

Comparison of Stimdate with Ritalin in Children and Adolescents with Attention Deficit Hyperactivity Disorder: A Double-Blind, Randomized Clinical Trial

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Objectives: The aim of this randomized clinical trial was to assess the efficacy of stimdate compared to ritalin in the treatment of children with attention deficit hyperactivity disorder (ADHD).

Method: Sixty four subjects (45 boys and 15 girls) aged 5-13 who were diagnosed with ADHD based on (DSM-IV-TR) criteria were selected for this study. The subjects were randomly assigned to two groups: one group with 30 subjects received stimdate and the other group of 30 subjects received ritalin for 6 weeks. Treatment outcomes were assessed using the Attention Deficit Hyperactivity Rating Scale administered at baseline and on weeks 2, 4 and 6 following the treatment. A two-way repeated measures analysis of variance (time- treatment interaction) was used.

Results: There were no significant differences between sex, age, weight, and ethnicity of the participants in the 2 groups. Both groups showed a significant improvement during the 6 weeks of the treatment period, and this improvement was due to the parents' ADHD Rating Scale during the treatment.

Conclusion: Based on the results of this study, no significant difference was observed between the two medications, and it seems both drugs behave in a similar way. In addition, stimdate appears to be effective and well tolerated for ADHD in children and adolescents in Iran.

Keywords: *Adolescents, Attention deficit disorder with hyperactivity, Children, Generic drugs, Methylphenidate*

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Attention-deficit hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood. The incidence of ADHD is 5–10% in children and the symptoms are known to persist into adulthood in 10–60% of the cases (1). The etiology of ADHD is not understood, yet potent drugs are being employed for its medical management while safe and effective alternatives are being neglected. Neurochemical studies suggest alterations in catecholaminergic-mainly dopaminergic and noradrenergic-transmitter functions markedly contribute to the symptoms of ADHD. The ADHD symptoms are significantly ameliorated by agents that specifically influence these neurotransmitter systems; animal studies implicate those areas of the brain where these neurotransmitters are most dominant.

In conjunction with psychosocial interventions such as parent training, contingency management, and social skills training, stimulant pharmacotherapy has been used for the treatment of ADHD for many decades in (2, 3).

Although stimulants are highly effective in controlling

the symptoms of ADHD, some children will not respond to, or do not tolerate them. Thus, the desire for safe and effective non-stimulant medications has risen during the past several years (4-10).

In Iran, ADHD signs and symptoms are regarded as being ordinary in some families, especially when boys are concerned. Furthermore, pharmacotherapy for ADHD children is regarded unfavorably by parents (6). Greenhill study showed that release methylphenidate (MPH), administered once daily in the morning is effective and safe in controlling ADHD symptoms throughout the day (11). Children suffering from ADHD respond differentially to treatment with ritalin (12). Seventy five percent of children respond to the first stimulant medication trial (13-15).

There are many reasons for considering pharmacotherapy other than stimulants in the treatment of ADHD. For instance, the stigmatization that arises from the ingestion of a controlled substance as children treated with standard release stimulant medications must typically take at least 1 dose during school hours. Alternative medications that have been studied in the

treatment of ADHD include Bupropion, Clonidine, Guanfacine, Moclobemide, Theophylline, Passiflora, Selegiline, Modafinil and Atomoxetine (1, 16-29).

These alternative medications may increase the patients' respond rate to treatment. Clinicians and researchers are still looking for a medication with an immediate onset and benefits throughout the day, with few or no side effects and no potential for abuse while being relatively inexpensive and effective for most patients (1, 30-33). Nevertheless, MPH is still the first line for treatment of ADHD in the majority of counties including Iran. Considering the annual use of this drug in Iran and its importation from different counties possibly with different qualities, national production of MPH with standard quality would be an advantage.

The main aim of this study was to evaluate the treatment efficacy of stimdate (produced as the generic of methylphenidate in Iran by Mehr Daru Company) in children and adolescents with ADHD as compared to treatment with ritalin.

Materials and Method

Sixty subjects (45 boys and 15 girls) aged 6–15 who were diagnosed with ADHD according to (DSM-IV-TR) (34) criteria were randomly selected to take part in this study. Exclusion criteria included a current diagnosis of any other axis I psychiatric disorders, substance abuse or dependency, mental retardation, a history of seizures or any other serious medical disorders and use of any psychotropic drugs in the 6 weeks prior to the study. The diagnosis of ADHD was made by 2 child and adolescent psychiatrists, using the Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS) (35) to confirm the diagnosis. Participants were recruited from the outpatient clinic of the author in Tehran. Prior to the study, written informed consent was obtained from the parents of the subjects. In addition, the parents permitted the publication of the results. The design was a double-blind, randomized clinical trial. All the participants were randomly assigned by a pharmacist to either a group receiving a 2.5 mg/bid Ritalin or a group receiving the same dose of stimdate. At the beginning of the treatment; the doses were titrated to the highest dose level (1 mg/kg/day Ritalin or stimdate, or a maximum of 40 mg/day)., The doses were reduced when the participants experienced any undesirable side effects. The average daily doses of stimdate and ritalin were 25 mg. The medications were tablets taken orally twice a day (at 7.30 to 8:00 a.m. and 12 to13:00 p.m.). The participants continued to take their maximum

