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Statistical Evaluation of Treatment Compliance In Children With Attention Deficit Hyperactivity Disorder

Duygu MURAT[1*], Uğur TEKİN[2]
[1] Special Child and Adolescent Psychiatry Clinic, İstanbul, Turkey
[2] Clinic of Child and Adolescent Psychiatry, University of Health Sciences, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey
[*1] duygucalisir44@yahoo.com, [2] drutekin@hotmail.com

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Abstract: Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder. Pharmacological treatment is the first option in the treatment of ADHD. Long-term treatment is required, as the course of the disease often continues throughout life. Long-term adherence to treatment in ADHD is important in terms of reducing the risk of substance use, accidents, and risk-taking behaviours. Medication adherence is very important for the successful outcome of the treatment. In this study, we aimed to evaluate the factors that may affect treatment adherence in the Turkish sample. We found that 39.6% of children with ADHD had high medication adherence accordingly Morisky Medication Adherence Scale. Medication adherence of boys and girls were similar. When the education level of mothers was compared, the education level of mothers with high medication adherence group was higher than those with poor medication adherence group, and this difference was statistically significant (p=0.013). We can say that highly educated families who learn that ADHD is a neurodevelopmental disorder and can realize the risks that may arise as a result of being untreated are more careful about drug use.

Key words: Attention Deficit, Hyperactivity, Medication Adherence, Statistical Evaluation.

Dikkat Eksikliği Hiperaktivite Bozukluğu Olan Çocuklarda Tedavi Uyumunun İstatistiksel Değerlendirilmesi

Öz: Dikkat Eksikliği Hiperaktivite Bozukluğu (DEHB) nörogelişimsel bir bozukluktur. DEHB tedavisinde ilk seçenek tedavi farmakolojik tedavidir. Hastalığın seyri çoğu zaman yaşam boyu devam ettiği için uzun süreli tedavi gerekir. DEHB' de tedaviye uzun süreli uyumun olması, madde kullanımı, kaza ve riskli davranışlar riskini azaltabilmektedir. Tedavinin başarılı seyretmesi için ilaç uyumu çok önemlidir. Bu çalışmada tedavi uyumunu etkileyebilecek faktörleri Türkiye örnekleminde değerlendirmeyi amaçladık. Çalışmamızda Morisky İlaç Uyum Ölçeği' ne göre DEHB' li çocukların %39,6'sının ilaç uyumunun yüksek olduğunu saptadık. Kız ve erkek çocukların ilaç uyumu ise benzerdi. Annelerin eğitim durumları karşılaştırıldığında, ilaç uyumu yüksek olan grubun annelerin eğitim düzeyi, ilaç uyumu kötü olan gruba göre daha yüksekti ve bu fark istatistiksel olarak anlamlıydı (p=0,013). Sonuç olarak DEHB' nin nörogelişimsel bir bozukluk olduğunu öğrenen ve tedavi edilmediği takdirde ortaya çıkabilecek riskleri fark edebilen eğitim seviyesi yüksek ailelerin ilaç kullanımı konusunda daha dikkatli olduklarını söyleyebiliriz.

Anahtar kelimeler: Dikkat Eksikliği, Hiperaktivite, İlaç Uyumu, İstatistiksel Değerlendirme.

1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized by inattention, hyperactivity and impulsivity. The prevalence of ADHD was found 11% in children and adolescent [1]. In a multi-center study conducted in Turkey included 5830 children, the prevalence of ADHD was found 12.4 % [2]. ADHD symptoms continue in adolescence and adulthood in 40-60% of those diagnosed with ADHD in childhood [3,4]. Pharmacological treatment is the first option in the treatment of ADHD. Stimulants (methylphenidate) and non-stimulants (atomoxetine and guanfacine) are medications with proven effectiveness in the treatment of ADHD. Adding behavioral therapy to drug therapy in ADHD positively affects the course of the disease [5]. Long-term treatment is required, as the course of the disease often continues throughout life.

