



Research Article

JMR 2020; 6(5): 216-218

September- October

ISSN: 2395-7565

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www.medicinarticle.com

Received: 03-09-2020

Accepted: 24-09-2020

Impact of methylphenidate and atomoxetine on sleep in children with ADHD

Elif Gokce ERSOY SIMSEK¹, Saniye Tulin FIDAN²

^{1,2} Eskisehir Osmangazi Univ Child and Adolescent Psychiatry Dept, Eskisehir Turkey

Abstract

Aim: Our purpose in this study is to determine the effects of methylphenidate and atomoxetine on the sleep of children with attention-deficit/hyperactivity disorder (ADHD). **Methods:** Eighty-one children admitted to a child psychiatric inpatient service with ADHD participated in a double-blind, crossover study in which 42 subjects received extended release methylphenidate, and 39 subjects received atomoxetine only one dose in the morning daily at least for 6 months. Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (KSADS-PL) and Child Sleep Habits Survey (CSHS) were applied to all children. **Results:** There was a sleep problem in 81% (n = 34) of the patients using methylphenidate and 89.7% (n=35) of the group using atomoxetine. When we evaluated according to the CSHS cut-off score, whether having a sleep problem or sleep problems, and there was no statistically significant difference between the two groups (p> 0.05). We are not able to find significant difference between two groups in terms of bedtime resistance, sleep duration, sleep anxiety, night awakenings, parasomnia, sleep-breathing problems, and daytime sleepiness subtest and total sleep scores (p> 0.05). There was a significant difference in sub-test of the falling asleep duration. It was found that the methylphenidate group had a longer falling asleep time duration (p <0.05). **Discussion:** Sleep-related complaints in children diagnosed with ADHD are not uncommon in clinical practice. It is known that 25-55% of children with ADHD often report various sleep problems and in addition, more sleep problems are reported by their parents. In our study, when the total scores of CSHS filled by the family were evaluated, this rate was found to be 85%. There was no difference in the frequency of sleep problems between the group using methylphenidate and the group using atomoxetine. In our study, there was significant difference between the group using methylphenidate and the group using atomoxetine in terms of delay in falling asleep. In many studies based on both objective and subjective measurements, psychostimulant drugs have been reported to be associated with difficulty falling asleep and prolonged sleep latency. Sleep disorders are common in ADHD. It is important that child and adolescents with ADHD must be evaluated the sleep habits before medical treatment to identify the etiology of sleep disorders.

Keywords: Attention-deficit/hyperactivity disorder, Child, sleep, Atomoxetine, Methylphenidate

INTRODUCTION

Attention deficit / hyperactivity disorder (ADHD) is a common neurodevelopmental disorder manifested by inattention, impulsivity, and hyperactivity, and is estimated to affect approximately 5.3% of children and adolescents worldwide (1). It has been reported that the frequency of sleep disorders in individuals with ADHD is 25-55% (2,3,4).

Sleep problems lead to serious impairments in children's mental, cognitive functions and social and academic skills (5). The relationship between ADHD and sleep is versatile and complex. Sleep-related problems may have a specific feature of ADHD, and sleep problems may aggravate ADHD symptoms or cause the development of ADHD-like symptoms (6,7).

The relationship between ADHD and sleep problems is further complicated by the use of psychostimulants in the treatment of ADHD. In some studies, it has been stated that psychostimulants have a negative effect on sleep (8,9). On the contrary, there are studies showing that psychostimulants have no effect on sleep (10) or the effect of improving sleep problems (11).

In addition, although there are studies reporting insomnia as a side effect in the treatment of ADHD with a nonstimulant drug, atomoxetine (12), in many studies, it has been stated that somnolence is a more common side effect (13,14).

For these reasons, it is recommended to identify primary sleep disorders before ADHD drug treatment is initiated (15).

In our study, it was aimed to compare the effects of methylphenidate and atomoxetine treatment on sleep habits in children and adolescents who followed and diagnosed as ADHD in Eskisehir Osmangazi University Faculty of Medicine Child and Adolescent Psychiatry Outpatient Clinic.

