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# Comparison of Horse and Cow Milk on the Symptoms of Attention Deficit Hyperactivity Disorder in Children: A Cross-Over Clinical Trial Study

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## Abstract

Numerous researchers have examined the effect of diet on Attention Deficit Hyperactivity Disorder (ADHD). The purpose of this study is to compare the symptoms of ADHD in children fed horse milk versus conventionally fed cow's milk. Thirty patients aged 6 to 14 with ADHD were randomly selected and divided into two groups in this randomized double-blind cross-over study. All patients completed a 45-day period of consuming 250 mL horse or cow milk, as well as continued Ritalin (1 mg/kg) treatment. The wash out period was considered one week. Symptoms are recorded using the Conners rating scale (CS). The CS of the parents decreased significantly (P value≤0.001) in the group that first received horse milk, but increased (P value=0.007) after consuming cow's milk. After consumption of horse milk, the parent's CS was significantly different from that of cow milk (P value= 0.001). Teachers' CS decreased significantly following horse milk consumption (P=0.001) and increased significantly following cow milk consumption (P=0.028) in this group. The average teacher's CS after cow milk differed significantly from that after horse milk (P value= 0.024). The CS of the parents did not change significantly (P value=0.913) in the group that first consumed cow's milk. However, it was significantly decreased (P value=0.004) after receiving horse milk. The CS of the teachers in this group did not change after the cow's milk (P value=0.282). However, following the administration of horse milk, the mean of CS decreased significantly (P=0.003). The average of the teacher's CS after consuming cow milk differed significantly from that of horse milk (P value= 0.010). In both groups, there was no significant difference in the mean of parents and teachers CS before and after the washout period (P>0.05). According to the study, horse milk consumption was significantly more effective than cow milk at lowering scores.

**Keywords:** Attention deficit disorder with hyperactivity; Diet; Milk; Complementary therapies; Integrative medicine; Traditional persian medicine

## Introduction

Attention deficit hyperactivity disorder (ADHD) is one of children's most frequent neurodegenerative disorders [1]. It is characterized by difficulties paying attention, excessive activity, and a lack of self-control [2]. Age, sex and ethnicity affect the prevalence of this disorder [3,4]. ADHD is more prevalent in males and affects between 5-10% of children in elementary school [5]. In Iran, this disorder affects 9.7% of the population [6]. This disorder usually starts at

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2-4 years of age and continues frequently until adulthood [1,7,8]. ADHD is a multi-factorial disorder that is influenced by both genetic and environmental factors [9]. A number of studies have shown that genes associated with serotonin, dopamine, and norepinephrine receptors and transporters are involved in the disease [9,11-13], despite the fact that the precise biological nervous mechanism of the disease is still not well understood [10]. Environmental factors that may contribute to ADHD include thyroid diseases, hypoxia, and fever, as well as exposure to chemicals, heavy metals, and organic pollutants. Additionally, nutritional factors affecting the infant following birth have been linked to ADHD [14-17]. Aside from that, diet has been implicated as a contributing factor to ADHD [6,18-20]. Currently, treatment options for ADHD include behavioral therapy, psychotherapy, and medication treatment. Typically, drug treatment entails long-term use of stimulants such as methylphenidate, dexamphetamine, and their derivatives, which increase dopamine and norepinephrine activity [21,22]. Around 30% of patients treated with stimulants do not improve clinically or do not tolerate the drug [23]. On the other hand, there are some adverse effects associated with drug use, including appetite and weight loss, growth disorders, abdominal pain, headaches, sleeping problems, and even elevated blood pressure [24,25]. The long-term results of treating and not treating ADHD children in adulthood are disappointing [26,27]. Some families are hesitant to use stimulant drugs, or to discontinue them abruptly, or to experiment with complementary and alternative medicine (CAM) [28,29], herbal therapies [30,31], and dietary supplements [32-34]. Studies have shown that using a proper diet may reduce ADHD symptoms and that it can be used in conjunction with drug treatment as a support [35,36]. Humans have long consumed horse milk. In the clinic, we observed that symptoms of hyperactivity, asthma, and acne improved in children who used horse milk for various reasons. Therefore, to further investigate and reduce the possibility of bias, we decided to measure the validity of this hypothesis through a clinical trial in ADHD patients.

