Statin Use and the Prevalence of Depressive Symptoms in Patients with Stable Coronary Heart Disease: A Prospective Cohort

BACKGROUND

- Major depression is hypothesized to have an immune related origin, and statins have an immunomodulatory effect.
- Statin use may have an effect on prevalence of depression in patients with coronary heart disease.

OBJECTIVE

- To evaluate the association between statin use at baseline and depressive symptoms during follow-up in patients with coronary heart disease.

METHODS

- **Design:** Multi-site, non-blinded prospective cohort study; duration of 6 years; participants enrolled by convenience sampling through mailed invitations.
- **Inclusion criteria:** At least one of the following: a history of myocardial infarction, angiographic evidence of at least 50% stenosis in one or more coronary vessels, prior evidence of exercise-induced ischemia by treadmill or nuclear testing, a history of coronary revascularization, or a diagnosis of coronary artery disease by an internist or cardiologist.
- **Exclusion criteria:** History of myocardial infarction within the past 6 months; deemed themselves unable to walk one block; planned on moving out of the area within the 3 years following initiation of the study.
- **Primary outcome measure:** Mean depression score (from 9 item Patient Health Questionnaire, or PHQ) at baseline.
- **Secondary outcome measures:** Presence of depressive symptoms (score of ≥10 on PHQ) at baseline and during follow-up; change in PHQ score at baseline and during follow-up; new onset depression during follow-up for those without depression at baseline (score of <10).
- **Treatment groups:** No controlled treatment groups; statin user (n=629) and nonuser (n=336) cohorts were determined at baseline assessment by whether or not participants brought in a medication bottle for simvastatin, simvastatin plus ezetimibe, pravastatin, rosuvastatin, atorvastatin, fluvastatin or lovastatin.
- Depressive symptoms were determined by scores of the PHQ at baseline, 1, 2, 3, and 4 year follow-up, and end of treatment assessment.
- Patients were included in the analysis if they completed two assessments.
- Power of study was not determined.

RESULTS

- Fifty-nine participants died prior to completing the first follow-up survey and were not included in the study. There were 965 participants who completed the study (at least two surveys). 85% of participants completed 80% of possible assessments.
- **Primary outcome measure:** Mean PHQ scores were statistically lower in users compared to nonusers at baseline (5.1±0.3 vs. 5.9±0.3 SE).
- **Secondary outcomes measures:** Presence of depression was lower in users than nonusers at baseline (17% vs. 24%; $p<0.02$) and during follow-up (28% vs. 40%; $p<0.01$). Baseline statin use was strongly predictive of subsequent PHQ depression scores as a continuous variable (β coefficient= -0.45; $p=0.02$); users have 33% decreased odds of having depression during follow-up than nonusers (OR=0.67; 95% CI, 0.48-0.92; $p=0.015$). No

difference in depression reported between those who did or did not continue to use statins ($p>0.40$), although no data for this analysis was not given. There was no difference between those who did die (n=137) and those who did not die (n=828) during follow-up; no data was given for this analysis either. In patients without depression at baseline, statin use was strongly predictive of subsequent depressive symptom scores (β coefficient= -0.48; $p=0.01$); users were less likely to have depression during follow-up as well (18% vs. 28%; $p<0.01$). Statin use decreased odds of developing depressive symptoms during follow-up by 40% (0.62; 95% CI, 0.41-0.95; $p=0.026$).

STRENGTHS

- Potential for a long follow-up period
- Specifically designed to evaluate depressive symptoms
- Surveys did not allow for researcher bias

LIMITATIONS

- Significant differences in age and gender between cohorts at baseline
- Higher rates of males in cohorts yet depression happens more commonly in females
- Pulled nearly 50% of participants from Veteran's Affairs clinics
- Convenience sampling could lead to unforeseen selection bias
- Undeterminable misclassification of statin use at baseline
- Undeterminable multivariable adjustments
- Only one method of determining if depressive symptoms were present
- Lack of causality, power, and follow-up with statin use during study period
- No follow-up with anti-depressant use after baseline
- Inadequate frequency of assessments
- Minimum of two assessments being used for evaluation (not enough to show trends)
- No analysis between duration of statin use and depressive symptoms and/or depression
- Standard error of mean used instead of standard deviation
- Lack of clinical significance despite statistical significance
- Cannot be extrapolated to other or similar audiences
- Chance of Type II error and missing data for the analysis of risk of death between cohorts and depression among those who did or did continue to use statins

CONCLUSION

- No clinical implications have arisen from this study due to its limitations.
    - Differences in PHQ scores may not vary enough to change therapy recommendations or management of symptoms.
    - Differences between cohorts and differences between study population and the general population do not allow for extrapolation of results.
    - There are too many limitations to assume an association.
- A randomized, double blind, controlled trial would be ideal to obtain causality, especially since the large weaknesses of the trial came from lack of control over the sampling and treatments.
    - However, such a study could be considered unethical because of the strong evidence behind statins reducing the risk of cardiovascular events in this population.
    - An alternative would be to compare statin users to patients who had previously tried and failed statin therapy in another, more tightly controlled prospective cohort study.

Reference:

Otte C, Zhao S, Whooley MA. Statin Use and Risk of Depression in Patients With Coronary Heart Disease: Longitudinal Data From the Heart and Soul Study. Journal of Clinical Psychiatry. May 2012; 73(5):610-5.

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