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Original Article

Is chronotype a risk factor for nocturnal non-dipping hypertension in children?

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ABSTRACT

Objectives: Chronotype is an individual circadian rhythm pattern affecting vascular tone and blood pressure. We aimed to investigate the effect of chronotype on nocturnal dipping in children with essential hypertension. This study was conducted considering that the habit of sleeping late at night has become widespread in children, especially during adolescence, potentially leading to the non-dipping phenomenon. With this study, we wanted to draw attention to the importance of sleep patterns and quality.

Material and Methods: This is a cross-sectional study, which was performed at Adiyaman University Faculty of Medicine between July 15, 2022, and March 15, 2023. All patients received 24-hour ambulatory blood pressure (BP) monitoring with essential hypertension based on the American Academy of Pediatrics guidelines. A chronotype questionnaire was administered to collect data from the participants.

Results: A total of 49 patients were included in the study, comprising 14 (29%) girls and 35 (71%) boys. The mean age of the patients was 13.9±2.3 years. Based on the chronotype questionnaire, 2 (4%) patients were identified as morning type, 23 (47%) as evening type, and 24 (49%) as intermediate type. Chronotype was not significantly associated with hypertension stage (p = 0.88) or the dipping phenomenon. In the intermediate type group, nighttime systolic BP dipping was 9.9±6% and in the evening type group, nighttime systolic BP dipping was 9.8±4.9% (p = 0.88). In the intermediate type group, nighttime diastolic BP dipping was 12.7±7.3% whereas in the evening type group it was 14.4 ± 6.4% (p = 0.58). Chronotype was not significantly associated with hypertension type [(p = 0.95) for systolic hypertension, (p = 0.58) for diastolic hypertension].

Conclusion: Chronotype affects nocturnal dipping in essential hypertensive children. In our study, the very low number of the morning type suggests that there are problems with sleep patterns and quality, especially late falling asleep, among adolescents. Sleep health, quality, and average daily sleep duration, and how they affect blood pressure levels in children, are a public health problem.

Keywords: children, chronotype, dipping phenomenon, hypertension

INTRODUCTION

Hypertension (HT) is a major health concern due to its high prevalence in the general population. In childhood, the prevalence of HT ranges from 4.9% to 7%, although regional and genetic differences exist.[1-3] The suprachiasmatic nucleus of the hypothalamus, also known as the biological clock, regulates the circadian rhythm. The circadian rhythm is involved in the regulation of the sleep-wake cycle, body temperature, and the release of hormones such as melatonin and cortisol. Chronotype represents individual circadian preferences that affect our physiology and psychology. Several modifiable and non-modifiable determinants that affect chronotype include genetics, family structure, environmental, social, and cultural factors, dietary habits, and urban lifestyle. Generally, humans can be categorized into three chronotypes: morning (preferring to go to bed earlier), evening (preferring to go to bed

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later), and intermediate (falling between morningness and eveningness) chronotypes.[4-6]

Healthy and sufficient sleep is crucial for the neurocognitive, cognitive, and emotional development of children and adolescents.[7] Circadian rhythm is a reflection of changes in vascular tone, blood pressure (BP), and coagulation balance, hunger-satiety cycles, and physical activity rhythms. Circadian rhythm disorders are known to be a risk factor for the development of cardiovascular disease (CVD).[8] In healthy individuals, arterial blood pressure typically decreases by approximately 10% at night compared to daytime, although this variation differs from person to person. Known as the "dipping phenomenon", this condition is associated with blood pressure variability regulated by neuroendocrine factors acting on the sympathetic nervous system and baroreceptors. A decrease in nighttime arterial BP is a normal part of circadian rhythm, and its absence is called the "non-dipping phenomenon". Abnormal parasympathetic and increased sympathetic nervous system activities have been implicated in this phenomenon.[9-11] In children, sleep health (sleep duration, timing, and efficiency) is one of the key family-level factors influencing hypertension.[12] However, limited data are available on the daytime course of blood pressure in relation to chronotype profiles. This study aimed to determine the relationship between chronotype and nocturnal BP dipping in children with essential hypertension. To the best of our knowledge, this is the first study to investigate whether blood pressure levels differ among chronotypes (morningness, intermediate, and eveningness) using 24-hour ambulatory BP monitoring (ABPM).

MATERIALS AND METHODS

Research and Publication Ethics: The study received the appropriate Institutional Review Board (IRB) approval. This study was conducted with the approval of the Ethics Commission of the Firat University Hospital, No. 17.07.2022-9571. Informed consent was obtained from the participants and the parents of the participants under 18 years of age.

