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The Efficacy of Magnesium Supplementation in Children With Attention Deficit Hyperactivity Disorder under Treatment With Methylphenidate: A Randomized Controlled Trial

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Abstract

Objectives: The prevalence of attention deficit hyperactivity disorder (ADHD) in children has been rising more rapidly in recent years. Studies have shown that attention to the nutritional deficiencies in these children can be effective in controlling symptoms. Therefore, we decided to examine the magnesium supplementation in children with ADHD under treatment with methylphenidate.

Materials and Methods: The study was conducted on 40 children with ADHD. The children were randomly assigned to 2 groups. The intervention group (n = 20) received magnesium tablets (10 mg/d) with methylphenidate (0.5 to 1 mg/kg/d) for eight weeks and the control group (n = 20) received placebo with methylphenidate (0.5 to 1 mg/d). Both groups were assessed before and after the intervention using the Conner's parent rating scale.

Results: At baseline, the mean total score was 74.4 ± 10.4 in the intervention group and 76.8 ± 6.6 in the control group ($P=0.79$). At the end of the study, the total score of Conner's Parent Rating Scale was 61.9 ± 11.1 in the intervention group and 68.8 ± 7.3 in the control group ($P=0.02$). There was also a significant difference between the groups in the scores of the inattention subscale at the end of the study ($P=0.001$).

Conclusions: The findings of the present study suggest that magnesium supplementation with methylphenidate can be effective in reducing ADHD symptoms.

Keywords: Attention deficit hyperactivity disorder, Magnesium, Methylphenidate

Introduction

Attention deficit hyperactivity disorder (ADHD) is the most common psychiatric disorder among school-age children. It can affect the quality of life of the children and impose a long-term economic burden on the family and community (1,2). The disorder is multifactorial and the exact etiology is unknown. However, genetic and environmental factors such as nutrition appear to play a key role in this disorder (3,4).

Magnesium as a mineral and intracellular cation is involved in more than 325 metabolic reactions including energy production pathway (5). Magnesium is also involved in the synthesis of neurotransmitters such as dopamine and impairment of the dopaminergic system has been widely discussed in the ADHD (6,7). Studies have shown that magnesium deficiency and hypomagnesaemia is a common deficiency in children with ADHD and supplementation with magnesium or at least including sufficient magnesium in their diet can have beneficial effects on the symptoms of the ADHD (8-10). A comprehensive study conducted by Huss et al showed that magnesium supplementation with zinc and polyunsaturated fatty acids (PUFAs) can be effective in reducing symptoms (11). Another report on 75 ADHD children who had magnesium deficiency showed that the recovery from hyperactivity was seen in the children who received standard treatment plus magnesium (12). Previous studies showed that the effect of magnesium supplementation alone as an adjunct to methylphenidate was very limited and there was no article that had the same dose and duration of supplementation as our study.

Therefore, the present study was performed to determine the effect of magnesium supplementation in children with ADHD under treatment with methylphenidate.

Materials and Methods

Study Design and Subjects

The present study was a double-blind randomized clinical trial performed on 40 children with ADHD who referred to a child and adolescent psychiatric center for the first

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Key Messages

- Identification of complementary therapies in ADHD children such as supplementation with magnesium may help more decrease the symptoms.
- After 8 weeks of magnesium supplementation, the total and non-attentions scores decreased significantly in the intervention group compared to the control group.
- A daily dose of 10 mg magnesium in the 8 weeks seems to be effective and safe.

time. The convenience sampling method was used.

The inclusion criteria include: being 7-12 years old, being diagnosed with ADHD by a child psychiatrist (subspecialized in children and adolescent psychiatry), not having contraindications for magnesium supplementation such as kidney failure, having an intelligence quotient (IQ) of >70, having no mental disorders based on the K-SADS form, being treated with methylphenidate tablets at a therapeutic dose of 0.5-1 mg/kg/d, parents' consent, oral satisfaction of children, and having no special diet.