The amount of fat, cholesterol, and casein (milk protein) in horse milk is lower than in cow's milk. The distribution of triglycerides and diglycerides in horse and human milk is similar, and the proportion of PUFA in horse milk is higher than that of human and cow milk. According to its structural characteristics, it is possible that horse milk is more suitable for humans and feeding human babies than cow milk [37]. Also, horse milk has more amounts of alpha-linoleic acid and linoleic acid, which are the precursors for the production of omega 3 and 6 [38]. In general, horse milk is rich in essential fatty acids, especially linoleic acid, which is beneficial for human health because the body is unable to produce it [38]. Mare milk is a suitable alternative for children properties with beneficial effects on the intestinal microbiome; these are just a few of the benefits of the milk chosen for this trial [41]. The purpose of this study is to compare the efficacy of horse and conventionally fed cow milk in treating ADHD symptoms.

## Materials and Methods

This study is a double-blind randomized clinical trial on ADHD patients. The RCT has been registered with the Iranian Registry of Clinical Trials (IRCT) and has been assigned the registration number IRCT20170823035862N1 (https://www.irct.ir/search/result?query=IRCT20170823035862N1). The protocol has been approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences (Ethics Committee Approval Code: IR.SSU.REC.1396.52). Parents signed the informed consent, and patients over the age of ten also signed the informed consent.

With a significance level of 0.05 and a test power of 80%, and based on previous studies, the standard deviation value is considered to be S=5 to achieve a clinically significant difference in Conners mean score (CS) (at least 2.5) in the two types of interventions, a sample of 32 people was used.

$$n = \frac{\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2 \times s^2}{(\overline{x}_1 - \overline{x}_2)^2}$$

The study included patients aged 6-14 years who were referred to Shahid Sadoughi Hospital. The initial diagnosis of ADHD was made using the Conners criterion and a face-to-face interview with the patient and his or her parents by a pediatric psychiatrist. Exclusion criteria included autism spectrum disorder, mental retardation, schizophrenia, psychosis, mood or personality disorders, predominantly inattentive ADHD, and premature or dysmature birth.

Patients were randomly assigned to one of two groups using a random number table.

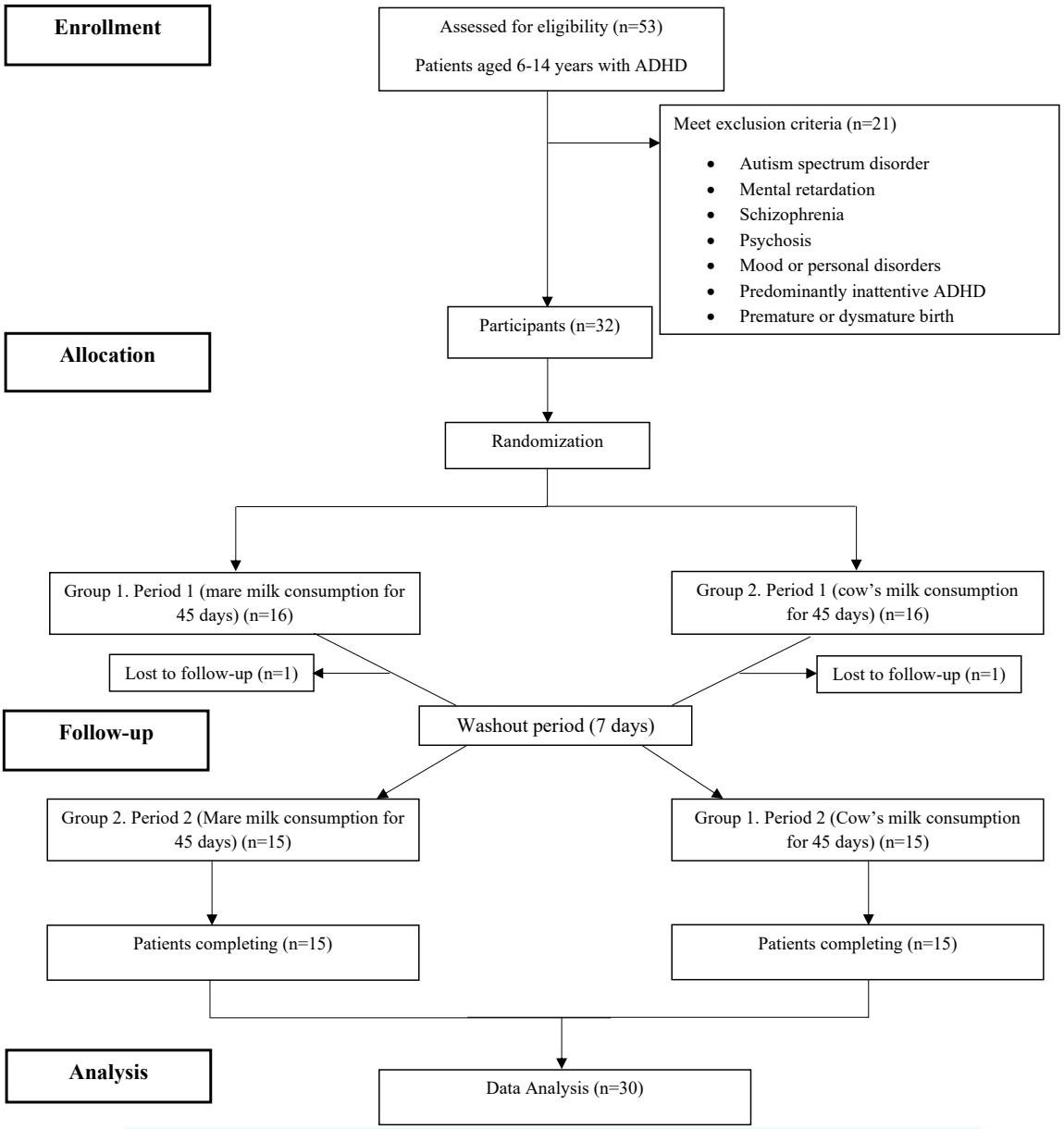
Both types of milk have the same smell, color, and taste.