1.1. Treatment Compliance and Attention Deficit Hyperactivity Disorder

Treatment compliance is defined as the regular and correct use of medication by the patient at the time and amount recommended by the clinician. Factors affecting the treatment compliance may be separated to three factors. The first one is factors related to parents and children, the second one is related to medication type and third one is related to the health system [6]. While the parents who understand that ADHD is a neurobiological

* Corresponding author: duygucalisir44@yahoo.com ORCID Number of authors: [1] 0000-0001-6372-2930, [2] 0000-0001-6720-4292

disease continue the treatment, the others do not even accept the treatment [7]. Parental anxiety about drug side effects makes it difficult to initiate medication for children with ADHD [8]. Therefore, in addition to providing medical treatment to children with ADHD, it is also important to provide psychoeducation to parents. Factors related to children such as older age, comorbid Oppositional Defiant Disorder and reluctant to take medication affects negatively the treatment compliance. Side effects of drugs used in ADHD, such as loss of appetite, insomnia, and increased irritability, also worsen drug compliance [9]. Difficulties in reaching a child and adolescent psychiatrist in Turkey and making appointments to continue the follow-up also complicate treatment compliance. Having information about ADHD, the effects and side effects of drugs, being under the age of 12 and being a girl, easily accessible to the health system increase treatment compliance [10]. In recent years, the use of pharmacotherapy in children and adults with ADHD has been increasing [9,11]. Long-term adherence to treatment in ADHD is important in terms of reducing the risk of substance use, accidents, and risk-taking behaviors [12,13]. Although the effectiveness of drug therapy in ADHD is high, medication non-compliance is common in both young people and adults, with rates varying between 13 and 87% [14]. Poor adherence to treatment may result in persistence of ADHD symptoms. Poor adherence to treatment decreases the child's functionality and the clinician's evaluation of the effectiveness of the treatment, while increasing health expenditures [15]. Medication adherence is very important for the successful outcome of the treatment.

The long or short-acting drug used in ADHD, the duration of treatment and drug side effects affect adherence with treatment [16,17]. The patient's age, gender, and co-morbidities also affect treatment adherence [18,19]. In a study on those who could not continue their ADHD treatment between the ages of 6-45, it was determined that the age with the highest probability of discontinuation treatment was 15-21 [20].

There are many factors that impair treatment compliance in ADHD and it is difficult to evaluate [21]. In this study, we aimed to evaluate the factors that may affect treatment adherence in the Turkish sample. If we can understand the factors that impair medication adherence, it will be possible for us to take the necessary precaution for long-term treatment in ADHD. Children with ADHD will have better long-term academic success, social relationships and quality of life, if treatment continues for a long time. They will not affected by the negative consequences of ADHD.

2. Material and Method

2.1. Participants

Ethics committee approval of the study was obtained from the ethics committee of Bakırköy Dr. Sadi Konuk Training and Research Hospital. Our study group consisted of 96 children diagnosed with ADHD. Parents and their children who volunteered to participate in the study and those who wanted to continue the treatment at least 6 months were included. Children with Neurological Disease, Autism Spectrum Disorder, Mental Retardation and Participants who refused to use of medications were excluded from the study.

Sociodemographic information form, Morisky Medication Adherence Scale and Conners' Parent Scale Long Form were given to the families participating in the study. In the Sociodemographic data form, the child's age, gender, age of the parents, education and employment status of the mother and father, marital status of the mother and socio-economic level of the family were asked. According to the data of the Morisky Medication Adherence Scale, participants were divided into 2 groups as high medication adherence and poor medication adherence. High adherence group consisted of children with medium and high scores, and the poor adherence group consisted of children with low scores in Morisky Adherence Scale. Using the Clinical Global Impression Scale (CGI), clinicians evaluated disease severity, improvement, and severity of adverse events.

2.2. Measurements

2.2.1. Clinical Global Impression Scale (CGI)

Clinical Global Impression Scale consists of 3 fields, which include the disease severity, improvement and severity of the side effect. The Clinical Global Impression Severity of disease (CGI-S) was developed by the American National Institute of Mental Health and published in 1976. It was developed for the purpose of evaluating the clinical course of psychiatric disorders. CGI-S is a seven-value Likert-type scale. It is evaluated between 1 and 7 points according to the severity of the disease at the time the scale was filled; 1 = Normal, not ill, 2 = Borderline mental illness, 3 = Mildly ill, 4 = Moderately ill, 5 = Significantly ill, 6 = Severely ill, 7 = Severe degree ill. Second part (Clinical Global Impression-Recovery) shows how much the patient has changed since the beginning of treatment. It is useful to evaluate between 1 and 7 points. 1=Healed a lot, 2=Much improved, 3=Minimal recovery, 4= No Change 5=Minimum worsening, 6=Very worsening, 7=It has deteriorated a lot. The third part of the scale is the Clinical Global Impression-Side Effect, it is evaluated over 4 points. These are; 1.

None, 2. Does not significantly affect the functionality of the patient, 3. Significantly affects the functionality of the patient, 4. Influencing at a level that negates the benefits of the therapeutic effect.

