Original Article

Factors Associated with Premature Treatment Discontinuation among Thai Children and Adolescents with Attention Deficit Hyperactivity Disorder [ADHD]

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Objective: To identify factors that contributed to premature treatment discontinuation among Thai children and adolescents with attention deficit hyperactivity disorder [ADHD].

Materials and Methods: This was a retrospective study. The parents of ADHD subjects were divided into three groups which were based on their children's adherence to treatment: 1) early discontinuation [ED] group, 2) late discontinuation [LD] group, and 3) control group. The possible factors that might cause treatment discontinuation were collected through chart reviews and interviews (telephone or face-to-face) by trained personnel. The Chi-squared and Kruskal-Wallis tests were performed when appropriate to identify the associated factors. Multivariate logistic regression analyses (backward stepwise method) were also utilized.

Results: A total of 375 parents of ADHD patients were recruited. The parents were separated into 3 groups where 195 parents were in the control group, while 105 and 75 were in the ED and LD groups, respectively. Multiple logistic regression analyses revealed that factors associated with treatment discontinuation were increased age (adj. OR = 1.19), family income > 50,000 baht/month (adj. OR = 2.48), parents' knowledge of "Treatment of ADHD is unnecessary." (adj. OR = 1.37) and "Medication for ADHD is an essential intervention for ADHD" (adj. OR = 0.61). The reasons for treatment discontinuation between ED and LD revealed that patients in the LD group experience more "intolerable side effects" (38.7% vs. 22.9%) and less "improved or cured children" (16.0% vs. 29.5) compared to those in the ED group.

Conclusion: The significant factors that predicted premature treatment discontinuation among Thai children and adolescents with ADHD were the age of the patients, family income, parents' lack of knowledge of ADHD, and negative parental attitudes toward the pharmacological management of ADHD.

Keywords: Treatment discontinuation, Attention deficit hyperactivity disorder, ADHD, Children and adolescents, Non-adherence

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Attention deficit hyperactivity disorder [ADHD] is characterized by a persistent, maladaptive and developmentally inappropriate pattern of inattention and hyperactivity-impulsivity[1]. It is one of the most common behavioral disorders in children and adolescents. A systematic review in 2007 revealed that the worldwide-pooled prevalence of ADHD was 5.28%[2]. The prevalence rate of ADHD among Thai school-aged children in 2013 was 8.1%[3], an increase from 5.1% in 2002[4].

ADHD usually has an onset in childhood and often persists into adulthood. The pathophysiology of ADHD is related to abnormalities in the noradrenergic and serotonergic systems of the brain, which causes impairments in the child's self-inhibition as well as executive functions. These impairments contribute to

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significant negative impact on the child's various developmental areas such as learning, emotion, interpersonal, and self-esteem. Furthermore, if left untreated, ADHD can create a tremendous financial burden for the patients and their families[5,6]. Early detection and intervention are recommended to prevent those detrimental outcomes[7].

Effective treatment for ADHD patients included pharmacological, psychosocial, behavioral, and combined interventions. Nevertheless, positive changes in a child's behaviors and overall functions often take time to emerge, necessitating good adherence to the treatment by both the family and the child[8]. ADHD treatment discontinuation is a critical issue that needs addressing and requires an exploration of the underlying factors. The long-term outcomes of ADHD patients can be predicted not only by the effectiveness of the treatment but also by the adherence to the treatment[9,10].

The rate of treatment discontinuation or non-adherence among ADHD patients ranges between 13.2 to 64%[11]. Multiple factors contributed to the treatment discontinuation among children and adolescents with ADHD. One of the most common factors that led the patients to stop ADHD medication is its side effects. Other factors included the type of medication, the dosage which caused inconvenience, the parents or guardians' attitudes toward ADHD, and perceptions regarding their roles in the treatment process[12]. A national retrospective, cohort study in Korea on treatment discontinuation revealed that a better understanding of ADHD treatment could lead to improved adherence and persistence of treatment[9]. In addition, clinicians can also help ADHD patients improve their behavioral problems and decrease the deleterious effects at academic and social functions in several ways. Specifically, clinicians can educate the patients and their parents about ADHD, have an inclusive decision-making process on treatment plans, and frequently monitored the treatment's effectiveness to identify any unacceptable medication side effects or other difficulties[13].