Milk bottles were coded, and patients, patients' families, and the investigator had no idea what was in each bottle before collecting questionnaires.

Due to irregular milk consumption, two patients were removed from the study during the first week. All patients completed a 45-day period of consuming horse milk and a 45-day period of consuming cow's milk, as well as continued drug treatment (Ritalin 1 mg/kg). Each group consumed 250 mL of pasteurized milk (63 °C/30 minutes) per day. One week passes between two doses of milk, which is referred to as the washout pe-

riod. Since the study was cross-over and each person is compared with himself, we did not limit the time of consumption and the way of consumption. We only emphasized that each person should use both kinds of milk at the same time and if using sweetener, use the same sweetener in both periods.

The improvement in symptoms, the dosage of the essential drug for symptom control, and any complications were all documented. If there were symptoms of cow or horse milk allergy, the study excluded the patient and information was recorded about the condition. After data collection, it was analyzed using STAT-I-14 software and cross-over data analysis. Finally, using the data model cross over, the effects of the two treatments were identified, and the carry-over effect was calculated.




CONSORT Diagram. Legend: The diagram indicates how many individuals were screened and c ompleted the intervention

## Results

Thirty ADHD patients were randomly assigned to one of two groups. Twenty-two (73.3%) of the patients were male, while eight (26.7%) were female. The patients' average age was 8.9 years. All patients completed a 45-day course of horse milk and a 45-day course of cow milk, as well as continued drug therapy.

### *Parents' CS*

In the t-test, the average CS of parents in the group that used horse milk first and then cow's milk was 80.13 ± 18.56, ranging from 44 to 104, which decreased to 59.80 ±11.12, ranging from 40 to 79 (P value≤0.001), and the effect size was 20.33 [95% CI 11.71;28.94]. Following the washout period, the average CS increased to 68.07 ±17.77 (ranged from 40 to 95), while cow's milk consumption increased the mean to 74.87± 15.84 (ranged from 47 to 98) (P value= 0.007), and the effect size was -6.80 [95% CI -11.46; -2.13]. The average CS of parents was lower at the end of the study than at the start, but the mean of CS was significantly different at the end of the two milk consumption periods (P value= 0.001), and the effect size was -15.06 [95% CI -22.75; -7.37]. (Table 1).

