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Research Article

Effects of Stimulants on Sleep Parameters in Children with Attention Deficit Hyperactivity Disorder

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Abstract

Objectives: This study aims to evaluate the effects of methylphenidate (MPH) on sleep parameters and BMI in attention-deficit/hyperactivity disorder (ADHD) children.

Methods: Eighty five ADHD children were enrolled and daily sleep diaries were evaluated after taking medication. This cross-sectional case-control study also included ninety five healthy children. BMI Z scores were measured at baseline and at last follow-up.

Results: Eighty five patients (mean [standard deviation] age: 14,02 [±1.6] years, 65 (77%) males) were included. When we compared ADHD and healthy control group, we observed significant statistical difference between two groups on the mean total scores of CSHQ and PSQI ($p<0.05$). For CSHQ, subscales about sleep delay, sleep duration and daytime sleepiness are also significantly higher in ADHD group ($p<0.05$). For PSQI, subscales about sleep disturbance, sleep latency and subjective sleep quality differed significantly. MPH treatment was associated with a notional reduction in body mass index standard deviation scores (SDS).

Conclusion: These findings indicate children with ADHD under stimulant treatment experience more sleep problems than healthy peers accorrding to both self and parent reports. MPH slightly descreased BMI-sds in this group of ADHD patients followed naturalistically over 32.2 months.

Keywords: Attention-deficit/hyperactivity disorder, body mass index, child, methylphenidate, sleep

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Attention deficit hyperactivity disorder (ADHD) is one of the most common psychiatric disorders in childhood. Attention Deficit Hyperactivity Disorder is a disorder diagnosed according to DSM-V, with symptoms of inattention and/or impulsivity - hyperactivity observed before 12 years of age and with symptoms in at least two different environments.[1]

Sleep-related problems play an important role in child development. Inadequate sleep leads to serious deterioration in social and academic functioning of the child, such as attention, impulsivity, behavioral problems, and falling school achievement.[2] Sleep problems in children with normal development have been reported in 2-20%.[3, 4] Sleep problems are reported to occur in approximately 50-70% of ADHD patients.[5–7] Delay of falling asleep, night waking, morning awakening problems, daytime sleepiness, snoring, parasomnias and night terror are common sleep problems in ADHD.[8, 9] In addition, the risk of falling asleep is another important sleep problem seen temporarily in childhood.[10] In meta-analysis studies on sleep problems in ADHD, although parents reported high rates of subjective sleep problems in their children with ADHD, it was reported that objective sleep tests had lower rates of problems.[7, 11]

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However, sleep-onset latency, apnea/hypopnea rate increase have been reported in objective sleep tests. Furthermore, sleep efficiency, sleep time and average sleep time decreased in polysomnography.[7] In ADHD, there is a correlation between daytime hypersomnia and excessive diurnal motor activity. In EEG studies, low stimulation has been reported in frontal, central and midline areas.[10] It has been suggested that the interaction between ADHD and sleep is related to hypo-arousal condition (similar to narcolepsy), delayed sleep onset latency, respiratory-related sleep problems, restless leg syndrome and epilepsy/EEG interictal discharges.[10] However, in sleep studies with both subjective and objective sleep tools, a consistent result has not yet been found. Although MPH is known to be relatively well-tolerated, adverse effects such as appetite reduction, nervousness, headache, irritability, anxiety, and nail biting are prevalent. MPH also has a negative effect on sleep, due to either a direct or a secondary "rebound" effect.[12, 13] In one study, nearly a third of ADHD children who were treated with stimulant increased sleep latency or insomnia every night.[14]

Decreased appetite is the most frequent adverse event of stimulants, but it is not necessarily related to a decrease in height. The association between stimulants and a delay in growth is still unclear and a focus of controversy. In a recently published birth cohort study that included patients with ADHD followed for 26.2 years, stimulants were not associated with a reduction in final adult height.[22] A group of patients with ADHD without pharmacological treatment was also included. Neither ADHD itself nor stimulants were associated with differences in the magnitude of peak height velocity (PHV) and final adult height. Our study aims to evaluate the effects of the acute impact of methylphenidate (MPH) on sleep parameters and the effects of the chronic impact of methylphenidate (MPH) on BMI in these patient group and compared with healthy children.

