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Effects of cigarette smoking on respiratory problems and functional levels in multiple sclerosis patients

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ABSTRACT

Objective: The aim of the study was to investigate the effects of smoking on respiratory symptoms and functional levels by questioning use of cigarette in Multiple Sclerosis (MS) patients.
Methods: A questionnaire was sent via e-mail to the 135 MS patients, who clinically diagnosed with MS and EDSS score was determined.Perceived dyspnea was assessed by the mMRC scale.The severity of dyspnea and fatigue perceived during rest and effort was assessed by the mBORG scale.Functional levels of the patients were assessed by asking the average daily walking distance and the average sitting time daily.
Results: The mean EDSS score of the smoker and the non-smoker group were 2.85 ± 0.75, 2.96 ± 1.03 respectively($p = 0.48$).There was no statistically difference found between groups in terms of age,height,weight,BMI,gender,EDSS scores($p > 0.05$).The rate of cough, sputum and severity of perceived dyspnea was statistically higher in the smoker group($p < 0.05$).The mean walking distance daily of the smokers was statistically lower ($p < 0.001$).The smoker group had a high level of sedanter lifestyle($p < 0.05$).
Conclusion: It has been proven that smoking increases respiratory problems even in MS patients with a good EDSS score.Moreover, these problems lead to a further reduction in the functional levels of the patients, in addition to the disease progression.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease with multifactorial etiology characterized by neuroinflammatory and neurodegenerative pathological phases (Briggs et al., 2014). Studies demonstrate that autoimmunity plays an important role in MS etiology (McFarland and Martin, 2007). Diseases like MS arise from not only individual genetic susceptibility but also environmental factors, that influence both incidence and clinical progression of the disease. Environmental risk factors affecting MS risk include low exposure to ultraviolet radiation and lack of vitamin D, Epstein-Barr virus and smoking (Wingerchuk, 2011, 2012). In many retrospective and prospective studies cigarette smoking has been proven to increase the risk of MS (Hawkes, 2007). Moreover tobacco use is the most important cause of preventable death that constitutes over 6 million premature deaths worldwide (WHO, 2013)

Epidemiological studies focusing on cerebrovascular disorders associate smoking with the pathogenesis and / or progression of a number of important neurological diseases. These include silent cerebral infarction (Howard et al., 1998), stroke (Mannami et al., 2004), small vessel ischemic disease (due to anticoagulant and atherogenic effects of smoking) and cerebral aneurysms (Mast et al., 1998; Miller et al., 1998). It has also been demonstrated that there is a strong correlation between smoking and the increased risk of MS (Hedström et al., 2013; Salzer et al., 2013).

Although some neuropathological effects of smoking are dependent on specific nicotine-acting pathways, precise cerebrovascular harmful mechanisms triggered by smoking are still unclear. However, recent studies clearly show that smoking can lead to the loss of function and integrity of the blood-brain barrier which is an important prodromal factor in the pathogenesis of neurological diseases. Cigarette smoke contains a large and still unclear number of highly reactive oxidative species, causing oxidative and inflammatory damage. It has also been reported that reactive oxidative species and inflammation are involved in the central mechanisms that initiate and promote the progression of the disease in neurological diseases such as MS, Alzheimer's disease,

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stroke, small vessel ischemia (Naik and Cucullo, 2015).

Studies of MS progression have proven that disease progression in smokers is faster (Manouchehrinia et al., 2013). In addition, the incidence of MS was increased with smoking as well (Di Pauli et al., 2008). Clinical trials have reported decreased indolamine 2,3-dioxygenase activity, altered cytokine and chemokine levels, and decreased number of T cells in smokers (Correale and Farez, 2015). This clinical course shows that autoimmune development contributes to the progression of the disease. Because indolamine 2,3-dioxygenase has been shown to reduce inflammation in autoimmune encephalomyelitis (Kwidzinski et al., 2005). It is already known that smoking is related to the susceptibility of various autoimmune diseases (Hardy et al., 1998; Saag et al., 1997). In addition, there are not many studies on this matter. This suggests that the issue is still a matter of research.

Dyspnea, that defined “the experience of breathing discomfort with qualitatively different senses of varying intensity” is a critical symptom because of predictor of hospitalization and mortality. It is a common, distressing symptom of neuromuscular and cardiopulmonary diseases. Dyspnea first emerges with physical effort, then goes further (Parshall et al., 2012). It is also increases with smoking (Miedinger et al., 2006).

Therefore, our study aims to investigate the effects of smoking on respiratory symptoms such as dyspnea,cough, sputum, fatigue and functional levels by questioning use of cigarette in MS patients.

2. Materials and methods

2.1. Study population

A questionnaire was sent via e-mail to the 135 MS patients, who clinically diagnosed with MS and Expanded Disability Status Scale (EDSS) score was determined, in the Department of Neurology in Dokuz Eylul University. The inclusion criteria were to be diagnosed with MS, volunteer to participate, self-sufficient and able to walk without help for about 12 h a day. The exclusion criteria were to be mentally inadequate, having EDSS score above 4, missed survey responses, not being voluntary, having an MS attack in the last 6 months, having cognitive and psychological problems. The patients were divided into two groups: smokers ($n = 68$) and non-smokers ($n = 67$). The flowchart of the study is shown in Fig. 1.