tolerated dose for a period of 42 days. All participants, parents and the rater were blind to each participant's medication. The parents' ADHD rating scales were obtained at approximately 4:00 to 6 p.m. on the relevant days at baseline and on weeks 2, 4 and 6 following the treatment. The trial was conducted in accordance with the Declaration of Helsinki, 1975 revised in 2000, and according to the Good Clinical Practice Guidelines.

The effectiveness of ritalin and stimdate on ADHD symptoms was assessed using the Attention Deficit Hyperactivity Rating Scale (31), administered at baseline and on days 14, 28 and 42 following the treatment.

The Attention Deficit Hyperactivity Rating Scale includes 14 items rated from 0 (normal) to 3 (severe) scales, yielding a total score out of 42 which constitute the outcome measure for ADHD. This rating scale has been successfully used in previous studies (32), and has also been used in Iran in many studies (1, 6, 17, 36 and 37).

An assessment of each participant's medical history, physical examination, measures of blood pressure and heart rate was performed at baseline. Drug-induced side effects observed by investigators or reported by parents were taken in to account and the side effects of ritalin and stimdate were also considered.

To ensure that participants took their medications accurately, parents were asked to supervise ingestion of the medications, and to count the pills following each administration. The data were analyzed using SPSS for Windows (Version 11.0). Two-way repeated measures analysis of variance (time- treatment interaction) was used.

Results

Sixty children (45 boys and 15 girls) aged 6–15 participated in the study. The number of clients who completed the trial and were assessed by the Parent form of the Attention Deficit Hyperactivity Rating Scale was 24 for the ritalin group and and 30 for the stimdate group respectively. Only 6 participants dropped out of ritalin treatment either because they experienced adverse side effects or their parents did not complete the parents' ADHD rating scale; no participants dropped out of the stimdate group. There were no significant differences between the subjects' characteristics such as sex, age, ADHS scores, weight, and ethnicity. The mean age of the participants was 9.29 years for the stimdate group and 9.21 years for the ritalin group (Table 1).

Table 1. Baseline data

	Stimdate Group	Ritalin Group
Girls	8	7
Boys	22	23
Age (Mean ±SD)	9.29 ± 2.58 (year)	9.21 ± 2.45 (year)
Weight (Mean ±SD)	31.26 ±9.18 Kg	30.46±6.23Kg
Ethnicity	All Persian	All Persian

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Table 2: Baseline and endpoint of two groups

	Week 0 (Mean±SD)	P	Week 6 (Mean±SD)	P
Stimdate	39.71±9.45	ns	16.45±10.20	ns
Ritalin	39.24±8.12		16.12±11.01	

Parent ADHD Rating Scale

There were no significant differences between the two groups at day 0 (baseline) on the Parent ADHD Rating Scale ($t = 0.34$, $df = 58$, $P=0.79$). Both groups showed a significant improvement over the 6 weeks of the treatment. The difference between the two groups was not significant as indicated by the effect of group, and the between-subjects factor ($F = 0.003$, $df = 1$, $P=0.98$). The behavior of the two treatment groups was homogeneous across time (groups by time interaction ($F = 0.09$ $df = 1.75$, $P=0.89$)). The baseline and endpoint of the two groups are presented in table 2.

Table 2

Discussion

Attention-Deficit Hyperactivity Disorder (ADHD) is a common psychiatric disorder in children and adolescents. To date the stimulants are considered highly efficacious and safe for ADHD treatment and have been the mainstay for over 60 years (1, 8, 17 and 38).

In this double-blind randomized controlled study of children with ADHD the authors detected a statistically significant effect of stimdate and ritalin on ADHD children. No significant differences were observed between the two groups on the Parent Rating Scale scores. In addition, stimdate showed a tolerable side effect profile in comparison to ritalin.

In this study, ritalin and stimdate were effective in reducing the symptoms of ADHD, and the parents were satisfied with the medication.

The short period of the study and small sample size should be taken into account as the limitations of this study. Therefore, further research on the subject is recommended. In addition, although adequate care was taken to ensure that the treatment allocation had become blind, some parents may have guessed whether their children were receiving ritalin or stimdate.

Conclusion

Stimdate was well tolerated in Iran and the clinical response was comparable to ritalin, suggesting that stimdate is a successful stimulant treatment for children and adolescents with ADHD.

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