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Sex differences in nicotine dependency and depressive tendency among smokers

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ABSTRACT

Depressive tendency and nicotine dependency are factors related to the failure of smoking cessation. Women generally have a higher depressive tendency and difficulty in smoking cessation than men. However, the impact of sex differences on the relationship between nicotine dependency and depressive tendency remains unclear. We evaluated 727 patients (496 men and 231 women) who visited our outpatient clinic for smoking cessation therapy and compared various parameters measured between sexes during consultation. Age, duration of smoking, and daily cigarette consumption were significantly higher in men during the first visit. Women had significantly higher self-rating depression scale (SDS) scores and took significantly more antidepressant drugs than men. The SDS score significantly correlated with the Fagerström test for the nicotine dependence score and with daily cigarette consumption in women, but not in men. Thus, the present study demonstrates the differential relationship of depressive tendency with tobacco use or nicotine dependency in men and women, which might reflect sex differences in response to psychological stress.

1. Introduction

Sex affects several conditions. Over the past few years, studies have shown that risk factors for the same condition may differently affect men and women and that the efficacy of the same drugs may differ in men and women. Typically, the occurrence of lifestyle-related diseases, such as alcoholic hepatitis, myocardial infarction, and chronic obstructive pulmonary disease, is more common in men. In contrast, depression, dementia, autoimmune diseases, and osteoporosis are increasingly common in women. Sex differences greatly affect the pathology of and prognosis for cardiovascular disease. Women are more sensitive to risk factors and are more likely to develop tobacco-related diseases, such as cardiovascular disease (Prescott et al., 1998; Bosetti et al., 1999; Mähönen et al., 2004; Oda et al., 2006; Sasaki et al., 2006; Huxley and Woodward, 2011), stroke (Peters et al., 2013), and chronic obstructive pulmonary disease (de-Torres et al., 2005; Sin et al., 2007). Women smokers encounter various health-related problems, including female-specific hazards such as cervical cancer, menstrual disorders, and infertility, as well as general health risks caused by smoking in both sexes (Mackay and Amos, 2003).

The smoking rates of both men and women have declined in several developed countries. In Japan, the prevalence of smoking among men has decreased from a peak of 83.7% in 1966 to 30.3% in 2014. In contrast, the prevalence among women has not decreased but remained stable at approximately 10% for 50 years (CDC, 2012; Ministry of Health, Labor and Welfare, 2014). Smoking may be a part of an unhealthy lifestyle, i.e., a lack of exercise and overeating due to psychosocial stress (Suzuki et al., 2016). Several patients have a poor lifestyle with multiple bad habits, such as obesity due to overeating, diabetes, and smoking. An individual succumbs to stress if psychosocial stress persists, and the individual shows depressive tendencies. Depressive tendency has been suggested to be associated with smoking (Lasser et al., 2000). Furthermore, anxiety and depression have been reported to be caused by smoking (Goodman and Capitman, 2000). Smokers with a history of depression are less likely to discontinue smoking during the smoking cessation therapy (Mendelsohn, 2012). A previous study has reported that women with a history of a major depressive disorder are more likely to resume smoking than men (Rodríguez-Cano et al., 2017). These subjects may have difficulties in maintaining long-term smoking cessation even with successful smoking

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cessation therapy (Hitsman et al., 2013). In addition to depression, the number of cigarettes smoked per day and nicotine dependency are factors related to the failure of smoking cessation (Tunstall et al., 1985; Blazić-Cop et al., 2001; Chatkin et al., 2004; Green et al., 2006; Panday et al., 2007; Ziedonis et al., 2008; Mendelsohn, 2012; Hitsman et al., 2013). Women generally have a higher depressive tendency and lower success rate for smoking cessation than men. Women who attempt to quit smoking but fail to do so resume smoking sooner than men (Ward et al., 1997; Cepeda et al., 2004). However, in Japan, women consume fewer cigarettes daily. Whether sex differences affect the relationship between nicotine dependency and depressive tendency remains unclear. The analysis of sex differences in individuals undergoing smoking cessation therapy would lead to better approaches to smoking cessation that can modify sex differences. Thus, our study aimed to examine the interaction among metabolic parameters, depressive tendencies, and factors related to smoking in men and women participating in an outpatient smoking cessation program and to evaluate sex differences in these factors.

2. Materials and methods

2.1. Subjects

This was a prospective study conducted at the National Hospital Organization, Kyoto Medical Center, from April 2007 to July 2013. Subjects included in this study were patients who consulted the smoking cessation clinic to receive treatment, those who provided informed consent, and those who consented to participate in this study during the enrollment period. Our study continuously recruited participants over a 6-year period, and the self-rating depression scale (SDS) scores were analyzed during the initial visit of patients to the smoking cessation clinic. Potential participants were not arbitrarily excluded, and a total of 727 patients were enrolled. Various parameters were evaluated in these patients during the initial consultation.

