Journal of Clinical Lipidology (2015) 9, 226–233

Journal of Clinical Lipidology

Gender-related lipid and/or lipoprotein responses to statins in subjects in primary and secondary prevention

Giuliana Mombelli, MD*, Raffaella Bosisio, PhD, Laura Calabresi, PhD, Paolo Magni, MD, PhD, Chiara Pavanello, PhD, Franco Pazzucconi, MD, Cesare R. Sirtori, MD, PhD

Dipartimento Cardiotoracovascolare, A.O. Ospedale Niguarda Cà Granda, Milano, Italy (Drs Mombelli, Pavanello, Bosisio, and Sirtori); and Department of Pharmacological Sciences, Università degli Studi di Milano, 20133 Milano, Italy (Drs Calabresi, Pazzucconi, Magni, and Sirtori)

KEYWORDS:
Gender;
HMG-CoA reductase inhibitors;
Ischemic heart disease;
Lipid disorders/ atherosclerosis;
Risk factors

BACKGROUND: Cardiovascular risk in men rises around the fourth decade of life, whereas women appear to be protected by sex hormones until menopause. This, in turn, tends to negatively affect the lipid profile. Since the 1980s, the incidence of cardiovascular diseases has been reported to progressively decline in men, but it has persisted almost unchanged in women. Major clinical trials on statins have been mostly conducted in men and have fostered the introduction of these agents into clinical practice worldwide. However, only few reports have examined a possible differential activity of statins in the 2 genders, providing in some cases opposite findings.

OBJECTIVE: To evaluate gender-related differences in statin responses.

METHODS: Variations of lipid profile after 1-year of treatment with different statins in 337 dyslipidemic patients (171 men and 166 women).

RESULTS: In this series of patients, a significantly attenuated reduction of total cholesterol and low-density lipoprotein cholesterol in women vs men on drug treatment was noted after adjustment for dose and statin power (low-density lipoprotein cholesterol: $-28.5 \pm 11.8\%$ in men vs $-22.7 \pm 11.8\%$ in women; $P < .001$).

CONCLUSIONS: The present study indicates that statin treatment has a reduced effectiveness in improving the plasma lipid profile in dyslipidemic women vs men. Whether such gender-related differences may have an impact on clinical outcomes remains to be elucidated.
© 2015 National Lipid Association. All rights reserved.

Cardiovascular diseases (CVDs) are the leading cause of morbidity and mortality in women after the age of 50 years in most developed countries.[1] Cardiovascular (CV) morbidity and mortality start to increase at the age of 40 years in men and about 10 years later in women.[2] However, in specific conditions, such as immediately after a coronary event or a percutaneous transluminal coronary angioplasty, mortality appears to be higher in women than in men,[3] and long-term mortality data after acute myocardial infarction are worse in older women than in men of the same age.[4]

* Corresponding author. Dyslipidemia Center, Niguarda Cà Granda Hospital, Piazza Ospedale Maggiore 3, 20162 Milan, Italy.
E-mail address: giuliana.mombelli@ospedaleniguarda.it
Submitted June 9, 2014. Accepted for publication December 4, 2014.

1933-2874/© 2015 National Lipid Association. All rights reserved.
http://dx.doi.org/10.1016/j.jacl.2014.12.003

In men, the presence of risk factors determines the onset of coronary artery disease (CAD) from the third to fourth decade onward, whereas in women, the presence of sex hormones during the reproductive life is associated with a relative risk reduction, the onset of arterial disease being postponed until after surgical or natural menopause.[5,6] CV events are less frequent in women until the fifth to sixth decade. Since the mid-1980s, the incidence of CAD in men has declined progressively, whereas it has remained fairly constant in women.[7,8]

Because statins provide the most effective pharmacologic approach to the reduction of CV risk, a possible differential response both in terms of risk and of lipid changes in the 2 genders has been investigated by some authors. An early meta-analysis by Walsh and Pignone[9] on studies conducted with cholesterol-lowering drugs in women reported a definite reduction in CV events in secondary prevention, but this did not clearly occur among those in primary prevention. The meta-analysis on 11 randomized secondary prevention studies by Gutierrez et al[10] came to the same conclusion, that is, statin therapy is an effective strategy in the secondary prevention of CV events in both sexes. More recently however Petretta et al[11] examined the impact of gender in the primary prevention of CV events and of total mortality with statin therapy. Although a clear reduction of risk, but not of total mortality, was noted in men, statin treatment in women did not appear to exert a clear beneficial effect on total mortality or CV events.