The exclusion criteria were as follows: a history of other psychiatric disorders based on the K-SADS form, change in treatment process, discontinuation of medication for any reason such as drug side effects, and magnesium use in the last two months. The studied samples were divided into two groups of 20 people.

Treatment of the intervention group was started with methylphenidate (0.5-1 mg/kg/d) and magnesium (10 mg). The control group was treated with methylphenidate (0.5-1 mg/kg/d) along with placebo. There was no significant difference between the two groups in terms of methylphenidate dose. The present study was performed for 8 weeks. Symptom severity was measured using Conner's Parent Rating Scale before and after the intervention.

Assessment of ADHD Symptoms

The present study was conducted using Conner's parent rating scale only due to the restriction of access to teachers and also payment for presenting the questionnaire to teachers.

This scale has 4 sub-scales and if completed by parents, it can diagnose 74% of students with ADHD. Additionally, this scale has a validity of 0.75 and was approved by psychiatrists (13).

Khushabi et al evaluated the correlation of each question with the whole questionnaire as well as the validity of the test (α = 0.93) using Pearson's correlation and Cronbach's alpha. They showed that the instrument accurately measured ADHD subscales (14).

Adverse Effects and Dietary Intake Assessment

Adverse effects of supplementation or methylphenidate therapy were screened using self-designed questions after the intervention. Moreover, a 24-hour dietary recall was completed for measuring magnesium dietary intake before and after the intervention.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) version 16.0 was used for the analysis. Independent *t* test or Mann–Whitney U test (depending on the presence or absence of normal data distribution) were used to compare the two study groups and Wilcoxon test was used for intra-group comparisons before and after the intervention.

Results

Participants

The mean age of the children in the intervention group was 9.0 ± 1.6 and it was 9.3 ± 1.4 in the control group with no significant difference between the two groups (P=0. 85). Moreover, there were no significant differences in the distribution of gender and age (Table 1).

Comparison of Conner's Parents Rating Scores in Two Groups

Table 2 compares the mean ± SD values of the total and subscales scores of Conner's questionnaire at the baseline and end of the study. At baseline, there was no significant difference between the two groups in terms of total and subscales scores of the Conner's questionnaire but at the end of the study there was a significant difference between the two groups in all subscales in intra-group comparison (P = 0.001).

In addition, there was also a significant difference between the two groups after the intervention in the comparison of the groups in terms of total and inattention subscale scores (P = 0.02 and P = 0.001, respectively).

Measurement of Side Effects

According to Table 3, no serious side effects were observed in either of the two study groups. There was no significant difference between the two using the chi-square test (P = 0.870).

Table 1. Socio-demographic Characteristics of Intervention and Control Groups

	Intervention Group (n = 20)	Control Group (n = 20)	*P* Value
Gender[a]			
Male	65.00 (13)	35.00 (7)	0.93
Female	70.00 (14)	30.00 (6)	
Age (year)[b]	9.00 ± 1.60	9.30 ± 1.40	0.85
Height (cm)[b]	128.70 ± 16.26	130.81 ± 17.10	0.89
Weight (kg)[b]	29.97 ± 5.60	31.10 ± 6.24	0.87
Age of father[b]	39.96 ± 8. 60	40.45 ± 9.19	0. 95
Age of mother[b]	34.81 ± 8.10	35.30 ± 7.9	0.83

[a] Expressed as percent (number); [b] Expressed as mean ± SD.
P≤0.05 was considered statistically significant.

