The relationship between dipping-non-dipping arterial blood pressure pattern and frequency of restless leg syndrome with related factors

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ABSTRACT

Objective: The lack of nocturnal decline in blood pressure (BP) is associated with an increase in cardiovascular events. Restless leg syndrome (RLS) is an uncomfortable feeling in which the patient wants to budge the legs with ache in the legs. RLS also increases the hypertension and cardiovascular risk. In this study, we aimed to evaluate the relationship between dipping and non-dipping blood pressure patterns with RLS and its severity.

Methods: Two hundred patients who had 24-hour ambulatory blood pressure monitoring (ABPM) were enrolled into this cross-sectional study. They were classified by blood pressure pattern as dipping and non-dipping. Then, 100 patients with the dipper pattern and 100 patients with the non-dipper pattern were chosen. A questionnaire for RLS diagnosis that was prepared by the International RLS Study Group was given performed to the patients.

Results: RLS symptom score was higher in patients with non-dipping blood pressure patterns (NDBPP), and patients with NDBPP had more severe RLS. Beside this, there were no differences in terms of RLS frequency in dipping and non-dipping blood pressure patterns.

Conclusion: As a conclusion, dipping and non-dipping blood pressure patterns do not increase RLS risk. But, if patients with NDBPP have RLS, they have more severe RLS. So, we suggest that evaluating a patient with a non-dipping blood pressure pattern, considering RLS, would be helpful to ameliorate the quality of life of the patient *(Anatol J Cardiol 2015; 15: 284-8)*

Keywords: dipping- non-dipping arterial blood pressure pattern, restless leg syndrome

Introduction

Blood pressure (BP) has a diurnal rhythm that is characterized by low values during sleep. Blood pressure gradually decreases during sleep (1, 2). The decrease in blood pressure at night is known to be approximately 10% (3). If the decline does not occur or occurs less than the expected value, this situation is named non-dipping blood pressure pattern (NDBPP) and has shown to be associated with cardiovascular risk (4, 5). Considering that even small changes in nocturnal blood pressure may affect cardiovascular risk, it can be noticed that diseases affecting nocturnal blood pressure and disrupting the sleep quality may affect cardiovascular risk, too.

Restless leg syndrome (RLS) is a condition characterized by an urge to move the legs, accompanied by unpleasant sensations or discomfort. The symptoms are exacerbated at night and at rest, and they are partially or totally relieved with activity. The prevalence of RLS in the general population ranges from 5%-10% (6). Diseases disrupting sleep quality influence blood pressure and are associated with NDBPP (7, 8).

The process in which nocturnal blood pressure variation becomes blunted remains unclear, but a number of factors have been identified as potential mechanisms underlying the deficits in nighttime blood pressure reduction. Blood pressure dipping seems to be related to the pattern of sleep stages during the night (9). Stress hormones seem to be a particularly salient factor in impacting nocturnal blood pressure, as well. In sleep apnea patients, treatment results in normalization of sleep and a parallel reduction in both nocturnal blood pressure and stress hormone levels (10) (e.g., cortisol, epinephrine, and norepinephrine). RLS is a disease affecting sleep quality and duration. RLS patients have higher cardiovascular disease prevalence. The relationship between hypertension and RLS is well known. Studies conducted in European countries with broad participation demonstrated higher hypertension frequency in RLS patients (11-13). The small number of studies about the relation-

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Accepted Date: 29.01.2014 **Available Online Date:** 16.04.2014

DOI:10.5152/akd.2014.5381

ship between RLS and dipping-non-dipping blood pressure patterns (DBPP-NDBPP) performed to date has given conflicting results. Besides, the differences of DBPP-NDBPP in influencing the severity of RLS and the effects of drugs used have not been investigated. In the present study, we aimed to evaluate this relationship for the first time.