2.2.2. Morisky Medication Adherence Scale

It is a self-filled scale measuring drug compliance developed by Donald E. Morisky [22]. The scale consists of four two-choice (yes/no) closed-ended questions. If all questions are answered “no”, medication adherence is considered high, if “yes” is answered for one or two questions, medication adherence is considered medium, if yes to three or four questions, medication adherence is considered low. The validity and reliability study in our country was carried out by Yılmaz to measure adherence to antipsychotic treatment [23].

2.2.3. Conners’ Parent Rating Scale Long Form

Conners' Parent Rating Scales are the most used tools for evaluating problem behaviors in children/adolescents, especially ADHD, monitoring the effects of the treatment. The scale developed by Conners consists of seven subscales: Cognitive Problems-Inattention, Oppositional, Hyperactivity, Anxiety-Shyness, Perfectionism, Social Problems, and Psychosomatics [24]. The validity and reliability study in our country was carried out by Kaner [25].

2.3. Statistical Analysis

SPSS version 24 was used to analyze the data of the study. The normal distribution of continuous variables between the two groups was evaluated using the Shapiro Wilk Test. Parametric tests were used for data with normal distribution, and nonparametric tests were used for data with non-normal distribution. The Independent Sample t-test was used to compare the continuous variables with normal distribution with the group, and Mann-Whitney-U test was used to compare quantitative data without parametric distribution. Chi-square test was used to compare the categorical variables in the data. Spearman correlation analysis was used for the evaluation of the relationship between treatment adherence scale scores and disease severity.

3. Results

Total 96 children and adolescents with ADHD between the ages of 8 and 13 were included in the study. The mean age of the children and adolescents participating in the study was 10.4 years. 12.5% of the participants (n: 12) were female and 87.5% (n: 84) were male. We divided 96 children and adolescents with ADHD into 2 groups according to their scores on the Morisky Medication Adherence Scale. The study group consist of 38(39.6%) participant with high medication adherence and 58 (60.4%) participants with poor medication adherence. When we compared mothers and children's age of the high and poor medication adherence groups, there was no statistically significant difference ($p>0.05$). The educational status of the mothers was divided into pre-high school and high school and above. When the education level of mothers in two study group (high and poor medication adherence) was compared, the education level of mothers with high medication adherence group was higher than those with poor medication adherence group, and this difference was statistically significant ($p=0.013$).

Table 1. Comparing medication adherence and maternal education levels.

		High Medication Adherence		**Poor Medication Adherence**		
		n	**%**	**n**	**%**	**p**
Mother's Education	**Pre-High School**	16	43.2	40	69	**0.013**
	High School and University	21	56.8	18	31	

χ^2 test

As it can be seen in the Figure 1 below, the education level of the mothers of children with high medication adherence was higher than the other.

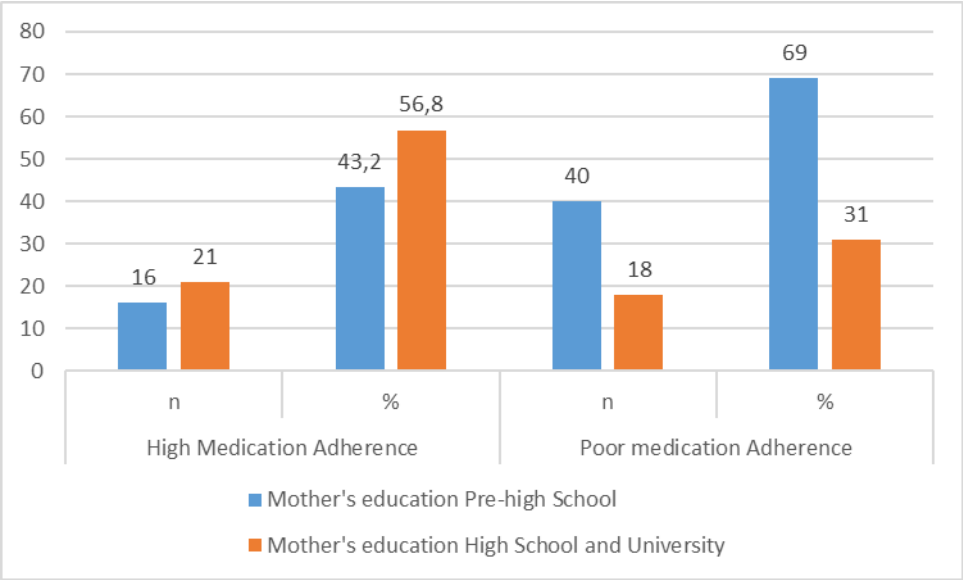

Figure 1. Medication adherence and maternal education levels.

When the father's education levels of those with high and poor medication adherence group compared, no statistically significant difference was found between the education levels of the fathers (p=0.557). When the working status of the mothers and fathers of the groups with high and poor drug compliance were compared separately, no statistically significant difference was found between the working status of the mothers and fathers (p>0.05).