*Corresponding author:

Elif Gokce ERSOY SIMSEK
MD

Eskisehir Osmangazi Univ
Child and Adolescent
Psychiatry Dept, Eskisehir
Turkey
Email: tulincps@hotmail.com

METHODOLOGY

This study was conducted with child and adolescents 42 taking extended release methylphenidate, and 39 taking atomoxetine only one dose in the morning daily, who were diagnosed and followed in Eskişehir Osmangazi University Child and Adolescent Psychiatry Outpatient Clinic at least for 6 months before the study. They were between 6 to 12 years old. Families of children and adolescents were informed about the purpose and content of the study and their written consent was obtained, indicating that they agreed to participate in the study. Exclusion criteria were determined as mental retardation, chronic and serious medical disease, seizure-like neurological disorder, and the presence of any other psychopathology other than ADHD.

Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) in order to exclude the cases having other psychiatric disorders were applied to all children and Child Sleep Habits Survey (CSHS) were used to evaluate by parents (16,17).

K-SADS-PL is a semi-structured diagnostic interview schedule designed to assess major psychiatric disorders in children and adolescents based on DSM-IV criteria (18). The reliability and the validity of the Turkish translation was conducted by Gokler et al. (19).

The Abbreviated Form of Child Sleep Habits Survey (CSHS) was filled by the parents to evaluate child and adolescents' sleep habits retrospectively over the previous week. The Abbreviated Form of Child Sleep Habits Survey (CSHS) consists of 33 items. Eight subscales were defined in the scale, which can be listed as bedtime resistance, delayed falling asleep, sleep duration, sleep anxiety, night awakenings, parasomnias, impaired breathing during sleep, and sleepiness during the day. As a cut-off score of CSHS, 41 points in total are accepted and values above this are considered as 'clinically significant'. The questionnaire also includes three open-ended questions about the child's sleep habits (bedtime, the amount of time he has been sleeping all day, and when he wakes up at night).

RESULTS

The study included 81 patients who were diagnosed with ADHD, 42 of whom were receiving methylphenidate and 39 were receiving atomoxetine treatment. 41 (50.6%) of the patients were male and 40 (49.4%) were female and the mean age was 9.2 ± 1.5 .

When it was evaluated whether there was a sleep problem according to the CSHS cut-off score, it was found that 81% ($n = 34$) of the patients using methylphenidate had a sleep problem, and 89.7% ($n=35$) of the group using atomoxetine had sleep problems, and there was no statistically significant difference between the two groups ($p > 0.05$).

The average nighttime bedtime time was $22:30 \pm 0:54$ (h: min) in those using methylphenidate; the mean morning waking time was $7: 05 \pm 0:11$ (h: min), the average night sleep time was $8:45 \pm 1:02$ (h: min) and the average night awake time was 7.8 ± 4.76 (minutes). In the group using atomoxetine, the average nighttime bedtime was $22:08 \pm 0:18$ (h: min); the mean morning waking time was $7: 31 \pm 0:55$ (h: min), the average night sleep time was $9:05 \pm 0:52$ (h: min) and the average night awake was 5.8 ± 5.1 (minutes). There was no statistically significant difference between the two groups in terms of mean nighttime, morning awakening time, sleep time and night awake time ($p > 0.05$).

There was not significant difference between the two groups in terms of bedtime resistance, sleep duration, sleep anxiety, night awakenings, parasomnia, sleep-breathing problems, and daytime sleepiness subtest

and total sleep scores ($p > 0.05$). A difference was found in terms of the delay score for falling asleep, which is another subtest, and the methylphenidate group was found to have a longer sleep time ($p < 0.05$).

DISCUSSION

Sleep-related complaints in children diagnosed with ADHD are common in clinical practice. It is known that 25-55% of children with ADHD often report various sleep problems and in addition, more sleep problems are reported by their parents (2,3). In our study, when the total scores of CSHS filled by the family were evaluated, this rate was found to be 85%. We are not able to find significance difference in the frequency of sleep problems between the group taking extended release methylphenidate and the group taking atomoxetine.