Methods

This cross-sectional study was performed between January 2012 and August 2012 in the Afyon Kocatepe University School of Medicine internal medicine, cardiology, and physical medicine and rehabilitation departments; 200 subjects, 100 of them with a dipping pattern and 100 with a non-dipping pattern, were chosen from patients to whom ambulatory blood pressure monitoring was applied before for any reason. Patients with dipping and non-dipping patterns were recalled to the hospital, and those who agreed to be included in the study were questioned for age, sex, family history, any risk factors, dietary compliance, drugs used, hypertension duration, neurological or other diseases that can cause RLS symptoms, and diseases affecting sleep quality, such as OSAS. Their medical histories were taken, and a general physical examination, including heart rate and arterial blood pressure, was performed. A questionnaire for the RLS diagnosis that was prepared by the International RLS Study Group was given to all patients A written informed consent form was obtained from each patient before the study. Our study was conducted in accordance with the ethical principles described by the Declaration of Helsinki.

Exclusion criteria

Neurological diseases that cause RLS symptoms (polyneuropathy, lumbosacral radiculopathy, amyotrophic lateral sclerosis, multiple myeloma, multiple sclerosis, Parkinson's disease, poliomyelitis, Isaac's syndrome, hyperekplexia syndrome) and other diseases that can cause RLS [iron, vitamin B12, and folate deficiency anemia (Hb for men <13 and for women Hb <12), uremia, amyloidosis, gastrectomy, cancer, peripheral vascular disease, chronic obstructive pulmonary disease, rheumatoid arthritis, and thyroid diseases] and patients with diseases affecting sleep quality, such as OSAS, were excluded from the study.

Ambulatory blood pressure monitoring application

The ABPM device (Tracker NIBP ABPM system, Del Mar Reynolds Medical Ltd, Hertford, UK), which measures blood pressure and the current pulse by the oscillometric method, was attached to the subjects. ABPM was performed according to guidelines (14). The device was programmed to take BP at least every 20 minutes, in such a way that at the end of the 24-hour period, a minimum of 16 valid daytime (06-22) and 8 valid nighttime (22-06) readings have been taken. Then, the number of valid readings was checked and repeated if necessary by informing this to the patient. In our study, ABPM of the patients was performed on a day of normal activities. The patients followed the doctor's instructions on chronic-use drugs and avoided taking showers and exercising for 24 hours before the examination. They brought a list of drugs with the times and dosages prescribed. The method and recommendations that daily activities be maintained during the examination were explained to the patient. Then, the patients were specified as to the activities to be performed during the 24 hours: at work, at home, at school, and both physical and resting activities. They took notes of meal times, and if consumption of alcohol, coffee, and cigarette was within the usual amount, the name, dosage, and times of the medications were taken, stressing events that occurred during the monitoring period. Besides, patients took notes on retiring and rising times, including during the day and the quality of sleep (good, satisfactory, unsatisfactory, or interrupted).

Patients whose mean systolic blood pressure was lower than 130 mm Hg and mean diastolic blood pressure was lower than 80 mm Hg were accepted as "normotensive." The upper values were accepted as "hypertensive." If the mean systolic blood pressures of the patients declined 10% or more at night, they were classified as "dippers," and if they decline less than 10%, they were classified as "non-dippers."

Determining RLS

For the diagnosis of RLS, a diagnostic questionnaire including diagnostic criteria for RLS that was developed by the International Restless Leg Syndrome Study Group was used. For a definitive diagnosis, the presence of four basic criteria was required.

1. Wanting to move arms and legs due to paresthesia
2. Continuing motor restlessness to soothe sensations of discomfort
3. Consistent or increasing complaints during rest, partial relief, or temporarily loss with movement
4. Increase in complaints in the evening and night (15)

Statistical analysis

Continuous variables were presented as mean±SD, and categorical variables were expressed as percentage. Kolmogorov-Smirnov test was used to evaluate of the distribution of variables. Student's t-test was used for continuous variables with normal distribution, and Mann-Whitney U-test was used for continuous variables without normal distribution. Chi-square and ANOVA tests were used for comparisons of the drug groups, and Pearson's and Spearman correlation analysis and Kendall's test were used to assess the relationships. A $p<0.05$ value was accepted as a significant level. For statistical calculations, SPSS statistical software (SPSS for Windows, version 17.0, Inc. Chicago, IL, USA) was used.