When the groups (high and poor medication adherence) were compared in terms of marital status of the mother, income of the family, and gender of the child, there was no statistical significant difference between the groups(p>0.05).

The mean score value of the subtests of the Conners' Parent Rating Scale was as seen in the Figure 2 below. Those with high medication compliance are shown in blue column, and those with poor medication compliance are shown in red column. Medication compliance was similar according to Conners' subtest scores.

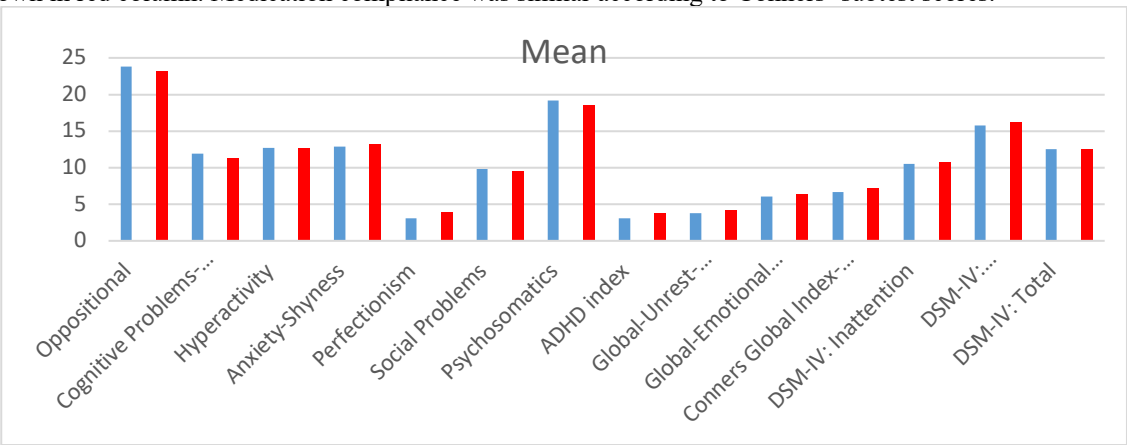

Figure 2. Conners' Parent Rating Scale scores and Medication Adherence.

There was no statistically significant difference between the Conners' Parent Rating Subscales scores of participants with high medication adherence and poor adherence groups.

Table 2. Conners' Parent Rating Scale scores and Medication Adherence.

Conners' Parent Rating Scale	Medication Adherence	n	Mean	Std. Deviation	Std. Error Mean	p values
Oppositional	High	38	23.79	10.81	1.753	0.775
	Poor	58	23.16	10.5	1.379	
Cognitive Problems-Inattention	High	38	11.89	6.5	1.055	0.683
	Poor	58	11.34	6.37	0.837	
Hyperactivity	High	38	12.71	6.42	1.042	0.944
	Poor	58	12.62	5.82	0.764	
Anxiety-Shyness	High	38	12.84	5.2	0.844	0.723
	Poor	58	13.24	5.5	0.722	
Perfectionism	High	38	3.11	2.19	0.355	0.121
	Poor	58	3.88	2.48	0.325	
Social Problems	High	38	9.84	4.91	0.796	0.733
	Poor	58	9.52	4.31	0.565	
Psychosomatics	High	38	19.21	7.25	1.176	0.683
	Poor	58	18.57	7.68	1.009	
ADHD index	High	38	3.05	2.67	0.433	0.273
	Poor	58	3.79	3.52	0.463	
Global-Unrest-Impulsıvıty	High	38	3.82	2.92	0.474	0.588
	Poor	58	4.19	3.52	0.462	
Global-Emotional Variation	High	38	6.03	3.8	0.616	0.713
	Poor	58	6.31	3.61	0.474	
Conners' Global Index-Total	High	38	6.68	3.86	0.626	0.561
	Poor	58	7.21	4.56	0.599	
DSM-IV: Inattention	High	38	10.55	6.34	1.029	0.892
	Poor	58	10.72	5.87	0.771	
DSM-IV: Hyperactivity-Impulsivity	High	38	15.79	8.08	1.31	0.816
	Poor	58	16.19	8.28	1.087	
DSM-IV: Total	High	38	12.53	6.34	1.029	0.986
	Poor	58	12.55	6.9	0.906	

Independent Sample T test

In our study, there was no statistically meaningful difference between severity of side effects and medication adherence.

Table 3. Side Effect Severity and Medication Adherence.