The possibility that a reduced lipid-lowering activity of statins may occur in women has been suggested by a number of authors. A multinational study[12] reported that women show a reduced cholesterol reduction after statins and a less frequent attainment of the cholesterol goals of the National Cholesterol Education Program Adult Treatment Panel III or of other national guidelines. A similar conclusion, that is, a reduced attainment of treatment targets, was also reached by the e-Registry in Germany.[13] Very recently, a retrospective study on 950 CAD patients followed by a large cardiology subspecialty of clinical practice, confirmed a different reduction in low-density lipoprotein cholesterol (LDL-C) levels between the 2 genders, in particular women being less likely to achieve their lipid goals.[14] We attempted to confirm these findings in a series of patients of both genders in predominantly primary, but also secondary prevention settings, followed for 1 year or longer and based on our findings offer potential explanations for such interaction.

Methods

Study subjects

In this retrospective observational study, we evaluated a total of 337 dyslipidemic Italian patients of the Lipid Clinic recruited from April 2010. They were selected from a sample of 7500 men and women regularly followed at the Clinic. Of the initial 7500 patients, we excluded from our analysis those who were well responding to diet alone, patients treated with nutraceuticals or fibrates and those who had experienced side effects with statins. Of patients treated with statins, we took into account only those with baseline LDL-C between 170 and 250 mg/dL and those who were on a stable statin dose for at least 1 year (Fig. 1).

The medication compliance was assessed for the duration of the study, considering that patients are regularly followed from the physicians of the Center. Every patient undergoes an average of 3 to 4 clinical examinations and laboratory analyses per year. Clinical and laboratory data are recorded into an electronic clinic chart (Lipid Chart). Dose changes or treatment suspension and adverse events or other particular conditions referred by the patients during the clinical examination are reported in the Lipid Chart. Adherence to treatment was verified with a questionnaire, asking whether patients took the medication, whether it was taken at the right time, and whether medication has stopped for any reason. Patients not entirely compliant were excluded from the analysis.

Total CV risk was estimated with the Systematic COronary Risk Evaluation (SCORE) algorithm, used in the clinical management of CV risk in European countries. Subjects were subdivided into 2 different SCORE charts (high and low risks) based on gender, age, total cholesterol (TC), systolic blood pressure, and smoking status, with relative risk chart, qualifiers, and instructions. Four different CV risk levels and LDL-C targets to be achieved are given: very high risk (LDL-C goal $<$70 mg/dL and/or $\geq$50% when target cannot be reached), high risk (LDL-C goal $<$100 mg/dL), moderate risk (LDL-C goal $<$115 mg/dL), and low risk (LDL-C goal not given).[15,16]

Laboratory procedures

A fasting plasma lipid and/or lipoprotein profile was measured at the baseline and after 1 year of treatment. Blood samples were collected in BD Vacutainer SST II Advance tubes after an overnight fast and centrifuged at 4°C at low speed. The determination of plasma concentrations of TC, high-density lipoprotein (HDL-C), and triglycerides was performed with certified methods using an auto-analyzer Integra 400 (Roche Diagnostics), as reported by a number of clinical studies in this Institution.[17] Concentrations of LDL-C were calculated using the Friedewald formula.[18]

Statistical analyses

Results are expressed as means $\pm$ standard deviation. Lipid values at baseline and after 12 months of treatment with statins were compared by paired t test (z test for binary data) for pretreatment and posttreatment in men and

Download English Version:

https://daneshyari.com/en/article/5985874

Download Persian Version:

https://daneshyari.com/article/5985874

Daneshyari.com