A preliminary survey by the Division of Child and Adolescent Psychiatry, Department of Psychiatry, Faculty of Medicine Siriraj Hospital, discovered that about half of the patients at the ADHD clinic discontinued their treatment prematurely. The primary objective of this study was to identify the factors associated with treatment discontinuation among Thai ADHD patients. The authors also explored possible differences in factors that contributed to treatment discontinuation between ADHD patients who discontinued in the early phase of their treatment, and those who discontinued in a later phase of the treatment. The findings from this study will help understand the factors which contributed to treatment discontinuation and ways to minimized them.

Materials and Methods

Study procedures

This was a retrospective study. The authors reviewed data from the psychiatric records of all ADHD patients who attended the child and adolescent psychiatry clinic at Siriraj Hospital and who had been diagnosed with ADHD between January 2003 and December 2007.

Participants

The participants consisted of parents of ADHD patients whose age was between 3 and 18 years old. The diagnosis of ADHD was made by experienced child and adolescent psychiatrists using the DSM-IV-TR criteria (American Psychiatric Association, 2000). The primary caregivers of the ADHD patients were invited to participate in the study. Based on their children's adherence to treatment, the participants were separated into 'regular follow-up group', and 'discontinuation group' (Figure 1). In the regular follow-up (or control) group, random recruitment process was undertaken in parents and children who had been routinely followed up at the clinic for at least a year and had never been lost follow-up for more than 6 months (n = 195).

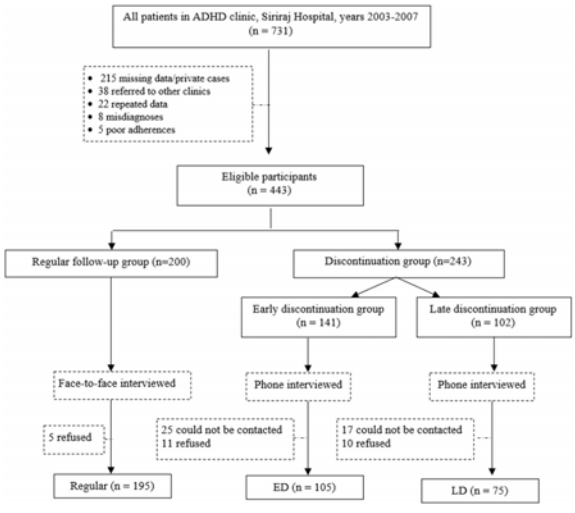

Figure 1. Participant flow diagram.

On the other hand, the discontinuation group was further divided into two subgroups. The first subgroup was an early discontinuation [ED] group. The parents of the ADHD patients in this group were seen in the clinic for under a year but were subsequently lost to follow-up, without a psychiatrist's agreement or referral to another clinic, for more than 6 months (n = 105). The second subgroup was late discontinuation [LD] group. The parents of the ADHD patients in this group had been seen in the clinic for over a year but were then lost follow-up, without a psychiatrist's agreement or referral to another clinic, for more than 6 months (n = 75). All patients who fell into the ED and LD groups were recruited for the study. The participants were excluded if: 1) parents of patients who were terminated by psychiatrists because of a significant improvement in ADHD symptoms; 2) the parents of patients who had been referred to other clinics; and 3) subjects who declined to participate in the present study (Figure 1).

Measures

The questionnaires used in the present study were designed to measure 3 factor-domains that could potentially be associated with treatment discontinuation. They included (1) characteristic features of ADHD patients and their parents; (2) severity of ADHD symptoms, measured by Conners' Teacher Rating Scale (Conners' Rating Scales, 1997) and the presence of comorbidity; and (3) parental knowledge and attitudes toward ADHD treatment.

The questionnaire that assessed parental knowledge and attitudes toward ADHD treatment was developed for this study. The Cronbach's alpha correlation coefficient of this questionnaire was 0.66.

The parents in the control group completed all questionnaires themselves. Parents who had difficulty reading or understanding the questionnaires were assisted in face-to-face interviewed by a trained social worker. The parents in the ED and LD group were interviewed via telephone by the same interviewer to gather the reasons for their child's treatment discontinuation.

Ethical considerations

The protocol for this study was approved by the Siriraj Institutional Review Board [SIRB], Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand (Si. 061/2007). Written, informed consents to participate in this study were obtained from the participants (both the children and their parents) prior to data collection.