			Medication Adherence		Total	P value
			High	Poor		
Side Effect Severity	none at all	n	16	22	38	0.718
		% within medication adherence	47.1%	38.6%	41.8%	
	not affect	n	14	28	42	
		% within medication adherence	41.2%	49.1%	46.2%	
	effect	n	4	7	11	
		% within medication adherence	11.8%	12.3%	12.1%	

χ^2 test

As it can be seen in the Figure 3 below, medication compliance was poor in all 3 groups, regardless of the severity of drug side effects.

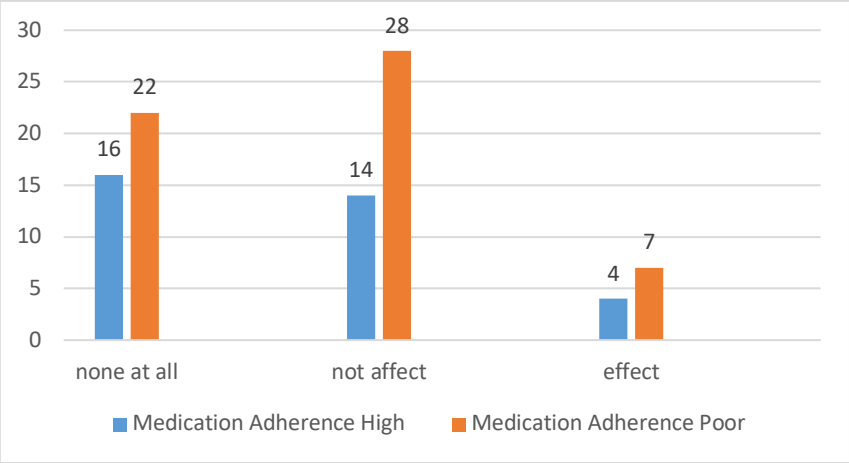

Figure 3. Side Effect Severity and Medication Adherence.

When we examined whether there is a relationship between the scores in the Morisky Medication Adherence Scale and the parameters in the Clinical Global Impression Scale, with Spearman's rho correlation analysis; there was no statistical significant correlation.

Table 4. Correlation analysis of Morisky Medication Adherence Scale and Clinical Global Impression Scale.

		CGI-Side Effect	CGI-Severity	CGI-Recovery
Medication Adherence Scores	r	-0.064	-0.133	-0.203
	p	0.544	0.207	0.055
	n	91	92	90

Spearman's rho correlation analysis

* Correlation is significant at the 0.01 level (2-tailed).

There was no correlation between the Conners' Parent Scale subtest and Morisky Medication Adherence scores.

4. Discussion

In our study, we found that 39.6% of children with ADHD had high medication adherence accordingly Morisky Medication Adherence Scale. In two different studies on drug adherence in ADHD, drug compliance was found in 21% and 45.6% of cases, respectively [26,27]. In our study, medication adherence of boys and girls was similar. In a study conducted in Korea, medication adherence of girls and boys was found to be similar [19]. The fact that our study did not have an effect of gender on medication adherence is compatible with the Korean study. In our study, the ages of children with high medication adherence and poor adherence were similar. In the literature, some of the studies indicated that small aged children had high medication adherence [28,29], and also showed that older aged adolescent had poor medication adherence [30]. In most of the studies, it was found that medication adherence decreased with increasing age. The reason why we did not find similar results in our study may be due to the close age ranges of the children. In the transition from childhood to adolescence as autonomy is gained, medication compliance decreases. The education level of mothers of children with high medication adherence was higher. We can say that highly educated families who learn that ADHD is a neurodevelopmental disorder and can realize the risks that may arise as a result of being untreated are more careful about drug use. Zheng at al. showed that in the training program about ADHD to parents and teachers, learning that ADHD is neurobiological disease and that medication therapy is the first choice increased treatment compliance [31]. We found that there is no correlation between the scores of Conners' Parent Scale subtest, Clinical Global Impression Scale and drug compliance separately. Navak at al. showed that drug adherence was found to be better in patients with low ADHD severity [32]. The inconsistency of the results of our study with the literature may be due to the methodological differences of the studies. Important limitations of our study were that we did not evaluate medication adherence according to the type of drug (stimulant and non-stimulant), the presence of psychopathology in the family and comorbidity of children.

In conclusion, adherence to treatment is an important factor in the treatment of ADHD, as in many medical and psychiatric conditions. In this multifaceted issue, our study indicates that high maternal education has a positive effect on the treatment of ADHD in children. Based on this finding, it can be speculated that mothers with higher education have better understanding of the nature and consequence of ADHD and how it can be managed.

However, given the vitality of treatment compliance in ADHD, more research is needed on our understanding of this issue and possible ways to cope with non-adherence.

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