Before and after cow's milk, parents' CS in the group that used cow's milk first, the average CS of the parent was 79.00± 14.17 (ranged from 57 to 104) and 79.33± 15.13 (ranged from 50 to 100), respectively (P value = 0.913). Following the washout period, the average CS was 77.60± 14.51 (ranged from 52 to 97) after horse milk consumption reached 64.07± 13.55 (ranged from 34 to 83), which was lower than the study's start time and also the end of the first milk consumption period; effect size was 13.53 [95% CI 4.97; 22.09] (Table 1). However, following horse milk consumption, the mean of CS was significantly lower (P = 0.004). Additionally, the mean of CS was significantly different at the end of the two milk consumption periods (P = 0.003), with an effect size of 15.26 [95% CI 6.13; 24.40]. In both groups, there was no significant difference in the mean of parents' CS before and after the washout period (first horse P value=0.059, first cow P value=0.092).

The treatment effect, period effect, and carryover effect in the ANOVA test for CS of parents were 0.0003, 0.4085, and 0.2332, respectively. These findings indicated that the treatment had a significant effect, however, there was no discernible difference in the analysis results based on the order of milk used first.

### *Teachers' CS*

In the T-test, the average of teachers' CS in the group that first used horse milk and then cow milk was 49.40 ± 20.78 (ranged from 20 to 99), which decreased significantly to 40.53 ±19.89 (ranged from 14 to 95), with an effect size of 8.86 [95% CI: 4.38; 13.35] (P value= 0.001). After the washout period, the average CS increased to 41.40±19.84 (ranged from 14 to 93), while after cow's milk consumption, the mean CS increased to 46.07 ±19.45 (ranged from 5 to 81) (P value= 0.028), and the effect size was -4.66 [95% CI -8.76; -0.57]. However, at the end of the study, the average CS of teachers was lower than at the beginning of the study, but the average CS of teachers differs significantly between the two milk (P value=0.024), and the effect size was -5.53 [95 % CI -10.22; -0.84] ( Table 2).

**Table 1.** Connor's' rating scales of parents

| Variables | MCS | | | | P value | | | | Treatment effect | Period effect | Carry-over effect | Effect size [ 95% CI] AFM | Effect size [ 95% CI] ASM | Effect size [ 95% CI] Comparison Between two milk |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | I | AFM | BSM | ASM | Pv.1 | Pv.2 | Pv.3 | Pv.4 | | | | | | |
| Mare then cow's milk | 80.13 ±18.56 | 59.80 ±11.12 | 68.07 ±17.77 | 74.87 ±15.84 | ≤0.001 | 0.059 | 0.007 | 0.001 | | | | 20.33 [11.71; 28.94] | -6.80 [-11.46; -2.13] | -15.06 [-22.75; -7.37] |
| Cow, then mare milk | 79.00 ±14.17 | 79.33 ±15.13 | 77.60 ±14.51 | 64.07 ±13.55 | 0.913 | 0.092 | 0.004 | 0.003 | 0.000 | 0.408 | 0.233 | -0.33 [-6.72 ; 6.05] | 13.53 [4.97 ;22.09] | 15.26 [6.13; 24.40] |

Mean of Connor's' rating scale( MCS), initial of study (I) ,After first milk(AFM), Before the second consumption of milk( BSM), After second Milk(ASM). Before and after the First milk consumption (pv.1), before and after washout period (pv.2), before and after the second consumption of milk (pv.3), after the first and second consumption of milk (pv.4)

**Table 2.** Connor's' rating scales of teachers

| Variables | MCS | | | | P value | | | | Treatment effect | Period effect | Carry-over effect | Effect size [ 95% CI] AFM | Effect size [ 95% CI] ASM | Effect size [ 95% CI] Comparison Between two milk |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | I | AFM | BSM | ASM | Pv.1 | Pv.2 | Pv.3 | Pv.4 | | | | | | |
| Mare then cow's milk | 49.40 ±20.78 | 40.53 ±19.89 | 41.40 ±19.84 | 46.07 ±19.45 | 0.001 | 0.091 | 0.028 | 0.024 | 0.027 | 0.318 | 0.098 | 8.86 [4.38; 13.35] | -4.66 [-8.76;-0.57] | -5.53 [ -10.22; -0.84] |
| Cow, then mare milk | 53.07 ±15.00 | 54.60 ±13.14 | 54.53 ±13.42 | 46.80 ±14.70 | 0.282 | 0.936 | 0.003 | 0.010 | | | | -1.53 [ -4.47; 1.40] | 7.73 [3.02 ; 12.43] | 7.80 [2.14 ; 13.45] |

