Comparison of Therapeutic Effects of Omega-3 and Methylphenidate (Ritalin®) in Treating Children With Attention Deficit Hyperactivity Disorder

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Objective: Attention deficit hyperactivity disorder (ADHD) is a fixed pattern of disregard and hyperactivity that is much more severe than what is normal in children of the same age. Multiple stimulant drugs are used for the treatment of children with ADHD; however, their side effects and efficacy are not clearly known. This study was designed to evaluate and compare the therapeutic effects of two drugs, that is, omega-3 and methylphenidate hydrochloride (Ritalin®), used to treat patients with ADHD.

Methods: This is a clinical trial using a parallel method performed on 85 children aged 6-12 years in Yazd city, Iran. The children were divided into two experimental groups and one control group. Thus, 29 subjects were treated with Ritalin®, 28 subjects received omega-3, and the remaining 28 received placebo. The data collection tools used in this study consisted of the Conners' Parent Rating Scale and Teacher Rating Scale. The scores obtained from these questionnaires were analyzed using chi-square test and paired t-test in PASW Statistics.

Results: The average age of the population was 8.22 (± 1.65) years. Significant associations were observed between Ritalin® therapy and the changes before and after the treatment, and the omega-3 treatment and the changes before and after treatment ($p < 0.001$). There was no significant association between the placebo group and the changes before and after the treatment ($p > 0.050$).

Conclusions: Omega-3 has significantly impacted both groups of hyperactivity-impulsivity and combined type. Due to its effectiveness in treating these two groups of patients with ADHD, its use is recommended.

Declaration of interest: None.

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Keywords: Attention deficit hyperactivity disorder (ADHD) • Methylphenidate • Omega-3 • Ritalin®

Introduction

Attention deficit hyperactivity disorder (ADHD) is a fixed pattern of disregard and hyperactivity that is much more severe than what is normal for children of the same age group (1). Cognitive, functional, and hyperactivity are obvious aspects of this disorder (2, 3) and it is usually observed with other psychiatric disorders such as depression, anxiety, conduct and learning disorders (4, 5). Based on the presenting symptom, ADHD can be divided into three subtypes—predominantly inattentive, predominantly hyperactive-impulsive, or combined if criteria for both types are met (6). The prevalence of this disorder has been reported to be 2-20% in the United States and also the prevalence of this disorder in boys is higher than girls (7). Stimulant drugs, such as methylphenidate, are used in the treatment of this disorder. About 75% of patients are responsive to this medicine. However, this medicine has possible risks, such as being carcinogenic (4), and causing drug abuse in children, and complications such as

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irritability, insomnia, anorexia, depression, and even child growth reduction. Moreover, an association has been observed between various behavioral disorders like ADHD and low plasma levels of long-chain unsaturated fatty acids especially omega-3 in these patients. Therefore, investigating the effect of food supplements containing these fatty acids and comparing the results with methylphenidate (Ritalin®) treatment in these patients seems necessary. By increasing the plasma levels of these fatty acids, these patients' symptoms, academic performance, and quality of life are improved and the possible complication of methylphenidate (Ritalin®) are avoided (8). This study was designed to evaluate and compare the therapeutic effects of omega-3 and methylphenidate (Ritalin®) drugs in treating patients with ADHD.

Materials and Methods

This was a double-blind, randomized, clinical trial performed using a parallel method on 85 children aged 6-12 years in Yazd city (Tamin Ejtemaei Central Hospital), Iran, from April 2010 to March 2011. Thus, 29 patients were treated with Ritalin® and 28 patients with omega-3, and the remaining 28 received placebos. The first 29 patients were treated with therapeutic doses (0.3-1 mg/kg) of Ritalin® 3 times a day, and the second 28 patients with therapeutic doses of omega-3 (1 g), one capsule per day for three days. Conners' Parent Rating Scale and Teacher Rating Scale were used in this study. Children with a score of higher than 65 on both scales, IQ of higher than 70 using the Kaufman Brief Intelligence Test, and whose parents gave an informed consent were included. However, children with occurrence of unintended side effect of methylphenidate, who had previous treatment of ADHD, who had taken omega-3 supplement during the previous 3 months, and who had severe psychiatric disorders were excluded from the study. The scores obtained from these questionnaires were analyzed using the chi-square test and paired t-test in PASW Statistics, (version 18.0; SPSS Inc., Chicago, IL, USA). The questionnaires were completed and collected by parents; then the questionnaires were reviewed and evaluated by researchers to find whether the children had the disorder in the opinion of their parents. The Teacher Rating Scale was given to the children's school to ask their teacher's opinion, and then the teachers forms were reviewed and evaluated by researchers. Children who had ADHD based on both questionnaires were introduced to professionals for treatment. To be categorized as ADHD, the child must have at least 6 signs of attention deficit or at least 6 symptoms of hyperactivity and impulsivity, or both. Moreover, individual score from each questionnaire should be equal to or greater than 12 and the overall score of each subject from the total of both questionnaires should be equal to or greater than 24. Cases that only showed signs of attention deficit in both questionnaires have been considered mainly as a type of inattentiveness. Cases which only show signs of hyperactivity-impulsivity in both questionnaires have been considered mainly as a type of hyperactivity-impulsivity. In addition, cases which showed signs of hyperactivity-impulsivity and attention deficit symptoms in both questionnaires have been considered as a combined type. The results of treatment were evaluated after 2 and 4 weeks, and again at the end of the treatment. The questionnaires were completed by the parents and the teacher of the treated subject and the scores were compared with that of questionnaires completed before the treatment.

