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Original article

Persistence With Statins in Primary Prevention of Cardiovascular Disease: Findings From a Cohort of Spanish Workers

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ABSTRACT

Introduction and objectives: The aim of this study was to assess patterns of treatment persistence in a cohort of male Spanish workers receiving statin therapy for primary prevention of cardiovascular disease.

Methods: This descriptive study was conducted within the framework of the prospective longitudinal Aragon Workers' Health Study (N = 5400). Incident male statin users were identified based on data collected from the regional government's medication consumption information system. Patterns of treatment persistence with statins prescribed for primary cardiovascular disease prevention were assessed and the relevance of potential predictors explored.

Results: Among the 725 new statin users, less than one third remained persistent during the 1 year of follow-up. About 15% of nonpersistent users discontinued statin therapy after dispensation of the first prescription; of these, 42.1% did not recommence treatment within the following year. Factors reducing the likelihood of treatment discontinuation were older age (HR, 0.55; 95%CI, 0.39-0.77) and cotreatment with antihypertensive drugs (HR, 0.68; 95%CI, 0.56-0.82). No association was observed between treatment persistence and cotreatment with antidiabetic or antithrombotic drugs, baseline low-density lipoprotein levels, or total cholesterol levels. However, persistence was influenced by the type of statin first prescribed.

Conclusions: Our analysis of a cohort of healthy male workers revealed poor statin persistence. These findings underscore the need for a better understanding of patterns of statin use, especially in apparently healthy individuals, and for the incorporation of patient behavior into prescribing decisions.

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Persistencia con estatinas en prevención primaria de enfermedad cardiovascular: resultados en una cohorte de trabajadores españoles

RESUMEN

Introducción y objetivos: El objetivo de este estudio es analizar el patrón de persistencia con estatinas en prevención primaria de enfermedad cardiovascular en una cohorte de trabajadores españoles.

Métodos: Este estudio descriptivo se llevó a cabo en el marco del estudio prospectivo longitudinal Aragon Workers' Health Study (n = 5.400). Se identificó a los nuevos usuarios de estatinas varones a partir de datos recogidos en el sistema de información de consumo farmacéutico de Aragón. Se analizaron los patrones de persistencia con estatinas prescritas en prevención primaria cardiovascular, así como los potenciales predictores.

Resultados: De los 725 nuevos usuarios de estatinas, menos de un tercio habían persistido durante el año de seguimiento. Alrededor de un 15% de los usuarios no persistentes interrumpieron la terapia con estatinas tras la dispensación de la primera receta y, el 42,1% de ellos no reiniciaron el tratamiento durante el resto del año. La mayor edad (HR = 0,55; IC95%, 0,39-0,77) y el cotratamiento con fármacos antihipertensivos (HR = 0,68; IC95%, 0,56-0,82) redujeron la probabilidad de que se interrumpiera el tratamiento. No se observó asociación entre la persistencia con el tratamiento y la toma concomitante de fármacos antidiabéticos o antitrombóticos, las concentraciones basales de lipoproteínas de baja densidad o las de colesterol total. Sin embargo, la persistencia sí estuvo influida por el tipo de la primera estatina prescrita.

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Conclusiones: Nuestro análisis en una cohorte de trabajadores varones sanos muestra una baja persistencia con estatinas. Estos resultados reflejan la necesidad de comprender mejor los patrones de utilización de estatinas, especialmente por individuos aparentemente sanos, y de incorporar la conducta del paciente a las decisiones de prescripción.

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Abbreviations

AWHS: Aragon Workers' Health Study

CV: cardiovascular

LDL-C: low-density lipoprotein cholesterol

INTRODUCTION

Statins, by reducing blood cholesterol levels, decrease cardio-vascular (CV) events and all-cause mortality in individuals with and without evidence of CV disease. While rates of statin use are high in most European populations, cholesterol control in these same populations is generally poor, decident that statin effectiveness may not correspond exclusively to the efficacy demonstrated in clinical trials, but rather is affected by real-life patterns of statin use. Among the contextual characteristics and behaviors that influence goal attainment, a key factor is "patient persistence" (i.e., whether the patient persists with treatment). Indeed, longer duration statin therapy is associated with improved clinical outcomes. Indeed, longer duration statin therapy is associated with improved clinical outcomes.