Table 2. The Comparison of the Conner›s Parent Rating Scale Scores in the Two Groups

Variable	Intervention Group	Control Group	*P* Value *
Total score			
Before	74.40±10.40	76.80±6.60	0.79
After	61.90±11.10	68.80±7.30	0.02
P value	0.001	0.001	
Hyperactivity			
Before	69.90±7.30	70.30±5.80	0.72
After	55.90±8.70	57.20±6.70	0.66
P value	0.001	0.001	
Inattention			
Before	74.90±8.40	77.50±7.60	0.54
After	59.80±6.20	68.70±80	0.001
P value	0.001	0.001	
Oppositional behavior			
Before	62.00±11.50	63.70±9.80	0.76
After	53.10±10.60	55.80±9.00	0.17
P value	0.001	0.001	

Table 3. Frequency of Adverse Effects in each Group

Type of Complication	Intervention group	Control group
Nausea and vomiting	3 (15%)	2 (10%)
Dizziness	0 (0%)	0 (0%)
Headache	1 (5%)	2 (10%)
Decreased appetite	1 (5%)	1 (5%)
Palpitations	0 (0%)	0 (0%)
Hypertension	0 (0%)	0 (0%)
Depression	0 (0%)	0 (0%)
Tic	0 (0%)	0 (0%)
Sleep disorder	1 (5%)	2 (10%)
Abdominal pain and cramps	0 (0%)	1 (5%)
Rash	0 (0%)	0 (0%)

Dietary Intake Measurement

Data obtained from 24-hour dietary recall questionnaire was analyzed by Nutritionist IV software in two groups, indicating that there was no statistically significant difference between the two groups (data not shown).

Discussion

In this study, after 8 weeks of supplementation, both groups had a significant improvement in comparison to the baseline, but in the intergroup comparison, there was a significant improvement in the total and inattention subscale scores of the Conner's questionnaire in the intervention group.

In a study by Mousain-Bosc et al, 22 pervasive developmental disorder or autism children as intervention group and 36 healthy children as control group were studied for six months. The children in the intervention group received vitamin B6 (0.6 mg/kg/d) and magnesium (6 mg/kg/d). The intervention group had lower magnesium levels than the control group. Magnesium regimen improved symptoms in 22 patients and had no side effects. After discontinuation of treatment, symptoms appeared within a few weeks (15). In addition, Kozielec and Starobrat-Hermelin conducted a study to evaluate magnesium levels in children with ADHD. Magnesium deficiency was found in 95% of those examined, most frequently in hair (77.6%), red blood cells (58.6%), and blood serum (33.6%) (16). In a study conducted by Elbaz et al, magnesium deficiency was found in 65% of the ADHD children and this deficiency was found to be correlated with hyperactivity, inattention, and impulsivity (6).

In another study, Huss et al studied the effects of zinc, PUFA, and magnesium supplementation in ADHD children. In this study, 810 children with ADHD, aged 5 to 12 years, were enrolled in the study. PUFA was administered in combination with zinc and magnesium for 12 months. Magnesium was given to these patients at a dose of 1 mg daily. After 6 months, the combination of omega-3, omega-6, zinc, and magnesium reduced symptoms in these patients (11). In the present study, magnesium supplementation along with methylphenidate leads to significant improvement in the total and inattention subscale scores of the Conner's questionnaire.

Limitations of Study

There were some limitations in our study. Due to budget constraints, we could not evaluate serum magnesium levels in children. In the present study, only Connor's Parent Rating Scale was used. This questionnaire has a standard structure to complete the diagnostic evaluation, but simultaneous completion of questionnaires by teachers and parents can give a different view of the child.

Conclusions

Based on the results of the present study as well as studies in this area, the use of magnesium as a supplement to mainstream treatments is an effective and safe method to relieve the symptoms of children with ADHD. Some of the differences observed in studies are due to differences in the samples, methodologies, and variables used. In conclusion, magnesium is tolerated well in children with ADHD and it can affect the recovery of a number of symptoms of the disorder.

Authors' Contribution

SGN and PK: concept and design the study. SGN and SHA: diagnosis and introduction of patients. SS: data collection and interpretation of the data. NY, SGN, and PK: wrote the manuscript with input from all authors. All authors discussed the results and contributed to the final manuscript.

Conflict of Interests

None to be declared.

Ethical Issues

This study was approved by Tabriz University of Medical Sciences,

IRAN. (Ethics No. TBZMED.REC 139) and registered at the Iranian Registry of Clinical Trials (identifier: IRCT2016062518927N4).