Methods

Study Setting and Subjects

The clinical sample consisted of children with a history of 85 ADHD cases who applied to Dokuz Eylul University Child and Adolescent Pyschiatry Outpatient Clinic after the ethics committee approval was obtained. Six participants for whom missing or erroneous entries in the data collection instruments were excluded from the study. The ninety five children who were appealed to our pediatrics outpatient clinic by parents for causes such as headache, acute infections but did not meet any diagnostic criteria effectuates healthy sample group. Finally, the data was collected on the total 180 cases that were subjected to statistical analysis after the ethics committee approval was obtained. The Dokuz Eylul University Ethics Committee approved the study.

After the participants who were included in the study were informed about the aim and method of the research, written consent was obtained from both groups. Height, weight and body mass index measurements of ADHD cases were obtained from hospital records. The participants who were appreciated with K-SADS-PL by blinded professionals completed a data form containing questions regarding sociodemographic and clinical features, Wechsler Intelligence Scale for Children-Revised (WISC-R) and Conners Parent Rating Scale-Revised Short Form (for only ADHD cases to support the diagnosis), The Pittsburgh Sleep Quality Index (PSQI) and Children's Sleep Habits Questionnaire (CSHQ)-Abbreviated Form (all participants). Weight, height, and BMI z scores were converted to age- and gender- corrected z scores using norms from the Turkish Population[15] at baseline and last follow-up.

Assessment Instruments

Sociodemographic Data Form: It is an information form filled by the researchers to obtain information about age, gender, education, family type, socioeconomic level, home conditions, status of parents, background and family history.

Conners Parent Rating Scale-Revised Short Form (CPRS-RSF): This form is widely used for the assessment of the prevalence of ADHD and its effect on diagnosis and treatment. Studies on the new version are described in U.S., and Canada. The validity and reliability study of the scale was conducted by Kaner (2013).[16]

The Pittsburgh Sleep Quality Index (PSQI): PSQI; It was developed in 1989 by Buysse et al. and Cronbach's alpha=0.80 to adequate internal consistency has been shown to have test-retest reliability and validity (Buysse, Reynolds, Monk, Berman and Kupfer, 1989). The validity and reliability study of the PSQI in our country was conducted by Ağargün et al.[17] (1999). In this study, Cronbach's alpha value was found to be 0.79 (Cronbach alpha=0.79). The PSQI is a self-report scale that assesses sleep quality and disorder over a period of one month.

Children's Sleep Habits Questionnaire (CSHQ)-Abbreviated Form: The Child Sleep Habits Questionnaire (CSHQ) Abbreviated Form, developed by Owens et al in 2000 to investigate the sleep habits and sleep related problems of children, consists of 33 items. As a cut-off point of the GHQ, the total score of 41 is accepted and the values above this are considered to be clinically significant.

Stastistical Analysis

Differences in all study variables were analysed by using the Statistical Package for the Social Sciences (IBM, NY), version 22 for Windows. Before the statistical analysis was performed,

Table 1. Sociodemographic data of the ADHD patients and control groups

	ADHD n=85	Controls n=95	p
Age* (mean±sds)	14.02±1.61	14.29±1.59	0.942
Gender, male, n (%)	65 (77.6%)	72 (75.6%)	
Mother's mean age (mean±SD)	34.06±3.82	36.41±5.82	0.382
Maternal education n (%)			
<8 years	12 (42.85%)	22 (44%)	0.542
>8 years	16 (57.15%)	28 (56%)	
Employment status n (%)			0.235
Homemaker	20 (42.85%)	35 (42.85%)	
Worker	8 (42.85%)	15 (42.85%)	
First BMI (sds)	18.28 (4.25)	17.49 (4.52)	0.544
Follow-up BMI (sds)	19.88 (5.4)	18.22 (5.32)	0.422
MPH duration of use (months) (sds)	32.22 (19.6)		
MPH mean dose (mg) (sds)	27.07 (9.89)		
WISC-R total score (sds)	89.45 (18.7)	86.25 (17.6)	0.315

ADHD: Attention deficit hyperactivity disorder; sds: Standard deviation scores; SD: Standard deviation; BMI: Body mass index; MPH: Methylpenidate; WISC-R: Wechsler Intelligence Scale for Children-revision. *p<0.05; **p<0.01.