Several studies have assessed rates of treatment persistence with statins for secondary prevention of CV disease. ^{5,6,8} However, less is known about treatment persistence in the case of statin use for primary prevention of CV disease in young people. Both primary prevention regimens and young age are associated with poorer treatment adherence, ^{9,10} probably because the users in question do not perceive themselves as being "sick". Describing patterns of statin treatment persistence in this type of population is essential to enhance persistence and ultimately improve the prevention of chronic conditions.

The objective of this study was to assess the pattern of persistence with statin therapy for primary prevention of CV disease in a cohort of male Spanish workers.

METHODS

Study Population and Data Sources

The Aragon Workers' Health Study (AWHS) is a prospective longitudinal study designed to characterize cardiometabolic factors and assess subclinical atherosclerosis in a middle-aged Mediterranean working population. For that purpose, we analyzed data from routine annual health examinations of workers at a Spanish automobile assembly plant in Figueruelas, Zaragoza (Spain), who voluntarily agreed to participate in the study. The cohort was recruited between February 2009 and May 2010, and consisted of 5400 workers. Participants aged 40 to 55 years were additionally invited to participate in triennial imaging examinations to assess the presence of subclinical atherosclerosis and complete additional questionnaires of CV and lifestyle factors. At baseline, 587 (94.5% men) were selected for this intensive followup group. Most of the workers witihin the cohort were involved in manual jobs (86.5% of men and 60.5% of women). Other baseline characteristics are shown in Table 1.11 The cohort showed a high prevalence of CV risk factors and subclinical atherosclerosis but a low prevalence of clinical CV disease. Active follow-up of participants is expected to continue through 2020. Further information on the AWHS can be found in Casasnovas et al.¹¹

We designed the present observational descriptive study to assess persistence with statin therapy in the AWHS cohort. Statin prescription data corresponding to AWHS participants was gathered from Farmasalud, the government medication consumption information system for Aragon, which is the Spanish autonomous community where the automobile factory is located. This database collects data on all prescriptions dispensed at pharmacies in Aragon through the public health care system (i.e., prescribed by either a company physician or a general practitioner from the public health care system). Prescriptions issued by private physicians, insurance companies, or in-hospital consumption, are not collected in Farmasalud. Each record in the data source corresponds to a prescription and contains the following information: an anonymous patient code, patient sex and birth date, dispensing date, Anatomical Therapeutic Chemical code of the prescribed drug, number of defined daily dose, and number of packages dispensed. Drugs were classified according to the 2015 version of the World Health Organization Anatomical Therapeutic Chemical code/Defined Daily Dose System. 12 Via an encrypted code provided by AWHS researchers, we identified prescriptions for statins, both alone (Anatomical Therapeutic Chemical code C10AA) and in combination with other lipidmodifying agents (C10BA), issued between January 1, 2010 and December 31, 2014.

From the AWHS database we gathered data on CV events experienced by AWHS participants (date and event type), as well as levels of total cholesterol and other lipid fractions recorded at annual medical examinations. The low-density lipoprotein cholesterol (LDL-C) value for each patient and examination was calculated using the Friedewald formula, 13 based on total cholesterol, high-density lipoprotein cholesterol, and triglyceride values.

Table 1
Aragon' Workers Health Study Baseline Characteristics

	Men (n = 5048)	Women (n = 351)
Age, y	49.3 (8.7)	40.8 (11.6)
BMI, kg/m ²	27.7 (3.6)	24.4 (3.8)
Systolic BP, mmHg	127.0 (14.7)	111.4 (13.2)
Diastolic BP, mmHg	83.8 (10.1)	76.4 (9.5)
Total cholesterol, mg/dL	212.4 (37.6)	204.3 (39.9)
HDL-C, mg/dL	52.4 (11.0)	66.5 (14.2)
Triglycerides, mg/dL	148.8 (106.1)	89.7 (75.5)
Glucose, mg/dL	98.3 (19.6)	91.2 (16.3)
Smoking		
Never	1796 ± 35.8	146 ± 41.8
Former	1359 ± 27.1	46 ± 13.2
Current	1862 ± 37.1	157 ± 45.0

BMI, body mass index; BP, blood presure; HDL-C, high-density lipoprotein cholesterol

Data are expressed as mean \pm standard deviation or no. (%). Reproduced with permission from Casasnovas et al. ¹¹

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