Results

In this study, of the 29 patients in the Ritalin® therapy group, 58.6% were males and 41.4% females (17 boys and 12 girls). Of the 28 patients in omega-3 therapy group, 46.4% were males and 53.6% females (13 boys and 15 girls). Moreover, of the 28 patients in the placebo therapy group, 64.3% were males and 35.7% females (18 boys and 10 girls). According to the obtained results, there was no statistically significant association between the frequency of sex in the 3 treatment groups ($p = 0.387$). From among the 85 patients, 20 patients had attention deficit disorder (ADD), 21 subjects had hyperactivity-impulsivity, and 44 were

mixed (combined type). There was no statistically significant association between the frequency of the disease type in the three treatment groups (p = 0.595). The average age of the target population was 8.22 (±1.65) years. The mean scores and standard deviations before the treatment were 24.20 (± 9.76) in the Ritalin® group, 25.89 (± 9.96) in the omega-3 group, and 22.58 (± 8.52) in the placebo group. In addition, the mean score and standard deviation after treatment was 17.81 (± 10.32) in the Ritalin® group, 18.44 (± 8.36) in the omega-3 group, and 22.66 (± 8.01) in the placebo group. Paired t-test and p = 0.001 showed a statistically significant association between treatment with Ritalin® and the changes before and after the treatment. It also showed a statistically significant association between treatment with omega-3 and the changes before and after the treatment. Nevertheless, paired t-test and p = 0.888 showed no statistically significant association between treatment with placebo and changes before and after the treatment (Table 1). On the other hand, using paired t-test and p > 0.050, no statistically significant association was observed between treatment with the two drugs and placebo, and changes before and after the treatment in ADD type (Table 2). On the other hand, the average score of hyperactivity-impulsivity type and its changes in the Ritalin® and omega-3 groups were significant. As a result, a statistically significant association was found between treatment with the first two intended drugs and changes before and after the treatment in the hyperactivity-impulsivity type. However, there was no statistically significant association between the placebo group and the changes before and after the treatment in hyperactivity-impulsivity type (Table 3). In assessing the mean scores of combined type and its changes in the three study groups (before and after the treatment) with paired t-test, P-values of 0.001, 0.001, and 0.290 were obtained in the three groups, respectively. The mean score of combined type and its changes were statistically significant in the Ritalin® and omega-3 groups. Thus, a statistically significant association was observed between treatment with the first two intended drugs and changes before and after the treatment in combined type. Nevertheless, there was no statistically significant association between the placebo group and the changes at the beginning and end of our study in the combined type (Table 4).

Table 1. Average scores of disease and its changes in the three study groups, before and after the treatment

Group	Number	Pre-treatment scores	Post-treatment scores	Changes	P-value*
		Mean ± SD†	Mean ± SD†	Mean ± SD†	
Ritalin	29	24.20 ± 9.76	17.81 ± 10.32	6.39 ± 5.39	0.001
Omega-3	28	25.89 ± 9.96	18.44 ± 8.31	7.44 ± 6.80	0.001
Placebo	28	22.58 ± 8.52	22.66 ± 8.01	-0.07 ± 2.66	0.888

* ANOVA; † Standard deviation

Table 2. Average scores of ADD type and its changes in the three study groups, before and after the treatment

Group	Number	ADD†			P-value*
		Pre-treatment scores	Post-treatment scores	Changes	
		Mean ± SD‡	Mean ± SD‡	Mean ± SD‡	
Ritalin	7	16.85 ± 3.83	4.77 ± 1.80	2.71 ± 3.30	0.073
Omega-3	4	15.50 ± 1.77	13.12 ± 2.25	2.37 ± 3.70	0.290
Placebo	9	15.11 ± 1.13	15.55 ± 2.74	-0.44 ± 2.77	0.645

*ANOVA; †Attention deficit disorder; ‡Standard deviation

Table 3. Average scores of hyperactivity-impulsivity type and its changes in the three study groups, before and after the treatment