In this study, there was a significant difference in terms of delay in falling asleep between the group using extended release methylphenidate and the group using atomoxetine. In many studies based on both objective and subjective measurements, psychostimulant drugs have been reported to be associated with difficulty falling asleep and prolonged sleep latency (9,20). In a study comparing the effects of methylphenidate taken 3 times a day and the effects of atomoxetine taken twice a day, it was shown with actigraph and polysomnography that both the parents and the children provided a better sleep quality according to their own reports (21).

However, in our study, a difference was found between methylphenidate and atomoxetine only in terms of delay in falling asleep, and no significant difference was found in terms of bedtime resistance, sleep duration, sleep anxiety, night awakenings, parasomnias, sleep-breathing problems, and daytime sleepiness. In addition, no significant difference was found in terms of total CSHS score, bedtime, morning wake-up time, and awake time at night.

Although it has been suggested that sleep changes seen in children with ADHD are mainly related to medications used in treatment (especially stimulants), current evidence suggests that drugs are only one possible reason to explain sleep disorders in children diagnosed with ADHD, and that sleep problems in these patients are multifactorial. In 2 meta-analysis studies, it was shown that age, gender, diagnostic criteria, determination of subtypes, sleep assessment tool (objective or subjective measurements), comorbidities and drug use were effective on the severity of the detected relationship (22).

Sleep problems that result in impaired or inadequate sleep can lead to increased fatigue, impulsivity, difficulty in concentration, behavioral problems and school failure during the day, and can negatively affect daily functionality in the mood, attention and behavioral areas, and lead to serious impairments in the child's social and academic functionality (23).

CONCLUSION

Therefore, ADHD should not be seen as just a daytime illness. Before starting treatment, patients should first be screened for primary sleep disorders that may require a different treatment. The clinician should ask the patient about problems with going to bed, falling asleep, maintaining sleep, waking up during the night, or unusual behaviors, snoring, trouble getting up in the morning, or sleepiness all day long. The optimal treatment for ADHD should include improving sleep hygiene and pharmacological regulations to reduce side effects on sleep.

Table 1: Comparison of Sub-Test and Total Scores of the Children's Sleep Habits Questionnaire

	Methylphenidate	Atomoxetine	p*
Bedtime resistance	9.3 (3)	10.2 (2.4)	>.05
Delayed falling asleep	1.5 (0.5)	1.2 (0.4)	<.05
Sleep time	4.5 (1.7)	3.6 (0.9)	>.05
Sleep anxiety	6.1 (2.4)	7.5 (2.5)	>.05
Waking up at night	5.3 (1.9)	4.3 (1.8)	>.05
parasomnia	8.9 (2.4)	10.7 (3.2)	>.05
Breathing problems while sleeping	3.4 (0.9)	4 (1.3)	>.05
Daytime sleepiness	14.3 (4)	13.8 (2)	>.05
CSHS total	50.3 (9.7)	52 (9.2)	>.05
Bedtime (h: min)	22:30 (00:54)	22:08 (00:18)	>.05
Morning wake up time (h: min)	07:31 (00:55)	07:05 (00:11)	>.05
Time spent awake at night (min)	7.8 (4.7)	5.8 (5.1)	>.05
Total amount of sleep (h: min)	08:45 (01:02)	09:05 (00:52)	>.05