Results

The mean age of 200 subjects included in the study was 51.8±14.2 years; 91 of our patients were male, and 109 were female. The number of hypertensive patients all in groups was

170 (85%); 46 patients (23%) were using an ACE inhibitor (ACEI), 43 (21.5%) were using an angiotensin receptor blocker (ARB), 33 (16.5%) were using Ca channel blocker (CCB), and 21 (10.5%) were using β-blockers (βBs). Also, 26 (13%) of all patients included in the study had RLS. The mean symptom score of the 26 patients with RLS was 13.65±SD. There were no statistical differences in terms of gender or the incidence of RLS in the dipping and non-dipping groups. The demographic and biochemical data of the two groups are demonstrated in Table 1.

When the patients were evaluated according to the characteristics of blood pressure (dipper or non-dipper), the incidence of RLS was 15 (15%) in the dipper group and 11 (11%) in the non-dipper group. There were no statistical differences in terms of the incidence of RLS between the two groups (Table 1).

The average severity score in dipper-RLS group was 11.4±3.2 and 16.8±6.7 in the non-dipper-RLS group. When these two groups were compared in terms of severity score, the severity score of the non-dipper-RLS group was significantly higher (p=0.002) (Fig. 1).

RLS symptom severity scores of the patients were grouped as mild, moderate, and severe; 10 (38.5%) patients had mild, 11 (42.3%) patients had moderate, and 5 (19.2%) patients had severe symptoms. Our patients did not have "very severe symptom scores." When the relationship between RLS and the antihypertensive drugs used by the patients was analyzed, we found no differences in terms of RLS or blood pressure patterns between the drug groups.

Discussion

The most important finding of our study was that the RLS severity score of patients with ND-BPP was higher than in patients with DBPP. Although the relationship between RLS and DBPP-NDBPP has been researched in previous studies, to the best of our knowledge, the influence of DBPP-NDBPP on the severity of RLS and the effects of the drugs used were evaluated in the present study for the first time. It is known that NDBPP increases cardiovascular disease risk (16-18). The OHASAMA study showed a 20% increased risk of cardiovascular disease, for 5% insufficient reduction of nocturnal blood pressure (4). Considering that even small changes in nocturnal blood pressure affect cardiovascular risk, it can be considered that diseases affecting nocturnal blood pressure and disrupting sleep quality affect the cardiovascular system (19). Eguchi et al. (20) reported that patients with a short sleep time had NDBPP. In 2011, a statistically significant relationship was found between RLS and hypertension in Nurses' Health Study II, which was performed with 65.544 female patients (21). The same results were obtained in the Sleep Heart Health National Sleep Foundation Poll and studies (12, 22). Beside this, some studies defend that RLS and hypertension are not related, or some defend a weak relationship (11, 12, 23). In our study, there was no relationship between the frequency of hypertension and RLS.

Table 1. Characteristics of patients with dipper and non-dipper pattern

Variables		Dipper pattern (n=100)	Non-dipper pattern (n=100)	*P*
Age, year		49.0±14.3	54.7±13.6	0.003
Gender*	Male	45 (45%)	46 (46%)	NS
	Female	55 (55%)	54 (54%)	
RLS frequency*		15 (15%)	11 (11%)	0.400
RLS severity score		11.4±3.2	16.8±6.7	0.002
BMI, kg/m^2		25.9	26.5	0.050
Hypertension duration		4.3±3.9	5.9±4.7	0.010
Drugs used	ACEI n (%)	18 (18%)	28 (28%)	NS
	ARB n (%)	20 (20%)	23 (23%)	
	CCB n (%)	17 (17%)	16 (16%)	
	βB n (%)	12 (12%)	9 (9%)	

All parameters were expressed as mean±standard deviation unless otherwise stated.
*Data was expressed as number (%).
P<0.05 value was accepted as the significance level, and the significant differences between the groups are shown in bold.
BMI - body mass index; BP - blood pressure; NS - not statistically significant; RLS - restless leg syndrome