Table 2. Child Sleep Habits Questionnaire (CSHQ) abbreviated form total and sub-scores of ADHD and the control group

	ADHD n=85 (mean±SDS)	Controls n=95 (mean±SDS)	p
CSHQ-Bedtime resistance	7.74±2.45	6.86±0.78	0.25
CSHQ-Sleep delay	1.64±0.75	1.23±0.42	0.02*
CSHQ-Sleep duration	4.55±1.58	3.56±0.61	0.03*
CSHQ-Sleep anxiety	4.79±1.67	4.65±0.87	0.32
CSHQ-Night wakings	3.84±1.02	3.7±0.77	0.72
CSHQ-Parasomnia	8.37±1.37	8.13±0.95	0.63
CSHQ-Sleep breathing problems	3.25±0.55	3.48±0.87	0.22
CSHQ-Daytime sleepiness	13.45±3.92	10.58±1.44	<0.001**
CSHQ-Total score	1.74±0.44	1.36±0.48	0.01*

ADHD: Attention deficit hyperactivity disorder; SDS: Standart deviation score; CSHQ: Child Sleep Habits Questionnaire Abbreviated Form. *p<0.05; **p<0.01.

it was checked whether the data met the assumptions of the parametric tests and the normal distribution and homogeneity of variance by using the Shapiro–Wilk test. Variables that don't show normal distribution were evaluated by Mann-Whitney U test. In the interpretation of the variables, descriptive statistical techniques and quantitative data analysis were used. Chi-square analysis was used to compare categorical variables between groups. The Pearson Correlation Test was used to determine the direction and level of correlation between the variables and the results were indicated by "r" (correlation coefficient) and "p"value (significance level). P<0.05 was considered statistically significant.

Results

Table 1 summarizes that main features of the participants and the identification of the clinical characteristics between groups. A total of 180 children and adolescents were included in the study, 85 in the ADHD group and 95 in the healthy control group. The mean age of the patient group was 14.02±1.61 and the mean age of the control group was 14.29±1.59. There was no statistically significant difference between the groups in terms of the mean age (p=0.942). Table 1 summarizes first and last visit follow-up body mass index points, WISC-R intelligence test scores, mean methylphenidate duration of use months and mean methylphenidate doses of ADHD cases. Also, No differences between groups showed on sex, parental education level and employment status (all groups), respectively (Table 1).

Table 2 summarizes the total and subscale scores of ADHD and control subjects from The Child Sleep Habits Questionnaire (CSHQ) Abbreviated Form. A significant difference was found between the two groups in terms of sleep delay, sleep

Table 3. The Pittsburgh Sleep Quality Index (PSQI) total and sub-scores of ADHD and the control group

	ADHD n=85 (mean±SDS)	Controls n=95 (mean±SDS)	p
PSQI-Subjective sleep quality	0.8±0.7	0.38±0.52	<0.001**
PSQI-Sleep latency	1.03±0.94	0.65±0.64	0.04*
PSQI-Sleep duration	0.18±0.45	0.12±0.33	0.62
PSQI-Sleep efficiency	0.3±0.66	0.12±0.33	0.18
PSQI-Sleep disturbance	1.18±0.54	0.31±0.55	<0.001**
PSQI-Daytime dysfunction	0.86±0.97	0.66±0.87	0.26
PSQI-Total score	4.34±2.22	2.25±1.4	<0.001**

ADHD: Attention deficit hyperactivity disorder; SDS: Standart deviation score; PSQI: The Pittsburgh Sleep Quality Index. *p<0.05; **p<0.01.

