearing stage) versus hydrophilic statins (**Table 2**). Multivariable linear regression model showed no difference in the average number of major spells in the past month between statin and no statin groups when controlling for age, sex, comorbidities, and previous IT injection (1.8 ± 3.9 vs 2.4 ± 5.1, respectively; $P = .43$). Even when statins were subdivided into lipophilic and hydrophilic, there was no difference in the average number of major spells in the past month when controlling for confounders (**Figure 1**). However, on multivariable logistic regression, patients on statins had lower odds (almost half the odds) of worse hearing (C or D) compared to patients not on statins when controlling for the same confounders (adjusted odds ratio = 0.46, 95% CI = 0.21-0.99, $P = .047$).

Discussion

Statins are lipid-lowering medications with additional pleotropic effects including reduction of oxidative stress and inflammation.[6] They have demonstrated protective effects against noise-induced HL and gentamicin ototoxicity in animal models.[9,10] However, there has been only 1 study at the clinical level which utilized database data.[7] To our knowledge, this is the first clinical study to investigate the association between statin use and MD activity at the patient level.

The frequency of major spells was similar when comparing patients on statins to those who are not. However, the odds of worse hearing among MD patients on statins was almost half (odds ratio = 0.46, $P = .047$). In a study by Kim et al., no association was noted between prior statin use and the odds of having MD. Nonetheless, on stratification, they noted lower odds of MD in middle-aged individuals on lipophilic statins.[7] This could possibly be due to the ability of lipophilic statins to cross the blood-brain barrier and reach the inner ear.[7,12] In our study, the type of statin did not make a difference.

Our study demonstrated that statin use did not affect the vertigo spells but could be associated with lower odds of worse hearing. HL has been identified as a major risk factor for adverse health outcomes including reduced quality of life, depression, dementia, and all-cause mortality.[13] Thus, protecting hearing could have considerable effect in MD patients.

This study has several limitations: (1) retrospective design, and (2) recall bias (patient with active disease may overestimate episodes whereas patients with inactive disease might underestimate. However, we expect this to be equal in both arms).

Conclusion

Statin use showed no decrease in frequency of major vertigo spells but did show a lower odds of HL among patients with MD. Although our study results are limited, the use of statins in patients with MD could be protective of cochlear damage and resulting HL. Further studies are needed to confirm our results.

Author Contributions

Mustafa G. Bulbul, study design, data acquisition, analysis and interpretation, and manuscript writing and revision; **Tyler Wanstreet**, data acquisition, analysis and interpretation, and manuscript writing and revision; **Amani Kais**, data acquisition, data interpretation, manuscript writing and revision; **Garrett H. Jones**, study design, data acquisition, manuscript revision; **Brian M. Kellermeyer**, study design, data analysis and interpretation, and manuscript revision.

Disclosures

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