Group	Number	Hyperactivity-impulsivity			P-value*
		Pre-treatment scores	Post-treatment scores	Changes	
		Mean ± SD†	Mean ± SD†	Mean ± SD†	
Ritalin®	8	17.25 ± 2.72	8.37 ± 4.35	8.87 ± 1.16	0.005
Omega-3	7	18.28 ± 2.82	12.28 ± 4.36	6.00 ± 3.14	0.002
Placebo	6	15.58 ± 1.46	17.16 ± 1.29	-1.58 ± 0.86	0.006

* ANOVA; † Standard deviation

Table 4. Average scores of combined type and its changes in the three study groups, before and after the treatment

Group	Number	Combined type			P-value*
		Pre-treatment scores	Post-treatment scores	Changes	
		Mean ± SD†	Mean ± SD†	Mean ± SD†	
Ritalin®	14	31.85 ± 8.51	25.30 ± 9.52	6.82 ± 5.09	0.001
Omega-3	17	31.47 ± 8.86	22.23 ± 8.42	9.23 ± 7.67	0.001
Placebo	13	31.00 ± 4.33	30.11 ± 5.05	0.88 ± 2.88	0.290

*ANOVA; † Standard deviation

Table 5. Comparison of rate of disease score changes in the three study groups

Group	Number	Average	SD†	MIN	MAX
Ritalin®	29	6.39	5.39	-2.5	17
Omega-3	28	7.44	6.7	-6.0	29
Placebo	28	-0.07	2.66	-3.0	6
Total	85	4.61	6.12	-3.0	29

† Standard deviation

Table 6. Binary comparison of rate of score changes due to treatment in the three groups

Groups compared		Average changes	P-value*
Ritalin®	Omega-3	-1.04	0.449
Ritalin®	Placebo	6.46	0.001
Omega-3	Placebo	7.51	0.001

* ANOVA

Moreover, by using analysis of variance (ANOVA) test, from the comparison of rate of disease score changes in the three study groups, a statistically significant difference was obtained (p = 0.001). This is an indication of a significant correlation in relation to the rate of score changes of ADHD disease in the three groups (Table 5). Furthermore, a statistically significant association was found in the analysis of treatment groups mutually between the placebo and Ritalin® and also placebo and omega-3. However, no statistically significant association was observed between the average of the changes of scores in the two groups, which were treated with Ritalin® and omega-3 (p = 0.449) (Table 6).

Discussion

The main objective of this research was to review and compare the therapeutic effects of Ritalin®, omega-3, and placebo in the treatment of ADHD. No statistically significant association was found between the two pharmacological treatments with the first comment in ADD type and also the placebo group and recovery changes. A statistically significant association was found between the two drugs and recovery changes in subtypes of hyperactivity-impulsivity and combined type. However, there was no statistically significant association between this drug and recovery changes in the placebo group in these two subtypes. A similar study was performed to evaluate the effects of eicosapentaenoic acid/docosahexaenoic acid (DHA) (omega-3) at high doses in ADHD patients. At the end of 8 weeks of study on 9 children of 8-12 years of age (6 boys and 3 girls), a reduction was observed in the symptoms of this disease (9). In a similar study which was performed in Japan in 2004, the children were randomly divided into two groups, one group was treated with DHA and the other was the control group. No statistically significant difference was observed in the 2 groups at the beginning and end of the 8 weeks (10). In a study performed in London in 2005, 43 children were placed in the control group and 53 children in the ADHD group. About 40% of the children with ADHD had fatty acid deficiency symptoms after laboratory study, but only 9% in the control group had this problem (10). In addition, Richardson and Puri have written in their reports about the reduction of symptoms and behavioral problems following treatment with supplements containing fatty acids (11). Previously, the effects of similar compounds, such as fish oil, have been investigated; however, it was only found to strengthen the short-term memory without any change in patients' ADHD symptoms (10). Furthermore, in another study in the US, the symptoms improved in Ritalin® users and showed clear changes compared with a placebo group (12).

Conclusion

The findings of the present study showed

the effective role of omega-3 in treating patients with ADHD. Thus, more attention should be given to screening, prevention, and treatment with omega-3 medicine and its effective role in the development of the brain and mental health, and increasing children's attention span and thinking ability. It is hoped that supplements with similar or better performance will be used as a substitute for drugs with more side effects.

Limitations

Difference in reliability of the questionnaires completed by parents and teachers was the main limitation. Moreover, our study duration was longer than expected due to the dropout rate.

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Authors' contributions

ND designed the study according to recent literatures and standard epidemiologic studies. HH collected data and also managed data sampling. AR supervised data sampling and participated in diagnosing and referring the patients as included samples. HRS reevaluated the clinical data, performed the statistical analyses, and revised the manuscript. MJ revised the manuscript and translate it, and obtained approval from the Ethics Committee and clinical registry for this study. All authors read and approved the final manuscript.

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