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Original Research Article

Frequency of cardiovascular diseases in the patients with restless legs syndrome

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ABSTRACT

Background: Restless Legs Syndrome (RLS) is a sensory-motor neurological disease characterized by discomfort, unpleasant sensations, an urge to move the legs. There are a lot of studies showing the association between Restless Legs Syndrome (RLS), Cardiovascular Diseases (CVD), Hypertension (HT) and Body Mass Index (BMI). The potential underlying mechanism of an increased risk of CVD in RLS is not clear but may involve hypertension, as Periodic Limb Movements during Sleep (PLMS) were shown to be related to blood pressure increases. These studies were inconsistent. The aim of this case control study was to show the prevalence of CVD in the patients with RLS compared with a control group.
Methods: A total of 37 newly diagnosed patients with RLS (group 1) who were applied to neurology polyclinic of Sakarya University Hospital between March 2016 and May 2017 and 37 control subjects (group 2) were included in this case control study. RLS was diagnosed using the criteria of the International RLS Study Group. Both groups were screened for HT, dyslipidemia, coronary artery diseases, atrial fibrillation. 24hour Ambulatory Blood Pressure Monitoring (ABPM) were enrolled for both groups. Interventricular septum was measured with echocardiography by cardiologist for diagnosis of left ventricular hypertrophy.
Results: There were no significant differences in sex (p:0.11) and age (p:0.33) between the two groups. Hypertension (p:0.001) and non-dipper hypertension (p:0.004), BMI (p:0.004), left ventricular hypertrophy (p:0,002) were found statistically significantly higher than the control group. There were no differences in atrial fibrillation (p:1) and hyperlipidemia (p:0.69) between two groups.
Conclusions: Patients with RLS should be followed closely for cardiovascular diseases.

Keywords: Coronary artery diseases, Hypertension, Restless legs syndrome

INTRODUCTION

Restless legs syndrome (RLS) is a sensory-motor neurological disease characterized by discomfort, unpleasant sensations, an urge to move the legs. This syndrome was first described in 1945 by Dr. Karl Ekbom.[1] The etiology of RLS has not been elucidated until today. The symptoms increase at night and at rest. Dysregulation of iron metabolism, dopaminergic dysfunction, genetic predisposition are the most common theories in the etiology of RLS.[2] RLS is divided to two groups named as idiopathic and secondary. Secondary RLS occurs due to conditions or diseases such as hemochromatosis, arthritis, chronic renal failure or pregnancy. Hypertension (HT), non-dipper hypertension, dyslipidemia, obesity, cigarette smoking are independent risk factors for cardiovascular diseases. The association between HT and RLS remains unclear in the literature.

Some studies suggest that RLS is more common in the patients with HT and the others suggest no relationship between HT and RLS.[3-6] Similar unclear less is also found in the studies showing the association between RLS, dyslipidemia, obesity.[7-10] The aim of present study was to show the frequency and association between RLS and cardiovascular diseases, HT, dyslipidemia.

METHODS

A total of 37 newly diagnosed patients with RLS (group 1) who were applied to neurology polyclinic of Sakarya University Hospital between March 2016 and May 2017, and 37 control subjects (group 2) were included in this case control study. RLS was diagnosed using the international restless legs syndrome study group questionnaire. This questionnaire consists of 4 questions.

- Do you have an urge to move your legs, accompanied by uncomfortable or disagreeable feelings?
- Do the uncomfortable or disagreeable feelings begin or worsen during inactive periods?
- Are the uncomfortable or disagreeable feelings reduced by activity?
- Are the uncomfortable or disagreeable feelings more prominent in the evening or at bedtime?

Positive answers to all questions were diagnosed as RLS. Exclusion Criteria for RLS were the patients with cushing's syndrome, hypo-hyperthyroidism, systemic inflammatory diseases (SLE, rheumatoid arthritis), pregnancy, lactation, chronic liver diseases, chronic renal failure, lumbosacral radiculopathy, polyneuropathy, amyotrophic lateral sclerosis, myeloma, diabetes mellitus, uremia, amyloidosis, hematological diseases gastrectomy, cancer, chronic obstructive pulmonary disease, smoking, peripheral vascular disease, congestive heart failure.

Hypertension has a diurnal rhythm. The blood pressure decreases approximately %10 at night normally. The patients with hypertension whose blood pressure is not decrease named as non-dipper hypertension ambulatory blood pressure monitoring device (Suntech Medical NC. Morrisville, USA Model Mobil Graph) were used for diagnosis of dipper, non-dipper hypertension. Electrocardiogram (ECG) with 12 derivation were used for diagnosis of atrial fibrillation. All patients and control group asked for diagnosis of dyslipidemia or using antilipidemic drugs. Patients, positive answers to this question were taken the dyslipidemia group.

Interventricular septum measurements were performed by the same cardiologist using Philips Matrix Epiq device (US314B0226) for diagnosis of left ventricul hypertrophy. Desis Ekoter Height and Weight Measurement Device were used for measuring height and weight of the patients and control group. BMI was calculated by patient's kg/patient's height cm^2. The control group was randomly selected among patients who presented to the internal medicine outpatient clinic. The institutional ethics committee approved the study protocol. Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study which was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" and approved by the institutional ethics committee. Data analysis was performed using SPSS for Windows17.0 (Statistical Package for Social Science, SPSS Inc., Chicago, IL, USA). Mean differences of continuous data were measured by t-test and median differences of categorical data were measured by Mann-Whitney U and Fisher's exact tests. A p value of <0.05 was accepted as statistically significant.