Definitions

After obtaining ethics committee approval, patients diagnosed with essential hypertension at the Pediatric Nephrology outpatient clinic of Adıyaman University Faculty of Medicine were prospectively evaluated between July 15, 2022, and March 15, 2023. The diagnosis of HT was based on the American Academy of Pediatrics (AAP) guidelines, which define HT as blood pressure values of ≥130/80 mmHg in individuals aged ≥13 years.[13,14] For children under 13 years, HT is defined as blood pressure at or above the 95th percentile for age, height, and sex. Children aged 11-18 years were included in the study, and all participants underwent 24-hour ambulatory blood pressure monitoring (ABPM). Patients with known chronic conditions that could cause hypertension and/or a history of drug use were excluded from the study. To assess individual sleep-wake cycles, the Turkish version of the Children's Chronotype Questionnaire (CCTQ), validated by Dursun et al., was administered.[15] Demographic characteristics, serum biochemical parameters, thyroid function tests, fasting lipid profiles, renin and aldosterone levels, eye examination findings, echocardiography, renal doppler ultrasonography findings, and 24-hour ABPM data were recorded.

Children's Chronotype Questionnaire (CCTQ)

CCTQ was created as an adaptation of the Morningness-Eveningness Scale for Children developed by Werner et al. and the Munich Chronotype Questionnaire developed by Zavada et al. and validated by Dursun et al. The CCTQ is a 10-item, parent-reported tool for children. Sleep/wake parameters, including sleep latency, bedtime, lights-off, wake-up time, daytime naps for scheduled days, and free days, are questioned. The scores for 10 questions are summed up to obtain an overall score, which is interpreted as follows: 23 or less, morning type; 24 to 32, intermediate type; 33 or higher, evening type. This questionnaire also allows for determining the average duration of sleep per day by noting the exact times the child sleeps and wakes up. If the child takes a nap during the day, that time is added to the sleep time to find out the total sleep time. The same calculation is made for both scheduled and free days. Average daily total sleep time was calculated as follows: total sleep time on scheduled days x 5 plus total sleep time x 2 on free days divided by 7.[12, 15,16]

Statistical analysis

IBM SPSS (Statistical Package for the Social Science) 26.0 software was used for statistical analysis. Descriptive statistics, numbers, and percentages for categorical variables, mean, and standard deviation for numerical variables were presented. The normal distribution for numerical variables was evaluated with the Shapiro-Wilk test. The Mann-Whitney U Test was used in the analysis of non-normally distributed variables, and the Independent Samples T-Test was used in the analysis of normally-

distributed variables. The Pearson Chi-square Test was used in the analysis of categorical data. In all statistical analyses, the significance value of $p<0.05$ was accepted.

RESULTS

A total of 49 patients were included in the study, comprising 14 (29%) girls and 35 (71%) boys. The mean age of the patients was 13.9±2.3 years. The mean body mass index (BMI) of the patients was 26.8±6.5 kg/m^2. Thirty-four (70.4%) of the patients were overweight, obese, or morbidly obese. The most common presenting symptom was headache (n=28, 57.1%), and 17 (34.8%) patients were asymptomatic. Hepatosteatosis was detected in 12 (24.5%) patients, and 6 (12.2%) patients had hyperlipidemia. Uric acid elevation was not found in any of the patients, and all had normal thyroid function tests and serum renin aldosterone levels. Renal Doppler ultrasound examinations were normal in all patients. Hypertensive retinopathy was identified in 8 (16.3%) patients, while 9 (18.4%) patients had microalbuminuria. Among the hypertensive patients, 29 (59.2%) had systolic HT, 3 (6.1%) had diastolic HT, and 17 (34.7%) had systolodiastolic HT. Stage 1 HT was diagnosed in 24 (49%) patients, while Stage 2 HT was diagnosed in 25 (51%) patients. Additionally, 23 (46.9%) patients exhibited nighttime systolic BP drops, and 34 (69.4%) patients had nighttime diastolic BP drops, categorizing them as nocturnal dippers. Considering the echocardiographic findings of the patients, left ventricular hypertrophy was detected in 2 (4.1%) patients. Based on the chronotype questionnaire, 2 (4%) of the patients were identified as morning type, 23 (47%) as evening type, and 24 (49%) as intermediate type. The average sleep duration did not have a significant effect on nocturnal systolic and diastolic blood pressure dipping ($p = 0.65$, $p = 0.55$, respectively). Clinical and demographic characteristics of the study population are presented in Table 1. Being a dipper or non-dipper was not significantly associated with age, BMI percentile, sleep time, neutrophil/lymphocyte ratio, and blood pressure measurements during sleep and wakefulness.