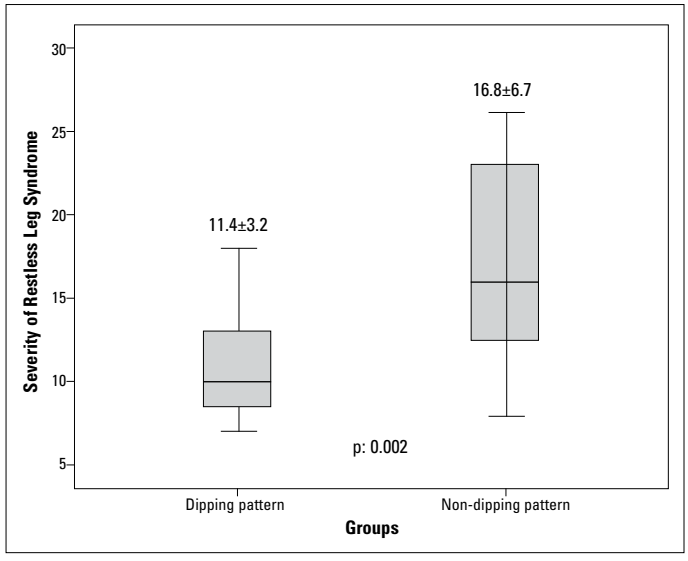

Figure 1. Restless legs syndrome severity of the groups (patients with dipping and nondipping blood pressure pattern)

When the patients with RLS were evaluated according to having DBPP or NDBPP, RLS was found to be related with NDP in a limited number of studies. Recently, in a study conducted by Erden et al. (24), it was shown that RLS was associated with the non-dipping pattern in patients with never-treated hypertension. However, the absence of a relationship between RLS and the diurnal rhythm of hypertension has also been reported. The possible cause may be the influence on NDBPP by diseases, which may cause activation of the autonomic nervous system or sympathetic system (12, 25). In our study, no relationship was found between RLS and DBPP-NDBPP. However, in our study, symptom severity scores of RLS patients with NDBPP were significantly

higher than in patients with DBPP. When the relationship between RLS and the antihypertensive drugs used by patients was evaluated, there were no differences in terms of the presence of RLS between drug groups. We believe that this result will be useful for clinicians in the treatment of hypertensive patients with RLS. There are limited studies about the effect of drug treatment type on blood pressure patterns. Recently, in a study by Kwon et al. (26), it was found that blood pressure medication type did not affect blood pressure patterns. In our study, when the patients were evaluated in terms of drug treatment type, there were no differences in terms of RLS or blood pressure patterns between the drug groups.

Study limitations

In our study, the lack of relationship between RLS and DBPP and NDBPP may be due to our strict patient selection criteria. In previous studies, patients with diseases that may cause RLS, such as neuropathy, anemia, coronary artery disease, chronic renal disease, obstructive sleep apnea syndrome, and thyroid disorders, were included; besides, the majority of our patients was using antihypertensive drugs for a long time. This condition may suggest that antihypertensive treatment reduces the frequency of RLS indirectly by reducing the cardiovascular risk. In the present study, the presence of obstructive sleep apnea was evaluated by the history of patients and their relatives. We did not evaluate patients with polysomnography to exclude diseases affecting sleep quality, such as OSAS. Besides, we had a small sample size of the drug groups. In this regard, drug monitoring studies starting new drug therapies in patients and determining their effects on both RLS and blood pressure pattern will shed light on this issue. We believe that more comprehensive studies including a neurological examination and evaluating the antihypertensive therapy with the exclusion of the reasons mentioned above will shed light on the relationship between RLS and DBPP-NDBPP.

Conclusion

According to the blood pressure pattern, the risk of RLS does not increase in patients with a dipper or non-dipper pattern. However, if patients with a non-dipper pattern have RLS, their RLS severity increases. In this respect, it can be concluded that evaluating a patient with NDBPP in terms of RLS would be helpful for the patient. If RLS is detected in a patient with NDBPP, clinicians should be more careful to improve the quality of life in these patients.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - S.M.U., Ş.Y.; Design - S.M.U., Ş.Y.; Supervision - S.M.U.; Materials - Ö.A., K.D.; Data collection &/or processing - S.M.U., F.Y., G.Y., A.A.; Analysis &/or interpretation -S.M.U., S.S.U., G.A.; Literature search - S.M.U., Ş.Y.; Writing - S.M.U., S.S.U.; Critical review - S.M.U., A.A., Ö.A., F.Y., K.D., G.Y., Ş.Y., G.A.

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