Statistical analysis

The baseline characteristics of the children and parents in the ED, LD and control groups were analyzed using descriptive statistics. Chi-squared tests were performed to measure the differences in their demographics and the reasons for the treatment discontinuation in certain groups. The Kruskal-Wallis test was also used to compare the differences in the knowledge and attitude toward ADHD of the parents in the groups. Multivariate logistic regression analyses (backward stepwise method) were also utilized to identify the risk factors for treatment discontinuation. All data were analyzed using SPSS version 18 (SPSS, Inc., Chicago, IL, USA).

Results

A total of 731 patients with ADHD attended the clinic from 2003 to 2007. Of those, 443 subjects were eligible; the children and their parents were allocated to the control and discontinuation groups according to the criteria previously described. Only 375 parents (84.6%) of the eligible parents could be reached and consented to participate in the study.

Details of the characteristics of the children and adolescents diagnosed with ADHD in this study are illustrated in Table 1. Most were boys (n = 303, 80.8%), and their mean age was 12.0 years. Children in the control group were younger than those in the discontinuation group, and about half of them studied in grades 4 to 6; children in the discontinuation group were mostly older children in grades 7 to 9 (Table 1).

The demographics of the parents revealed that in most families, mothers were the children's primary caregivers (Table 2). The parental occupation and family income were statistically different between the control and discontinuation groups; more than one in three parents in the control group were government officers or state enterprise employees. On the other hand, the parents' careers in both discontinuation groups were contractors, housewives, self-employed, cultivators, and students. There were no significant differences in the other demographic characteristics.

The reasons for ADHD treatment discontinuation are demonstrated in Table 3. The child's reported uncooperativeness with treatment (n = 54, 30%) was the most common reason. The other reasons included an inability to tolerate the side effects of the medications (n = 53, 29.44%), the inconvenience of traveling to the hospital (n = 44, 24.44%), having to

Table 1. Characteristics of children and adolescents diagnosed with ADHD in the 3 groups

Characteristics	Number (%) or mean ± SD			*p*-value
	Control (n = 195)	ED (n = 105)	LD (n = 75)	
Gender: male	154 (79.0)	86 (81.9)	63 (84.0)	0.608[a]
Age (years)	11.3±2.8	12.9±4.0	12.7±3.3	0.019[b,c]
Grade level				
<4	44 (22.6)	16 (16.3)	4 (5.6)	<0.001[a,d]
4 to 6	81 (41.5)	35 (35.7)	29 (40.3)	
7 to 9	55 (28.2)	56 (21.4)	25 (35.2)	
10 to 12	13 (6.7)	20 (20.4)	11 (15.5)	
>12	2 (1.0)	6 (6.1)	2 (2.8)	
T-score of hypersensitivity index	63.5±11.2	63.1±12.1	64.1±11.8	0.442[b]
Comorbidity: yes	77 (39.5)	51 (48.6)	35 (46.7)	0.261[a]

[a] The *p*-value from Chi-squared test; [b] The *p*-value from one-way ANOVA; [c] Control vs. ED: $p<0.001$, control vs. LD: $p<0.01$, ED vs. LD: $p = 0.091$, significant level at $p<0.016$; [d] Control vs. ED: $p<0.001$, control vs. LD: $p<0.001$, ED vs. LD: $p<0.001$, significant level at $p<0.016$

Table 2. Characteristics of parents of ADHD subjects in the 3 groups

	Number (%) or mean ± SD			*p*-value
	Control (n = 195)	ED (n = 105)	LD (n = 75)	
Relationship				
Father	38 (19.5)	16 (15.2)	17 (22.7)	0.398 [a]
Mother	139 (71.3)	84 (80.0)	53 (70.7)	
Relatives	18 (9.2)	5 (4.8)	5 (6.7)	
Gender: female	155 (79.5)	88 (83.8)	58 (77.3)	0.518 [a]
Age (years)	43.8±6.3	43.7±8.1	44.4±6.0	0.546 [b]
Occupation				
Government employee	70 (35.9)	15 (14.4)	20 (26.7)	0.003 [a, c]
Employee	35 (17.9)	21 (20.2)	16 (21.3)	
Housewife	32 (16.4)	21 (20.2)	20 (26.7)	
Private business	44 (22.6)	33 (31.7)	11 (14.7)	
Others	14 (7.2)	14 (13.5)	8 (10.7)	
Income (baht/month)				
<10,000	29 (15.1)	8 (7.9)	7 (9.6)	0.01 [a, d]
10,001 to 25,000	43 (22.2)	16 (15.8)	10 (13.7)	
25,001 to 50,000	65 (33.3)	25 (24.8)	22 (30.1)	
>50,000	57 (29.4)	52 (51.5)	34 (46.6)	

