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Is restless legs syndrome associated with Helicobacter pylori infection?

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ABSTRACT

Objective: In this study, we aimed to investigate the frequency of restless legs syndrome (RLS) in patients with and without helicobacter pylori (HP) detected in pathology.

Material and Method: This study was carried out prospectively between January-June 2019 with patients who had dyspeptic complaints and underwent upper gastrointestinal endoscopy and biopsy. The frequency of RLS was compared between the two groups by applying a questionnaire to patients with and without HP.

Results: The study was carried out with 96 patients, 72 HP positive and 24 HP negative. Fifty-two of the patients were women (54%) and 44 were men (46%). The mean age of patients was 44. When the positivity of patients in terms of HP was examined, 1+ HP in 24 patients (25%), 2+ HP in 24 patients (25%) and 3 + HP in 24 patients (25%) were detected. Thirteen patients were diagnosed as RLS with the questionnaires (14%). The average age of these patients was 41. Nine patients were women (69%) and 4 patients were men (31%). Only two of these patients smoked (15%). When patients were classified according to whether they had HP or not, the rate of RLS was 8.3% in patients who were HP negative, while this rate was 12.5% in patients with 1+ HP, 12.5% in patients with 2+ HP and 21% in patients with 3+ HP.

Conclusion: In this study, it was shown that the rate of RLS was 14% in patients with dyspeptic complaints who had endoscopy and the rate of RLS increased with HP severity.

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Introduction

Restless legs syndrome (RLS) is a disease that causes unpleasant or uncomfortable sensations in the legs and an irresistible urge to move them [1]. The onset and/or increase of symptoms at rest and relief with movement are typical and diagnostic for the disease [2]. RLS is one of the most common diseases of the nervous system and its prevalence varies between 2% and 10% [3]. It is more common in women and the elderly [4]. RLS has a familial predisposition, but the etiology of the disease is not fully known. Although most of them are idiopathic, secondary forms associated with iron deficiency anemia, chronic kidney failure, pregnancy and rheumatic diseases can also be seen [5]. RLS has been shown to be associated with many gastrointestinal diseases [6-8]. Bacterial overgrowth, infections such as HIV, Hepatitis C, and other gastrointestinal inflammatory or infectious diseases are blamed in the etiology of RLS [9-11].

Helicobacter pylori (HP) is a microorganism primarily associated with the gastrointestinal tract, but it has also numerous extra-intestinal manifestations. Although it was previously associated with many neurological diseases such as Alzheimer's, multiple sclerosis and Parkinson's [12-14], there is only one study investigating the relationship between HP and RLS [15]. In this study, the use of serological tests instead of the pathological Sydney classification for HP positivity and the low number of patients constitute important disadvantages for the study [16]. Therefore, the relationship between HP and RLS still remains unclear.

In this study, we aimed to investigate the frequency of RLS before HP eradication treatment in patients with and without HP detected in pathology.

Materialand Method

This study was carried out prospectively between January-June 2019 with patients who had dyspeptic complaints and underwent upper gastrointestinal endoscopy and biopsy. The frequency of RLS was compared between the two groups by applying a questionnaire to patients with and without HP. Seventy-two HP positive and 24 HP negative patients were included in the study. While patients with HP were included in the study group, patients without HP were included in the control group. Sydney classification is

used for HP entity. The frequencies of RLS were compared between the control and study groups. Patients with neurological or chronic systemic diseases (rheumatological diseases, iron deficiency anemia, diabetes, hypertension, heart failure, pulmonary disease, celiac disease, kidney disease, liver disease and inflammatory bowel disease), sleep disorders, pregnant women and patients with malignancy were excluded from the study. Also those who received any treatment for HP before the study; those who had taken a proton pump inhibitor, bismuth or antibiotics in the last 4 weeks were excluded from the study.

A face-to-face questionnaire of 6 questions was conducted with the patients, investigating the presence of RLS. In addition, the patient's smoking status, age, gender, and co-morbid conditions were recorded with this questionnaire. Those who answered positively to all 6 criteria were accepted as RLS.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc., Chicago, IL). The normal distribution of the data was evaluated with the Kolmogorov-Smirnov test. Among the numerical variables, those with normal distribution are shown as mean ± standard deviation, and those with normal distribution are shown as median (min-max). Categorical variables are expressed as numbers and percentages.

Written informed consent was obtained from all patients for the study. The study was conducted according to the ethical standards specified in the 1964 Declaration of Helsinki. Research and publication ethics were followed in our study. Ethical approval of the study was obtained from the ethics committee of XXXX University Training and Research Hospital, dated 30.10.2018 and numbered 2018-19/167.

