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Cigarette Smoking, Alcohol Consumption and Overweight in Multiple Sclerosis: Disability Progression

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Background. The rate at which disability progresses in multiple sclerosis (MS), and its severity, have been associated with modifiable lifestyle habits.

Objective. To investigate the risk of disability progression in MS patients according to tobacco and alcohol consumption and to the presence of overweight.

Methods. This was a follow-up of MS cases from a concluded case-control study (National Institute of Neurology and Neurosurgery, Mexico 2010–2013). The evolution in EDSS (Expanded Disability Scale Score) units was followed through a medical record review. Kaplan Meier statistics and multivariate Cox regression analysis were performed.

Results. Of 181 cases, 63.5% were women and 82.5% had relapsing remitting MS. Study duration was 19.95 ± 15.24 months. The disease progressed faster in daily smokers than in non-smokers ($p = 0.0168$). In overweight patients, disability progressed faster than in normal weight patients ($p = 0.0249$). Ex-consumers of alcohol had lower risk of progression than current consumers (HR = 0.33 CI 95% = 0.14–0.83, $p = 0.019$) and both daily and ex-smokers presented higher risk of progression than non-smokers (HR = 2.32 CI 95% = 1.14–4.72, $p = 0.020$ and HR = 3.56, CI 95% = 1.21–10.46, $p = 0.021$). Stratifying by gender, the effects of smoking and overweight were only found in men.

Conclusions. Smoking is associated with rapid disability progression in MS. Our results suggest that cessation of tobacco and alcohol consumption could be clinically beneficial. Although there is association between overweight and disability progression in men, a further exploration of gender differences is necessary to corroborate this finding.

Key Words: Cigarette smoking, Alcohol consumption, Overweight, Multiple sclerosis, Disability.

Introduction

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS). It is characterized by an inflammatory and demyelinating process, occurs predominantly in women and symptoms appear at an average age of 30 years old (1). Clinical progression and axonal damage level vary between individuals and the causes that lead to evolution from non-progressive to progressive forms are not fully known (2).

MS etiology has been linked to complex genetic susceptibility profiles accompanied by environmental conditions (3). Several risk factors for MS associated with disability progression are currently in debate: ethnicity, education, age at disease onset, early treatment, obesity during early life, diet, cognitive impairment at diagnosis, brain atrophy and comorbidity are some of the sociodemographic and

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clinical factors with conflicting results (4−9). On the other hand, well known risk factors as tobacco consumption are yet to be comprehended in the full extent of its impact on the progression of the disease (10).

Adverse health habits such as cigarette smoking, alcohol consumption, as well as reduced physical activity, have been reported frequently in MS patients (11); this implies a risk of developing other chronic diseases and theoretically all disease's outcomes can be affected by comorbidity (12). In a cohort study of 895 patients with MS, cigarette smoking was associated with severe and rapid progression of the disease (13).

Studies that addressed alcohol consumption and disability in MS show inconclusive results. Although alcohol consumption is not necessarily more frequent in MS patients (14), an association with mood disorders has been reported, making these patients particularly vulnerable to other complications (15). In contrast, other studies suggest that alcohol may have a protective effect on MS progression (as in other autoimmune diseases) (16).

Some studies report that young people with a background of obesity have increased risk of developing MS; although the pathophysiologic mechanism for this is not known, an association with vitamin D deficiency (common in overweight patients) has been proposed (17−19). Obesity in MS generates a state of cellular inflammation (20), in this context, recent studies elaborate the possible participation of the adipocyte which releases leptin and other adipokines. Leptin act a modulator of immune responses and induces a low grade inflammatory state (21) which could represent a risk for disease activity and long term progression (22).

Data on the distribution of MS in Latin America are limited, the prevalence rates estimated for Mexico range from 1.5−3 per 100 000 but there are reports of higher prevalence and of elevation of incidence up to ten times in some regions, explained by new and better protocols of diagnosis implemented in the country and to disease literacy (23−27). A recent descriptive study exposes clinical and demographic characteristics or 313 Mexican patients with MS with similar results to those reported in literature (28). To our knowledge, there is not background of follow up studies of Mexican patients with MS that explore disability and health behaviors trough time.

The aim of this study was to investigate the risk of disability progression in MS patients related to cigarette smoking, alcohol consumption and to the presence of overweight.

Methods

Study Design and Ethic Approval

This follow-up study is a secondary analysis derived from the case-control study Risk factors associated with multiple sclerosis in Mexico: A multicenter study conducted from 2010−2013 and approved by the Ethics, Biosafety and Research Committees of the National Institute of Neurology and Neurosurgery (*INNN*) and of the National Institute of Public Health (*INSP*) (approval number CI.790, No.684). With the authorization from the institutional authorities and committees, cases were followed through their medical records for an average of 20 months since the application of the original questionnaires.

Population

From the original case-control design (n = 615), we considered information on 205 diagnosed MS cases, according to the updated McDonald criteria (29). Inclusion criteria: ages over 18 years and centralized at the *INNN*. Exclusion criteria: background of any neurologic or psychiatric disease. For the medical record review, we excluded patients with less than two EDSS (expanded disability scale score) measurements from baseline, unavailable records and observations with data entry errors.

Measures or Interest

In the main study, after informed consent was obtained, structured interviews were conducted by trained personnel to obtain sociodemographic, clinical and nutritional information. This follow-up study was limited to data registered in the sociodemographic and clinical sections of the questionnaires.

Sociodemographic and clinical variables collected were: gender, education and access to social security, type of MS, EDSS baseline value, disease duration, age at diagnosis, medical history, number of relapses before baseline, and baseline treatment. Disease duration was calculated from diagnosis to the date of application of questionnaires (baseline).

Regarding exposure, questions in the main study were asked about smoking habits throughout life, frequency of consumption, average number of cigarettes smoked per day and time of cessation. Similarly, subjects were asked about alcoholic habit throughout life and frequency of consumption time. Current smoker and current consumer of alcohol were defined as a person that smoke or drunk an alcohol beverage in the las 30 d. Scales where obtained from the basic series of validated questions used in the Global Adult Tobacco Survey (30) and from a validated semi quantitative instrument elaborated for exploring nutritional intake including alcohol consumption (31,32).

Height and weight measurements reported in the original questionnaires were used to calculate the body mass index (BMI); these measurements were taken by standardized personnel with standardized instruments. Three categories where constructed according to the World Health Organization (WHO) criteria (33): normal weight (BMI of 18.5−24.9), overweight (BMI of 25−29.9) and obesity (BMI greater than 30).