[a] The *p*-value from Chi-squared test; [b] The *p*-value from one-way ANOVA; [c] Control vs. ED: $p<0.001$, control vs. LD: $p<0.001$; ED vs. LD: $p = 0.091$, significant level at $p<0.016$; [d] Control vs. ED: $p<0.001$; control vs. LD: $p<0.001$, ED vs. LD: $p<0.001$; significant level at $p<0.016$.

come during office hours (n = 44), and improved or cured children (n = 43, 23.89%). The significant differences between the ED and LD groups' reasons for discontinuation were "improved or cured children" ($p = 0.036$) in the case of the ED group, and "experiencing intolerable side effects" ($p = 0.022$) and "parent's negative attitudes toward treatment" (p-value = 0.039) for the LD group. None of the other reasons were significantly different.

The parent's knowledge and attitude toward

Table 3. Reasons for treatment discontinuation in the early- and late-discontinuation groups

Reasons for treatment discontinuation	Group: number (%)		*p*-value[a]
	ED (n = 105)	LD (n = 75)	
1) Improved or cured children	31 (29.5)	12 (16.0)	0.036[b]
2) Child's uncooperativeness with treatment	30 (28.6)	24 (32.0)	0.621
3) Inconvenience of coming during office hours	27 (25.7)	17 (22.7)	0.639
4) Inconvenience of travelling	27 (25.7)	17 (22.7)	0.639
5) Experiencing intolerable side effects	24 (22.9)	29 (38.7)	0.022[c]
6) Parent's fear of potential harm from medication	21 (20.0)	16 (21.3)	0.827
7) Parent's unwillingness to let the child be absent from school	17 (16.2)	15 (20.0)	0.510
8) Dissatisfaction with service	17 (16.2)	17 (22.6)	0.801
9) Dissatisfaction with staff	6 (5.7)	10 (13.3)	0.077
10) Relative's disagreement with treatment	8 (7.6)	5 (6.7)	0.808
11) Having financial problems	5 (4.8)	4 (5.3)	0.862
12) Teacher's disagreement with treatment	4 (3.8)	1 (1.3)	0.319
13) Not improved or worsened	3 (2.9)	1 (1.3)	0.494
14) Feeling stigmatized	2 (1.9)	2 (2.7)	0.732
15) Parent's negative attitudes toward treatment	0 (0.0)	3 (4.0)	0.039[d]

[a] The *p*-value from Chi-squared test; [b,c,d] ED vs. LD ≤0.001; significant level at $p<0.025$

Table 4. Parents' knowledge and attitudes toward ADHD in the 3 groups

Parents' knowledge and attitude toward ADHD (1 to 5, 5 = most agreeable)	Mean ± SD			*p*-value
	Control (n = 195)	ED (n = 105)	LD (n = 75)	
1) An ADHD child is just a naughty child. Nothing is wrong	2.4±1.2	2.7±1.4	2.4±1.3	0.158
2) Parents of ADHD children often fail to discipline their child	2.4±1.2	2.7±1.4	2.3±1.3	0.148
3) ADHD is not a serious problem	2.9±1.3	3.1±1.3	2.9±1.1	0.222
4) Treatment of ADHD is unnecessary.	1.5±1.0	2.1±1.3	1.9±1.2	<0.001 [a]
5) Medication treatment is an essential intervention for ADHD	3.8±0.9	3.1±1.3	3.4±1.0	<0.001 [b]
6) Medication for ADHD is safe	3.3±0.9	2.9±1.1	2.9±1.0	<0.001 [c]
7) If it is possible, I don't want my child to take any medication for ADHD	2.9±1.4	3.6±1.3	3.2±1.4	<0.001 [d]
8) Meditation practice is helpful for ADHD children	3.7±1.1	3.8±1.0	3.8±1.0	0.372
9) The child can grow out of ADHD	2.9±1.1	2.8±1.3	2.8±1.2	0.901

The *p*-value from Kruskal-Wallis test, significant level at $p<0.016$. [a] Control vs. ED: $p<0.001$, Control vs. LD: $p = 0.015$; [b] Control vs. ED: $p<0.001$; control vs. LD: $p = 0.003$; [c] Control vs. ED: $p = 0.020$, control vs. LD: $p = 0.003$; [d] Control vs. ED: $p<0.001$, control vs. LD: $p = 0.164$.