2.2. Procedures

2.2.1. Data collection

The body mass index (BMI) was calculated as the weight (in kg) divided by the height (in m) squared. The systolic (SBP) and diastolic (DBP) blood pressures were measured in a sitting position using an automatic electronic sphygmomanometer (BP-103iII; Nippon Colin, Komaki, Japan) after the patients rested for more than 5 min (McManus et al., 2003). The regular-sized cuff that is appropriate for the Japanese (arm length, 17–32 cm) was used as recommended. The expiratory CO concentration was measured by a nurse using the EC50 Micro Smokerlyzer^{R} (Bedfont Scientific Ltd., Kent, UK), which electrochemically measures the end-tidal CO concentration with a reported precision of $<2\%$ (Hald et al., 2003). The Fagerström test for nicotine dependence (FTND), a world standard test used to assess the physical dependence of nicotine, was used (Fagerström et al., 1990; Heatherton et al., 1991; Terry and Rustin, 2000). The score ranges from 0 to 10, with higher scores indicating more severe nicotine dependence. The number of cigarettes smoked daily was determined by asking the smokers the following question: “On average, in the past month, how many cigarettes did you smoke per day?” The Brinkman index was calculated by multiplying the daily number of cigarettes smoked by the number of smoking years. The severity of depression was assessed using the Zung SDS, which is a self-report questionnaire used to track changes in the depression levels over time in research studies or in the clinical course following treatment (Zung, 1965; Zung et al., 1965). All patients completed the questionnaires at the hospital clinic. Subsequently, the questionnaires were reviewed by a member of the study staff, and patients were instructed to redo the questionnaire if any omission was found (Hasegawa et al., 2008; Wada et al., 2008). A higher score indicated a more severe depressive state.

In the present study, we used the Japanese version of FTND and SDS, which are official questionnaires translated into Japanese and widely used in Japan. The Japanese versions of FTND and SDS are reportedly both reliable and valid. The test–retest correlation and the Cronbach's alpha of FTND were 0.75 and 0.66, respectively, and the score significantly correlated with the standard of satisfied criteria of nicotine dependence ($r = 0.70$; $p < 0.001$). The sensitivity and specificity of FTND were 0.75 and 0.80, respectively (Mikami et al., 1999). Similarly, the test–retest correlation, split-half correlation, and Cronbach's alpha of SDS were 0.85, 0.73, and 0.82, respectively (Kurimoto et al., 2011; Fukuda et al., 2011), and the score significantly correlated with the total number of items and psychological dependence-related items in the diagnostic guideline of dependence syndrome of the ICD-10 ($r = 0.76$, $p < 0.01$) (Ozaki and Wada, 2005).

The classification by the SDS score in the present study was performed based on the classification of the Japanese version of the Zung SDS, which represents the SDS score using the raw score opposed to the index. The mean ± standard deviation of the SDS score in Japanese was 35 ± 12 and 49 ± 12 points in the normal and neurotic patient groups, respectively. Therefore, the ranges of the SDS score were 23–47 and 39–59 points in the normal and neurotic patient groups, respectively. Patients were divided into the following three groups on the basis of these ranges identified by Zung: normal (score ≤ 38), borderline neurotic (score = 39–47), and neurotic/depressed (score ≥ 48).

2.2.2. Blood sampling

Blood examinations were performed during the first consultation to assess the biochemical and hematological profile of patients. Blood samples were obtained from the antecubital vein 2–3 h after lunch to determine hemoglobin A1c (HbA1c), triglyceride (TG), high-density lipoprotein-cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C) levels. The blood samples were immediately centrifuged at 3000 rpm for 10 min at 4 °C. The plasma levels of HbA1c and serum levels of HDL-C, and LDL-C were measured using an automatic analyzer (LABOSPECT 008; Hitachi High-Technologies Co., Ltd., Tokyo, Japan) with enzyme-based reagents (Kyowa Medex Co., Ltd., Tokyo, Japan) (Komiyama et al., 2015).

2.2.3. Statistical analysis

All statistical analyses were performed by a professional statistician using the statistical package for the social sciences (SPSS) Statistics 17.0 (SPSS Inc., Chicago, IL, USA). Normality was assessed using the Shapiro–Wilk test. Data on various parameters on patients during the initial consultation were compared using an independent *t*–test, Mann–Whitney *U* test, or chi–square test. The correlations between the FTND score and various parameters with respect to sex were examined using correlation analysis, and the factors related to the FTND score were analyzed using multivariate analysis. The correlation among the SDS and FTND scores and the number of cigarettes smoked daily was assessed using the Pearson correlation or Spearman rank correlation coefficient. The distribution of SDS scores for men and women were compared using a Mann–Whitney *U*–test.

2.2.4. Ethical aspects

Informed written consent was obtained from all participants. The study data were anonymized with no personal identifiers. The study protocol was approved by the Ethical Review Board, National Hospital Organization, Kyoto Medical Center.

3. Results

3.1. Participants

A total of 727 patients (496 men and 231 women), aged between 22 and 82 years were enrolled. Of the 727 participants, 147 (20.2%) received antihypertensive agents, 81 (11.1%) received statins, 69 (9.5%)