*p<0.05 CSHS: Child Sleep Habits Survey

REFERENCES

- Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *Am J Psychiatry*. 2007;164(6):942-8.
- Corkum P, Tannock R, Moldofsky H. Sleep disturbances in children with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 1998;37(6):637-46.
- Sung V, Hiscock H, Sciberras E, Efron D. Sleep problems in children with attention-deficit/hyperactivity disorder: prevalence and the effect on the child and family. *Arch Pediatr Adolesc Med*. 2008;162(4):336-42.
- Owens JA. Sleep disorders and attention-deficit/hyperactivity disorder. *Curr Psychiatry Rep*. 2008;10(5):439-44.
- Johnson KP. Pediatric sleep disorders. K Cheng, KM Myers (Eds.). *Child and Adolescent Psychiatry The Essentials*. Philadelphia: Lippincott Williams and Wilkins;2005.
- Cortese S, Lecendreux M, Mouren MC, Konofal E. ADHD and insomnia. *J Am Acad Child Adolesc Psychiatry*. 2006;45(4):384-5.
- Owens JA. Sleep disorders and attention-deficit/hyperactivity disorder. *Curr Psychiatry Rep*. 2008;10(5):439-44.
- Galland BC, Tripp EG, Taylor BJ. The sleep of children with attention deficit hyperactivity disorder on and off methylphenidate: a matched case-control study. *J Sleep Res*. 2010;19(2):366-73.
- Corkum P, Panton R, Ironside S, Macpherson M, Williams T. Acute impact of immediate release methylphenidate administered three times a day on sleep in children with attention-deficit/hyperactivity disorder. *J Pediatr Psychol*. 2008;33(4):368-79.
- Ashkenasi A. Effect of transdermal methylphenidate wear times on sleep in children with attention deficit hyperactivity disorder. *Pediatr Neurol*. 2011;45(6):381-6.
- Kim HW, Yoon IY, Cho SC, Kim BN, Chung S, Lee H, et al. The effect of OROS methylphenidate on the sleep of children with attention-deficit/hyperactivity disorder. *Int Clin Psychopharmacol*. 2010;25(2):107-15.
- Adler LA, Liebowitz M, Kronenberger W, Qiao M, Rubin R, Hollandbeck M, et al. Atomoxetine treatment in adults with attention-deficit/hyperactivity disorder and comorbid social anxiety disorder. *Depress Anxiety*. 2009;26(3):212-21.
- Yildiz O, Sismanlar SG, Memik NC, Karakaya I, Agaoglu B. Atomoxetine and methylphenidate treatment in children with ADHD: the efficacy, tolerability and effects on executive functions. *Child Psychiatry Hum Dev*. 2011;42(3):257-69.
- Block SL, Kelsey D, Coury D, Lewis D, Quintana H, Sutton V, et al. Once-daily atomoxetine for treating pediatric attention-deficit/hyperactivity disorder: comparison of morning and evening dosing. *Clin Pediatr (Phila)*. 2009;48(7):723-33.
- Cortese S, Brown TE, Corkum P, Gruber R, O'Brien LM, Stein M, et al. Assessment and management of sleep problems in youths with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2013;52(8):784-96.
- Owens JA, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. *Sleep*. 2000;15:1043-1051.
- Fiş NP, Arman A, Ay P, Topuzoğlu A, Güler AS, Gökçe İmren S, Ersu R, Berkem M. Çocuk Uyku Alışkanlıkları Anketinin Türkçe geçerliliği ve güvenilirliği. *Anadolu Psikiyatri Dergisi*. 2010;11:151-160.
- Brent, D., Kaufman, J., Ryan, N., Rao, U., Birmaher, B., Williamson, D., ... Ryan, N. (2003). Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): Initial Reliability and Validity Data. *Journal of the American Academy of Child & Adolescent Psychiatry*, 36(7), 980-988. <https://doi.org/10.1097/00004583-199707000-00021>
- B Gökler, F Ünal, B Pehlivan Türk, EÇ Kültür, D Akdemir, Y Taner. Reliability and Validity of Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version-Turkish Version (K-SADS-PL-T) Çocuk ve Gençlik Ruh Sağlığı Dergisi; 2004;11(3):109-116
- Ironside S, Davidson F, Corkum P. Circadian motor activity affected by stimulant medication in children with attention-deficit/hyperactivity disorder. *J Sleep Res*. 2010;19(4):546-51.
- Sangal RB, Owens J, Allen AJ, Sutton V, Schuh K, Kelsey D. Effects of atomoxetine and methylphenidate on sleep in children with ADHD. *Sleep*. 2006;29(12):1573-85.
- Hill CM, Hogan AM, Karmiloff-Smith A. To sleep, perchance to enrich learning? *Arch Dis Child*. 2007;92(7):637-43.
- Cortese S, Konofal E, Yateman N, Mouren MC, Lecendreux M. Sleep and alertness in children with attention-deficit/hyperactivity disorder: a systematic review of the literature. *Sleep*. 2006;29(4):504-11