Results

Demographic characteristics and data of the study are given in Table I. The study was carried out with 96 patients, 72 HP positive and 24 HP negative. Fifty-two of the patients were women (54%) and 44 were men (46%). The mean age of patients was 44. It was

observed that 30 patients were smokers (31%). When the positivity of patients in terms of HP was examined, 1+ HP in 24 patients (25%), 2+ HP in 24 patients (25%) and 3 + HP in 24 patients (25%) were detected. Thirteen patients were diagnosed as RLS with the questionnaires (14%). The average age of these patients was 41. Nine patients were women (69%) and 4 patients were men (31%). Only two of these patients smoked (15%). When the data of 83 patients who were not diagnosed with RLS were examined, the mean age of the patients was 45. In these group, 43 patients (52%) were female and 40 patients (48%) were male. Twenty-eight of these patients were smokers (34%). When patients were classified according to whether they had HP or not, the rate of RLS was 8.3% in patients who were HP negative, while this rate was 12.5% in patients with 1+ HP, 12.5% in patients with 2+ HP and 21% in patients with 3+ HP.

Discussion

In this study, we investigated the relationship between RLS and HP using a questionnaire method. As a result, the rate of RLS was found to be 14% in patients with dyspeptic complaints who underwent endoscopy. In addition, it was shown that the rate of RLS increased in correlation with the presence and severity of HP.

As it is known, HP is a microorganism that is associated with almost all kinds of diseases in modern medicine, but is considered an important predisposing factor especially for the development of gastric cancer and peptic ulcer [17]. In recent years, many studies have shown that HP plays a potential role in the pathogenic mechanisms of different extra-gastric diseases. The role of HP in idiopathic thrombocytopenic purpura, idiopathic iron deficiency anemia, and vitamin B12 deficiency has been previously established. There is also a growing body of evidence for the association of cardiovascular, metabolic, and neurological disorders with HP. One of the studies showing the relationship of HP with other diseases is our study.

The relationship between HP and RLS is one of the newly researched topics in the literature, about which there are only two articles. Although there is a study by Rezvani et al. in the literature, there are many methodological errors in this study. Although serology positivity was high in the country

where the study was conducted, the use of antibody determination by serology, which is not a reliable method for the diagnosis of HP, is one of the most important shortcomings of the study [15]. The fact that the HP rate is around 20-30% in the study and control group also supports our claim. In another study conducted with patients with dyspeptic complaints and diagnosed with RLS who underwent endoscopy, no relationship was found between RLS and HP positivity [18]. We think there are two possible reasons for this situation. First, the diagnosis of RLS was made similar to ours in this study, but although 6 criteria were taken for the diagnosis of RLS in our study, 4 criteria were taken in this study. Another reason is that since rapid urease test was used for the diagnosis of HP in this study, no relationship could be found between HP and RLS. In our study, pathological examination (Sydney classification) was used instead of rapid urease test.

Our study was designed differently from the other two studies above. In these studies, HP rate was investigated in patients with RLS, on the contrary, in our study, the rate of RLS was investigated in patients with and without HP. In addition, the risk between HP severity and RLS development was better demonstrated in our study.

In our study, the rate of RLS was found to be 14% when all patients were examined. In previous studies with different patient groups, it was stated that the rate of RLS varied between 2-10% [3].In a study conducted with pregnant patients, the rate of RLS in pregnant women was shown to vary between 10-34% [19]. In a study conducted with patients with migraine, it was reported that the prevalence of RLS was 19% in this patient group, and this rate was around 8% in the healthy control group [20].In our study, it was shown that the prevalence of RLS, which was 8% in the group without HP, increased to 21% as the HP severity increased in biopsy. Detection of RLS in one of every 5 patients with HP 3+ is the most important finding of our study. It should be kept in mind that this situation may be related to the HP-RLS relationship mentioned in our study, especially in patients with persistent joint-muscle pain, restlessness in the legs and dyspepsia, and that this situation can be resolved with HP eradication therapy.

The most important limitation of our study is the small number of patients. Another important limitation is that we could not provide information about the role of HP treatment in improving RLS symptoms. We expect prospective randomized studies on this subject in the future.

In conclusion, in this study, it was shown that RLS is common in people with dyspeptic complaints and the rate of RLS increases in correlation with the severity of HP.

Ethics Committee Approval: This research complies with all relevant national regulations, institutional policies and the principles of the Declaration of Helsinki. It was approved by the Ethics Committee of XXX University XXX Medical Faculty (approval number: 2018/19-167).

Informed Consent: All participants' rights were protected and written informed consent was obtained prior to the procedures according to the Declaration of Helsinki.

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