ADHD were also associated with treatment discontinuation (Table 4). Relative to the control group, parents in the two discontinuation groups were more agreeable with the statement "Treatment of ADHD is unnecessary" but less agreeable with "Medication treatment is an essential intervention for ADHD". The understanding of the safety of ADHD medications was significantly different between the control and LD groups, but not between the control and ED groups. Parents with the attitude of "If it is possible, I don't want my child to take any medication for ADHD" were statistically different at *p*-value <0.001 between the control and ED groups. There was no statistical difference in the knowledge of and attitude toward ADHD between the ED and LD groups.

Multivariate logistic regression analyses

Table 5. Multivariate logistic regression analyses predicting treatment discontinuation

	Univariable analysis		Multivariable analysis	
	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Age (years)	1.16 (1.08, 1.24)	<0.001	1.19 (1.10, 1.28)	<0.001
Income (baht/month)				
≤10,000	1		1	
>50,000	2.92 (1.44, 5.92)	0.003	2.48 (1.13, 5.48)	0.024
Patient's knowledge of ADHD (5 = agree)				
Treatment of ADHD is unnecessary	1.48 (1.22, 1.80)	<0.001	1.37 (1.11,1.70)	0.004
Medication for ADHD is essential intervention for ADHD	0.58 (0.47, 0.72)	<0.001	0.61 (0.48,0.77)	<0.001

The *p*-value from linear regression (backward stepwise method)

revealed that a 1-year increment in age increased the risk of treatment discontinuation by 19%. The patients whose parents earned more than 50,000 baht per month were 2.5 times more likely to discontinued ADHD medication than others. The knowledge of, and attitudes toward, ADHD could also predict treatment discontinuation. Increased scores for "Treatment of ADHD is unnecessary" could increase the discontinuation by 37%. In contrast, the increased scores for "Medication treatment is an essential intervention for ADHD" could reduce the discontinuation by 39%. Other beliefs about ADHD were not predictors for treatment discontinuation (Table 5).

Discussion

The present study aimed to find the factors contributed to treatment discontinuation among Thai children and adolescents with ADHD. The results showed the important predictors for treatment discontinuation are as followed: the age of the children, family income, and parental misunderstandings or negative attitudes toward ADHD and its treatment. This is consistent with the findings of a previous study[14]. Other studies have reported that the reasons for discontinuation of medication included the medication side effects, the patients' and/or parents' negative attitudes toward the medication, social stigma, and suboptimal outcomes after treatment[15,16].

Getting older is a risk factor for treatment discontinuation, whereas a young age is a protective factor against discontinuation[17]. Similar to other studies, there were evidences that the older children or adolescents were afraid of social stigmatization[18,19]. Being diagnosed with ADHD and having to take medication at school regularly made many ADHD adolescents feel embarrassed and different from their friends[20]. Parents had more impact in the decision making process regarding ADHD treatment when the children were younger. As the children become older, they tend to become more resistant and uncooperative. They may eventually decide to stop taking their medication[21]. In the present study, the authors also discovered that children who continued ADHD medication were significantly younger than those patients who discontinued the medication.

Although first-line medications of ADHD, like methylphenidate, help decrease the symptoms of hyperactivity, inattentiveness and impulsiveness[22,23], an inability to tolerate the medications' side effects is also a major reason for stopping the medication. Normally, medication side effects occur within a year, leading to many patients' decision to discontinued treatment[13,21]. However, in this study, the patients in the LD group were unexpectedly less able to bear the medication side effects than those in the ED group. The particular reason for this finding warrants clarification through future research.