Table 4. The effect of methylphenidate by sex

	Girls (n=20)			Boys (n=65)		
	Baseline (T1)	Follow-up (T2)	p	Baseline (T1)	Follow-up (T2)	p
Height-SDS	0.52 (1.32)	-0.43 (0.80)	**<0.001	0.72 (1.40)	-0.62 (4.42)	*0.003
Weight-SDS	0.23 (1.10)	-0.48 (0.62)	**<0.001	0.78 (1.21)	-0.44 (0.78)	**<0.001
BMI-SDS	-0.08 (1.10)	-0.20 (0.79)	**<0.001	0.38 (1.26)	-0.02 (0.70)	**<0.001

BMI: Body mass index; SDS: standard deviation score; n: number of patients. *p<0.05; **p<0.01. p values from paired t-tests.

Table 5. Table of correlations in the ADHD group

Correlations	Dif-Height	Dif-Weight	Dif-BMI
Age starting MP-SDS	-0.42 (0.432)	**-0.236 (0.004)	0.035 (0.212)
Dosage of MPH [mg]-SDS	0.017 (0.521)	-0.016 (0.212)	0.095 (0.114)
Duration of treatment-SDS	0.028 (0.227)	0.034 (0.237)	-0.080 (0.432)

BMI: Body mass index; MPH: Methylphenidate; SDS: Standard deviation score; Dif-BMI: Difference between baseline and follow-up BMI, in SDS; Dif-Height: Difference between baseline and follow-up height, in SDS; Dif-Weight: Difference between baseline and follow-up weight, in SDS. *p<0.05; **p<0.01. p values from Pearson correlation test.

duration, daytime sleepiness scores and total sleep scores (p<0.05). There were no differences in other sub-tests between bedtime resistance, sleep breathing problems, sleep anxiety, night waking and parasomnia scores (p>0.05).

Total and subscale scores of participants from The Pittsburgh Sleep Quality Index (PSQI) are reported in Table 3. All of the subscales, except use of sleep medication were higher in ADHD group. Total score and subscales about sleep latency, sleep disturbance and subjective sleep quality were significantly different (p<0.05). There was no significant difference in scores of sleep duration, sleep efficiency and daytime dysfunction.

If we divided the groups into girls (n=20) and boys (n=65), before starting treatment, girls showed height (baseline height-SDS: 0.52 [1.32], t=3.22; p**<0.001), weight (baseline weight-SDS: 0.23 [1.10], t=1.56; p=0.023) and BMI (baseline BMI-SDS: -0.08 [1.10], t=-0,84; p=0.580), and these differences were statistically significant except baseline BMI-SDS scores in Table 4.

Before starting treatment, in the group of boys showed height (baseline height-SDS: 0.72 [1.40], t=2.46; p**<0.001), weight (baseline weight-SDS: 0.78 [1.21], t=6.28; p**<0.001) and BMI (baseline BMI-SDS: 0.38 [1.26], t= 3.41 p**<0.001), and these differences were statistically significant.

However, considering whether patients were girls or boys, in the group of girls, height (baseline height-SDS: 0.52 [1.32]; follow-up height-SDS: -0.43 [0.80]; p**<0.001), weight (baseline weight-SDS: 0.23 [1.10]; follow-up weight-SDS: -0.48 [0.62]; p**<0.001) and BMI weight (baseline BMI-SDS: -0.08 [1.10]; follow-up BMI-SDS: -0.20 [0.79]; p**<0.001) were slightly affected by treatment. This effect was observed in the group of boys also. In such cases, height (baseline height-SDS: 0.72 [1.40]; follow-up height-SDS: -0.62 [4.42]; p**<0.001), weight (baseline weight-SDS: 0.78 [1.21]; follow-up weight-SDS: -0.44 [0.71]; p**<0.001) and BMI weight (baseline BMI-SDS: 0.38 [1.26]; follow-up BMI-SDS: -0.02 [0.70]; p**<0.001) were slightly affected by treatment.

Table 5 shows the correlations between age starting treatment, dosage of MPH and duration of treatment and growth parameters. A statistically significant positive cor-

relation was found between age starting MPH and differences in weight-SDS between baseline and follow-up (R=-0.236, p=0.004*). The dosage of MPH and duration of treatment did not correlate significantly with growth parameters.