2.2. Measurements

All assessments were conducted with a questionnaire sent to the patient via e-mail. Demographic and clinical characteristics of patients were questioned. Body mass index (BMI) of participants' were calculated by weight and height as kg/m2.

The EDSS scores were recorded from the hospital information management system as a result of the neurological assessment the neurologist performed last. EDSS is a method of quantifying disability in MS and monitoring progression in the level of disability over time. It is widely used in clinical trials and in the assessment of people with MS. The scale was developed by John Kurtzke in 1983 as an advance from his previous 10 step Disability Status Scale (DSS). The EDSS scale represents high levels of disability with an increase of 0.5 ranges from 0 to 10 (Kurtzke, 1983).

Modified Medical Research Council (mMRC) Dyspnea Scale, which consist of five-item scale based on a variety of physical activities that cause a feeling of dyspnea, was used to determine the severity of patients’ shortness of breath. The participants read and chose the most appropriate scale option between 0 and 4 that best describes the degree of their pulmonary distress (Bestall et al., 1999).

The severity of dyspnea and fatigue perceived during rest and effort was assessed by the mBORG scale which was developed by Borg. The aim was to simplify the scoring of related expressions, in order to be used by the less-educated population, which may not be familiarized with technical and mathematical expressions. This consisted of a vertical scale labelled 0–10, with corresponding verbal expressions of progressively increasing symptom intensity (Corcioli et al., 2017).

We asked two questions in the questionnaire to assess the amount of cigarette consumption. “How many years have you been smoking?” and “how many packs do you smoke on average per day?” Then we multiplied year and number of cigarette packs per day and expressed in “pack-years”.

The patients were assessed by the average walking distance daily, the average sitting time (sitting against the TV, reading the book, etc.), and the total time they did not have activity. Sedentary time was assessed from the response to the question, outside of work, how many hours a day do you spend watching television, sitting at a computer, or reading? Daily sedentary time levels were created for low (≤ 2 h), medium (3–4 h), and high (≥ 5 h) (Young et al., 2014). In addition, patients with admission to the hospital in the last 6 months because of respiratory complaints (dyspnea, cough, sputum, etc.) were questioned.

Patients were consenting to all procedures. This study has been approved by our institute's ethics committee.

2.3. Statistical analysis

We performed statistical analyzes using the IBM Statistical Package for Social Sciences (SPSS Inc.; Chicago, IL, USA) software for Windows version 20.0. Descriptive statistical methods (mean, standard deviation, frequency, percentage, and range) were used for evaluating data. Student's t test was used for comparing normally distributed parameters between the two groups and chi-square test was for comparing the difference between the ratios. The relation of smoking consumption with dyspnea parameters was evaluated using the Pearson correlation analysis. The significance level was determined at 95% confidence interval when $p < 0.05$.

3. Results

The mean age of the smoker group was 39.18 ± 10.33, and the non-smoker group was 36.75 ± 12.22 ($p = 0.21$). Moreover, 50.3% of the patients were smokers and 49.7% were non-smokers. The mean EDSS score of the smoker group was 2.85 ± 0.75, and the non-smokers group was 2.96 ± 1.03 ($p = 0.48$). When the gender distributions between the groups were examined, 64.7% of the smokers were female and 35.3% were male. Besides, 77.6% of the non-smoking group were female and 22.4% were male. When the proportion of patients diagnosed with respiratory and/or cardiac disease was examined, 11.8% of the smoker group had cardiac diseases and 5.9% had respiratory diseases. In addition, 13.4% of the non-smoker group had cardiac diseases and 4.5% had respiratory diseases. There was no statistically difference between groups in terms of age, height, weight, BMI, gender, EDSS scores, diagnosed respiratory and/or cardiac disease ($p > 0.05$; Table 1 and 2).

Not only the rates of cough (%67, $p = 0.04$) and sputum (%69, $p = 0.01$) symptoms, but also rate of admission to the hospital (%29, $p = 0.01$) because of respiratory complaints were higher in the smoker group. It was found that the severity of dyspnea and fatigue perceived during effort was statistically higher in the smoker group than the non-smoker group ($p < 0.001$). Additionally, according to mMRC, the severity of perceived dyspnea was significantly different between the two groups (smoker group 1.84 ± 0.97, non-smoker group 0.64 ± 0.51, $p < 0.001$; Table 2).

The smoker group that mean daily walking distance was 384.71 ± 235.57 was found to have a high level of sedanter. The non-smoker group's mean daily walking distance that have a low level of sedanter was 993.28 ± 605.40 ($p < 0.001$; Table 2, Fig. 2).

Furthermore, there were positive correlations between cigarette consumption and mMRC scale ($r = 0.33$, $p = 0.01$), effort dyspnea ($r = 0.36$, $p < 0.001$), resting dyspnea ($r = 0.28$, $p = 0.02$), daily