Other reasons for stopping treatment were inconvenient clinic opening hours and the commute to and from the Hospital. For some families, one visit of an ADHD patient resulted in the loss of a whole-day's family income as well as the child's absence from school for the day. This situation particularly affected low-income employees, like laborers, housekeepers and cultivators, who were mostly in the discontinuation groups. Therefore, the parents in the discontinuation groups stopped treatment because they gave a higher priority to working to earn money to meet necessary family expenses than to ADHD treatment and follow-

up. The significant difference in the occupations and family income levels of the control and discontinuation groups supports this interpretation of the findings. This issue has also been reported in a previous study[24].

Since ADHD is not a life-threatening condition like heart disease or infectious diseases, stopping ADHD medication does not suddenly affect the patients. Patients with ADHD normally take a long course of medication, perhaps for months or years, depending on the severity, type of symptoms, and whether they were diagnosed with comorbidities[25]. A decision to discontinue must be made in consultation with a psychiatrist. However, the present study found that approximately a half of the children in the discontinuation group stopped their medications without the agreement of their physicians because their symptoms had self-reportedly improved. Unfortunately, premature discontinuation can lead to symptom deterioration and suboptimal treatment outcomes[26,27].

Moreover, the parent's level of understanding of ADHD medication was related to the continuity of treatment[28]. Parent's lack of knowledge can lead to treatment discontinuation[14]. The present study confirmed that those parents with negative attitudes toward ADHD treatment in the ED and LD discontinuation groups seemed to believe that "Treatment of ADHD is unnecessary". On the other hand, good knowledge is associated with good adherence to the treatment of ADHD patients. It was shown that acknowledgement of the importance of treatment is essential for its continuation. If the patients and their parents understand ADHD and its management correctly, this knowledge may help increase the rate of continuation of their treatment[29].

To our knowledge, this is the first study to examine the differences between the factors associated with the stopping of ADHD treatment during and after the first year of treatment. In the present study, it was revealed that the reasons for treatment discontinuation were statistically different between the ED and LD groups. Patients in the LD group stopped their treatment because they couldn't tolerate the side effects, while patients in the ED group stopped their treatment because their ADHD symptoms had self-reportedly improved or been cured. The parents in the ED and LD groups showed no statistically significant difference in their knowledge of and attitudes toward ADHD.

There were several limitations of the present study. First, the questionnaires were completed by the primary caregivers without any direct input from children. Future research should obtain from the patients themselves as to the reasons why they chose to discontinue treatment. Second, the types and forms of medication could affect adherence. Unfortunately, this study did not collect data about the type of medication given to each patient. Third, a comparison of a symptom severity index before and after treatment was not undertaken. Finally, the population of the study largely lived in urban areas. The information in this study therefore may not adequately reflect the attributes of the parents of ADHD patients in rural areas: different demographics may reveal different results.

There should be a further study measuring the benefit of providing psycho-education, setting goals for treatment, and early detection of medication side effects. One should expect a reduction in the discontinuation rate if the aforementioned interventions are effective. Moreover, the details of the medication side effects should be ascertained to further differentiate the reasons for treatment discontinuation in the ED and LD groups.

To decrease the rate of treatment discontinuation, child and adolescent psychiatrists should (1) provide accurate knowledge of the disease and its management to patients and their parents[9], (2) increase awareness of both the patients and their parents of the need for treatment[30,31], (3) detect side effects early and gradually titrate the medication dosage, if necessary[32], and (4) set goals and plans for the ADHD management with both the children and their parents[14]. These interventions should improve the long-term outcomes and quality of life of ADHD patients.

Conclusion

The age of the children, family income, parental misunderstandings, and negative attitudes toward the pharmacological management of ADHD are considered the main predictors of treatment discontinuation among Thai children and adolescents with ADHD. Few differences were found in the two discontinuation groups. The parents in the ED group believed that their children were improved or cured. However, and as reported by the parents, the ADHD children in the LD group discontinued their treatment because they could not tolerate the side effects and/or had negative attitudes toward their ADHD treatment.

What is already known on this topic?

The causes and predictors of treatment

discontinuation, including the age of the children, parental knowledge of ADHD, and negative parental attitudes toward ADHD treatment, have been reported in many studies.

What this study adds?

To date, the differences between early and late discontinuation have never been identified. The present study showed significant differences in the reasons for treatment discontinuation in those two groups.

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Potential conflicts of interest

None.

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