Discussion

In this study, we found that sleep problems are more common in ADHD group. With the idea that sleep changes may be due to ADHD drugs (especially stimulants) in children with ADHD, studies have shown that these drugs are only one of the causes of sleep disorders in ADHD and children have more sleep problems than controls, independent of ADHD treatment. Among the most common sleep problems reported in children with ADHD are insomnia, resistance to sleep or bedtime, prolonged tiredness due to alertness, and daytime sleepiness. However, drugs used for ADHD and / or comorbid diseases also contribute to sleep disorders. It is considered important to determine the metabolic or neurological pathways that may be common for both sleep and ADHD and to determine the therapeutic targets for these pathways.[17]

The stimulants used in the first step caused sympathomimetic effects by increasing the amount of extracellular dopamine and noradrenaline, and thought to reduce the sleep awareness and fatigue awareness. The results of our study are one of the most common side effects associated with insomnia or sleep-stimulating drugs, delayed for more than 30 minutes, consistent with the literature. This is the situation when the child refuses to go to bed should be distinguished from resistance. Methylphenidate effect, whether the child has just started will vary according to the length of time. When the efficacy decreased, it was reported that there was more difficulty in falling asleep with rebound effect and lower dose of the drug before rebound facilitated falling asleep.

The relationship between sleep and medication is complex. However, it is well established that stimulants cause insomnia at the beginning. Stimulant drugs are associated with difficulty in falling asleep and short sleep time, as shown in a large number of studies using both objective and subjective measurements. Dose increase and short-term stimulant use have been shown to cause insomnia more frequently. Patients with a history of associated comorbid conditions such as insomnia or depression/anxiety may be worse in patients with dose changes (first dose, dose increase, drug naive), and sleep problems in younger children. These children are more vulnerable to sleep-related side effects of drugs.[18]

The use of atomoxetine in non-stimulatory agents used in the treatment of ADHD compared with methylphenidate; it is shown that it is easier to get up in the morning, it takes less time to fall asleep and sleeps better. Methylphenidate use decreases night wakings more than atomoxetine.[19]

In some studies about stimulant drugs used in the treatment of Attention Deficit Hyperactivity Disorder, although it has been reported that it may cause a delay in growth in children, it has been shown that although the most common side effect of stimulants, there is not any effect on height. For this reason, stimulant and growth retardation is still a controversial issue.

There have been limited researches into association between boys and girls growth with ADHD. In the current study, our sample which included 65 boys and 20 girls with ADHD, we had 3.2:1 ratio. A significant effect between gender (both boys and girls) and differences in all z-scores between baseline and follow-up, but, in the regression analysis, gender wasn't predicted difference and final anthropometric values. Our results coherent with the findings of study by Suarez et al.[20] (2017) which did not find interaction between boys and girls in the effect of MPH on growth. Also Biederman et al.[21] (2010) showed that effect of emotional disorders on z-scores which are greater weight in girls and with smaller height in boys.

Several explanations have been proposed to discuss these findings, but although we suggested that stimulants may function the pattern of delay in the rate of physical maturation. Therefore, no statements could be made on the influence of gender on weight and height change in ADHD sample.

This study suggests that ADHD treatment with stimulant drugs is not associated with significant changes in adult height or growth. In contrast to the previous studies, stimulant drugs contributed positively to the body mass of the case sample. This is because; limited number of samples, short follow-up period and not calculated z values. There is also a need for comparison with the Turkish population. In this study, we also found that sleep problems are more common in ADHD group. Further studies need to evaluate whether this higher incidence of sleep problems is due do methylphenidate use or the common aethiology with ADHD.

There are several limitations in our study. In spite of all these positive aspects, it can be mentioned that the age distribution is not homogeneous and the relatively small number is the limitation of our study. Self-evaluation of the scales used in the study, the fact that objective measurement tools such as polysomnography, actigraphy and MLST could not be included in the study are among the limitations of the study.

Disclosures

Ethics Committee Approval: The Dokuz Eylul University Ethics Committee approved the study (date: October 11th, 2018, number: 2018/25-11).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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