Chronotype was not significantly associated with hypertension stage ($p = 0.88$) or the dipping phenomenon. In the intermediate type, nighttime systolic BP dipping was 9.9 ± 6%, while in the evening type, it was 9.8 ± 4.9% ($p = 0.88$). In the intermediate type, nighttime diastolic BP dipping was 12.7 ± 7.3%, whereas in the evening type, it was 14.4 ± 6.4% ($p = 0.58$). Chronotype and systolic/diastolic/dipper blood pressures, hypertensive retinopathy, and microalbuminuria relationships are given

Table 1. Demographic and clinical features of the study population

Parameter	**Patients** (n=49)
Demographic parameters	
Sex (female/male)	14/35
Age (years)	13.9 ± 2.3
Height (cm)	165.4 ± 12.1
Body weight (kg)	74.1 ± 22.1
Nutritional parameters	
Body mass index (kg/m^2)	26.8±6.5
Distribution by BMI percentile	Lean: 0 (0.0%) Normal: 15 (30.6%) Overweight: 8 (16.4%) Obese: 11 (22.4%) Morbidly Obese: 15 (30.6%)
Presenting Symptom	
Nosebleed	1(2%)
Dizziness	1(2%)
Chest pain	2(4.1%)
Asymptomatic	17(34.8%)
Headache	28(57.1%)
Number of children per family	3.3±1.1
Intermediate type	3.5±1.0
Evening type	3.0±1.2
Chronotype	
Morning type	2(4%)
Evening type	23(47%)
Intermediate type	24(49%)
Average Sleep Time (hours)	8.5±1.2
Intermediate type	8.1±1.1
Evening type	9±1.3
Blood Pressure Parameters	
Daytime Systolic BP (SBP) (mmHg)	126 ±8.2
Daytime Diastolic BP (DBP) (mmHg)	74.2 ±8
Nighttime Systolic BP (mmHg)	114 ±10.2
Nighttime Diastolic BP (mmHg)	64.2 ±6.7
Nighttime Systolic BP Dippers (%)	9.6 ±5.5
Nighttime Diastolic BP Dippers (%)	13.2 ±7
Stage 1 HT (n)	
Intermediate type	11/23
Evening type	12/24
Stage 2 HT Intermediate type Evening type	 12/23 12/24

BMI: Body mass index, BP: Blood Pressure, HT: Hypertension

in Table 2. Chronotype was not significantly associated with hyperlipidemia, microalbuminuria, the presence of hypertensive retinopathy, or hypertension stage (p = 1.00, p = 0.701, p = 0.63, p = 0.88, respectively). The number of children per family was not associated with sleep duration or chronotype (p = 0.13, p = 0.96, respectively). The number of siblings had no effect on nighttime systolic dipper BP and nighttime diastolic dipper BP (p = 0.49, p = 0.14, respectively).

DISCUSSION

In this study, we aimed to investigate whether chronotype (morningness, intermediate type, and eveningness) has an impact on the expected physiological drop in nocturnal blood pressure. Although it is more commonly reported in adults, the relationship between sleep duration and blood pressure has also been demonstrated in childhood.[17] To the best of our knowledge, this is the first study to evaluate the effects of chronotype on nocturnal blood pressure fluctuations in hypertensive children by means of 24-hour ABPM. There are studies reporting that chronotype affects cardiovascular health by modulating physiological processes such as heart rate and blood pressure, and therefore, may predispose the individual to CVD.[17-19] In our study, we expected to see a decrease in physiologic BP drops in evening-type hypertensive children compared to their intermediate-type counterparts. However, we did not find a significant difference in terms of the effect of chronotype on nocturnal BP drops. We found no significant impact of chronotype on the nocturnal dipping phenomenon. Chronotype was not significantly associated with hypertension stage (p = 0.88) or the dipping phenomenon. In the intermediate type, nighttime systolic BP dipping was 9.9 ± 6%, while in the evening type, it was 9.8 ± 4.9% (p = 0.88). In the intermediate type, nighttime diastolic BP dipping was 12.7 ± 7.3%, whereas in the evening type, it was 14.4 ± 6.4% (p = 0.58). Previous studies have shown that obese children and adolescents sleeping less than 6 hours per day are at an increased risk of hypertension.[20,21] As reported in many studies, shorter sleep duration is associated with an increased likelihood of obesity and cardiovascular disease.[22] A link between habitual short sleep and increased body fat composition has been demonstrated in adolescents and adults.[23] Each one-hour increase in total sleep time has been shown to reduce the risk of obesity by 9.0%.[21,24] It was shown that insufficient, poor-quality sleep can lead to the development of HT and CVD by causing endothelial dysfunction and increasing the secretion of proinflammatory cytokines.[25] There are studies reporting a strong negative correlation between short sleep duration and elevated blood pressure.[26-29] In contrast to these reports, we did not observe any relationship between sleep duration and nocturnal dipping/non-dipping or blood pressure changes in our study. This may be related to the small sample size of subgroups. Since there were only two morning-type children in our study, all comparisons were made between evening-type and intermediate-type children. This may also be another reason for the dissimilar findings. Further studies involving a larger cohort that specifically compares morning-type and evening-type pediatric patients may yield statistically significant findings. Our results contradict some of the previous reports. In a study by Navarro-Solera et al., short sleep duration was found to be significantly associated with higher pulse pressure and mean arterial pressure in children aged 7 to 16 years.[30] Similarly, Peach et al. demonstrated that short sleep duration is a risk factor for HT.[29] Previous studies have shown that both sleep quality and duration are associated with systolic BP[26-31] and diastolic BP.[30] Contrastingly, in our study, systolic and diastolic blood pressures did not show any relationship with chronotype (Table 2). The CARDIA