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References

1. Nydén A, Myrén KJ, Gillberg C. Long-term psychosocial and health economy consequences of ADHD, autism, and reading-writing disorder: a prospective service evaluation project. J Atten Disord. 2008;12(2):141-148. doi:10.1177/1087054707306116
2. National Collaborating Centre for Mental Health. National Institute for Health and Clinical Excellence: Guidance. Attention Deficit Hyperactivity Disorder: Diagnosis and Management of ADHD in Children, Young People and Adults. Leicester, UK: British Psychological Society; 2008.
3. Sharma A, Couture J. A review of the pathophysiology, etiology, and treatment of attention-deficit hyperactivity disorder (ADHD). Ann Pharmacother. 2014;48(2):209-225. doi:10.1177/1060028013510699
4. Curtis LT, Patel K. Nutritional and environmental approaches to preventing and treating autism and attention deficit hyperactivity disorder (ADHD): a review. J Altern Complement Med. 2008;14(1):79-85. doi:10.1089/acm.2007.0610
5. Vormann J. Magnesium: nutrition and metabolism. Mol Aspects Med. 2003;24(1-3):27-37. doi:10.1016/s0098-2997(02)00089-4
6. Elbaz F, Zahra S, Hanafy H. Magnesium, zinc and copper estimation in children with attention deficit hyperactivity disorder (ADHD). Egypt J Med Hum Genet. 2017;18(2):153-163. doi:10.1016/j.ejmhg.2016.04.009
7. Gröber U, Schmidt J, Kisters K. Magnesium in prevention and therapy. Nutrients. 2015;7(9):8199-8226. doi:10.3390/nu7095388
8. Villagomez A, Ramtekkar U. Iron, magnesium, vitamin D, and zinc deficiencies in children presenting with symptoms of attention-deficit/hyperactivity disorder. Children (Basel). 2014;1(3):261-279. doi:10.3390/children1030261
9. Hariri M, Azadbakht L. Magnesium, iron, and zinc supplementation for the treatment of attention deficit hyperactivity disorder: a systematic review on the recent literature. Int J Prev Med. 2015;6:83. doi:10.4103/2008-7802.164313
10. Mahmoud MM, El-Mazary AA, Maher RM, Saber MM. Zinc, ferritin, magnesium and copper in a group of Egyptian children with attention deficit hyperactivity disorder. Ital J Pediatr. 2011;37:60. doi:10.1186/1824-7288-37-60
11. Huss M, Völp A, Stauss-Grabo M. Supplementation of polyunsaturated fatty acids, magnesium and zinc in children seeking medical advice for attention-deficit/hyperactivity problems - an observational cohort study. Lipids Health Dis. 2010;9:105. doi:10.1186/1476-511x-9-105
12. Starobrat-Hermelin B. [The effect of deficiency of selected bioelements on hyperactivity in children with certain specified mental disorders]. Ann Acad Med Stetin. 1998;44:297-314.
13. Conners CK, Sitarenios G, Parker JD, Epstein JN. The revised Conners' Parent Rating Scale (CPRS-R): factor structure, reliability, and criterion validity. J Abnorm Child Psychol. 1998;26(4):257-268. doi:10.1023/a:1022602400621
14. Khushabi K, Pour-Etemad H, Mohammadi M, Mohammadkhani P. Study of Prevalence of ADHD and Comorbid Disorders in Primary School Students of Tehran. Medical Journal of the Islamic Republic of Iran; 2006;20(3):147-150.
15. Mousain-Bosc M, Roche M, Rapin J, Bali JP. Magnesium VitB6 intake reduces central nervous system hyperexcitability in children. J Am Coll Nutr. 2004;23(5):545S-548S. doi:10.1080/07315724.2004.10719400
16. Kozielec T, Starobrat-Hermelin B. Assessment of magnesium levels in children with attention deficit hyperactivity disorder (ADHD). Magnes Res. 1997;10(2):143-148.