RESULTS

A total of 74 people was included in the data analysis. Patients were divided into two groups: group 1 (n:37), patients with RLS and group 2 (n:37), control subjects. The groups were determined to be homogenous in terms of age and gender (Table 1). Mean age of patients with RLS group was 47.7years and mean age of control group was 49.1years (p: 0.33). About 23 patients were female and 14 patients were male in RLS group, 21 patients were female and 16 patients were male in control group (p:0.11). There were no significant differences in sex and age between the two groups (Table 1). Hypertension, dipper hypertension and non-dipper hypertension were found to be statistically significantly higher in the patients with RLS (p:0,001, p:0,004, p:0,002). There were 15 patients with hypertension in the patients with RLS (40.5%). 11 patients had dipper hypertension (73.3%) and 4 patients had non-dipper hypertension (26.6%) from these 15 hypertensive RLS patients. There were 10 patients with hypertension in the control group (27%). 8 patients had dipper hypertension (80%) and 2 patients had non-dipper hypertension (20%) from these 10 hypertensive control group (Table 1).

Atrial fibrillation was found in 4 patients both RLS group and control group. 8 patients with RLS had dyslipidemia (%21.6) and 7 patients had dyslipidemia (%18.9) from control group. There were no significant differences in atrial fibrillation (p:1) and dyslipidemia (p:0.69) between the two groups (Table 1).

Interventricular Septum (IVS) were measured in both two groups. IVS were found 12mm in the patients with RLS and 11mm in the control group. Patients with interventricular septum bigger than 10mm diagnosed as left ventricular hypertrophy (LVH) LVH were found to be statistically significantly lower in the patients with RLS (p:0.002) (Table 1). Body Mass Index (BMI) were calculated in both two groups. Mean BMI levels were found 25.2kg/m^2 in the patients with RLS and 22.6kg/m^2 in the control group. BMI were found to be statistically significantly higher in the patients with RLS (p:0.004). (Table 1).

Table 1: Demographic and characteristic findings of the two groups.

Parameters	Restless leg syndrome, n:37		Control, n:37		P values
	n	%	n	%	
Age (year)	47.7		49.1		0.33
Gender male/female	14/23	37.8/62.2	16/21	43.2/59.4	0.11
Hypertension	15	40.5	10	27	0.001
Dipper hypertension	11	73.3	8	80	0.004
Non-dipper hypertension	4	26.6	2	20	0.002
Dyslipidemia	8	21.6	7	18.9	0.69
Atrial Fibrillation	4	1.08	4	1,08	1
LVH*	15	40.5	10	27	0.002
BMI (kg/m^2)*	25.2		22.6		0.004

*LVH: Left Ventricular Hypertrophy *BMI: Body Mass Index.

DISCUSSION

The main results of present study there was strong relationship between RLS and cardiovascular risk factors such as HT, non-dipper HT, obesity, low LVEF. The relationship between RLS and cardiovascular risks discussed in many previous studies. Pennestri MH et al, showed nocturnal blood pressure changes in the patients with RLS in 2007.[11]

Walters AS et al, showed the relationship between RLS and HT, heart disease, stroke in 2009.[12] The strong relationship between RLS and HT were found in many studies.[3,4,6] Some studies suggest that RLS and HT are not related or have a week relationship.[13-15] The mechanism of relationship between RLS and HT was unclear, the periodic limb movements during sleep were shown to be related with HT.[16] RLS make sleep impairment, decrease sleep quality and cause distress. All of these symptoms activate autonomic nervous system cause arterial baroreflex dysfunction and increase catecholamines.[17-18] Hypothalamic-pituitary-adrenal axis was activated by RLS, this activation increase nocturnal cortisol and blood pressure.[19] The findings are consistent with the literature. The patients are more hypertensive and have more non-dipper hypertension than control group.

Left ventricular hypertrophy (LVH) were found higher in the patients with RLS in this study. This was consistent with the literature. LVH was a major risk factor for cardiovascular outcomes, heart failure and cardiovascular mortality.[20] The mechanism of LVH in RLS was unclear but also same as the HT in RLS. Low sleep quality, activation of autonomic nervous system, high catecholamines and cortisol levels cause LVH in the patients with RLS.[16-19] Obesity is the one of the major risk factors of cardiovascular diseases. Many studies suggested relationship between RLS and obesity and a few studies no relationship between RLS and obesity.[21]

The mechanism of obesity in RLS is depended on vascular pathology and dopaminergic system.[21] the findings are consisting with the literature. Atrial fibrillation (AF) and dyslipidemia were found similar between RLS and control group. AF were found higher in the patients with obstructive sleep apnea. However, no information is available about the relationship between AF and Periodic Leg Movement during Sleep (PLMS) and also AF and RLS.

Mirza M et al, showed treatment of RLS influences progression of AF.[22] A few studies can be found in the literature about dyslipidemia and RLS. Also, the results are unclear. Yeon-Gyung B et al, found lower LDL and total cholesterol levels in the patients with RLS.[23] Dyslipidemia was found related with RLS in the studies showing all risk factors of cardiovascular events.[5,7-8] The mechanism was also unclear.

CONCLUSION

In conclusion, the findings were consistent with the literature. Patients with RLS should be followed closely for cardiovascular diseases. The main limitation of present study was the number of patients. It is too small when author looked at the other studies. There were no polysomnographic recordings showing the sleep quality.

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