Table 2. Chronotype and systolic/diastolic/dipper blood pressures, hypertensive retinopathy, and microalbuminuria relationships

	Intermediate type	Evening type	p
Daytime systolic BP (mmHg)	127.9±9.3	124.4±6.7	0.14
Daytime diastolic BP (mmHg)	74.8±8.9	73.8±7.4	0.70
Nighttime systolic BP (mmHg)	115.4±12.3	112.4±7.8	0.33
Nighttime diastolic BP (mmHg)	64.7±7.8	63.5±5.8	0.57
Nighttime systolic BP Dippers (%)	9.9±6	9.8±4.9	0.88
Nighttime diastolic BP Dippers (%)	12.7±7.3	14±6.4	0.58
Hypertensive retinopathy (+) (n)	3/23	5/24	0.63
Microalbuminuria (+) (n)	3/23	5/24	0.70

BP: Blood Pressure

sleep study has shown that not only reduced sleep duration but also poor sleep quality were associated with increased systolic and diastolic BPs.[32]

In our study, we also examined whether an increasing number of siblings negatively impacts sleep quality and nighttime blood pressure. Our findings indicated no significant association between the number of siblings and either sleep quality or nighttime blood pressure. Bal et al.[33] examined sleep duration and its effect on BP in 2.860 patients aged 11 to 17 years and showed that a sleep duration of 8 hours or less is an independent risk factor for pre-HT and HT. The consensus statement issued by the American Academy of Sleep Medicine recommends that adolescents 13 to 18 years of age sleep 8 to 10 hours per day.[34] In our study population, the average sleep time was 8.5±1.2 hours daily, and we did not observe a relationship between sleep time and BP variations. Again, this may be due to the insufficient number of morning-type children included in this study, which led to their exclusion from any comparative analyses. If there had been more morning-type children, we could have compared the evening-type and morning-type children and potentially found significant differences in blood pressure fluctuations at night. However, these findings suggest that adolescents may not have a morning-type chronotype due to their lifestyles. In our study, chronotype profile was not significantly associated with indicators of the clinical course of HT such as the presence of hypertensive retinopathy and microalbuminuria (p=0.63, p=0.70, respectively).

CONCLUSION

Our findings show that morning type chronotype is less common among children. The lack of an association between chronotype and dipper/non-dipper hypertension was attributed to the very low prevalence of the morning chronotype in our cohort. If the number of morning chronotypes had been sufficient, the effect of morning and evening chronotypes on dipper/non-dipper hypertension might have been more significant. On the other hand, this situation suggests that late falling asleep is a common problem among adolescents, which may have a negative impact on health in the long term. This indicates that sleep patterns in children are becoming disrupted. We believe our study will provide valuable insights for future research, as no similar studies exist in the pediatric age group. Multicenter, large-sample studies are needed in childhood. Further studies involving a larger cohort will be helpful for understanding the relationship between chronotypes and blood pressure changes.

Ethical approval

This study has been approved by the Ethics Commission of the Firat University (approval date 17.07.2022, number 9571). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: GI, EA; data collection: GI, EA ; analysis and interpretation of results: GI and EA; draft manuscript preparation: GI. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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