Mean of Connor's' rating scale (MCS), initial of study (I), after first milk (AFM), before the second consumption of milk (BSM), after second milk consumption (ASM). Before and after the First milk consumption (pv.1), before and after washout period (pv.2), before and after the second consumption of milk (pv.3), after the first and second consumption of milk (pv.4).

The average CS of teachers in the group who used cow's milk first was 53.07±15.00 (ranged from 28 to 76) and then changed to 54.60±13.14 (ranged from 30 to 76) (P value= 0.282). Following the washout period, the average CS was 54.53±13.42 (ranged from 28 to 75), and after horse milk consumption decreased to 46.80 ±14.70 (ranged from 23 to 82) (P value= 0.003) with an effect size of 7.73 [95% CI 3.02; 12.43]. (Table 2). Furthermore, at the end of the two milk consumption periods, the mean of CS was significantly different (P value = 0.010), and the effect size was 7.80 [95% CI 2.14; 13.45]. There was no significant difference in the mean of CS teachers before and after the washout period in either group (horse milk first P value= 0.091 and cow's milk first P value= 0.936). (Table 2). The treatment effect, period effect, and carryover effect in the ANOVA test for CS of teachers were 0.0278, 0.3185, and 0.0984, respectively. These findings indicated that horse milk had a significant effect on ADHD symptom improvement, but there was no meaningful difference in the results of the analysis based on which milk was started first. There were no side effects during this trial.

## Discussion

The growing use of CAM to treat ADHD places a premium on diet, nutrients, and gut health. The purpose of this study was to determine the effect of horse and cow milk (non-grass fed) on children's symptoms of ADHD. Our findings show that 250 mL of horse milk consumption reduced the average parent CS by 20 scores and a standard deviation of 15. In the end, the order in which the milk was used had no effect on the scores. Horse milk had a beneficial effect on reducing ADHD symptoms and improving sleep quality in our study, as reported in another article.

In comparison to conventionally raised cows with a low Omega 3 to 6 ratio in their lipid profile, mare milk is a good source of polyunsaturated fatty acids that may help alleviate ADHD symptoms [36, 42]. Nutritional deficiencies, particularly in fatty acids, can affect neurons and result in defects in neuroplasticity, which has been linked to ADHD [43]. The study discovered that some patients had low levels of this essential lipid and that supplementation with unsaturated fatty acids had a beneficial effect on ADHD, with individual responses varying. Six of our cases demonstrated an improvement of more than 25 CS, confirming the observation above. The presence of tryptophan and tyrosine in mare milk enhances the synthesis of melatonin and serotonin, both of which play critical roles in brain function improvement [44]. Although we did not examine the gastrointestinal microbiome of our participants following milk consumption, mare milk has the potential to alter the gastrointestinal flora due to its high biological content (lactose, lysosome, and lactoferrin). The gut-brain axis is a relatively new area of research that may help us explain the observation [45-47]. Allergies may be one of the reasons for the increase in CS caused by cow's milk consumption following mare milk consumption. Milk is one of the most frequently allergenic foods in children. Mare milk is an excellent substitute for children allergic to cow milk, and a trial of cow's milk protein elimination is a prudent decision in children with allergies and ADHD. There was no history of allergy to cow's milk in our case; additionally, we did not eliminate any other source of cow's protein during the trial. This does not rule out the possibility of intolerance to other components of milk, such as the bovine casein A1 protein, exacerbating the symptoms. According to some studies, some children with ADHD have a specific type of protein intolerance [48,49]. Several studies on mental diseases have shown that neuronal damage due

to oxidants plays an important role in these diseases. So that the relationship between ADHD and oxidative stress has been investigated in several studies [50,51]. Horse milk contains a higher concentration of vitamin C than cow milk, which may have a beneficial effect on ADHD symptoms due to its antioxidant properties [50-52].

According to Persian medicine, symptoms similar to ADHD are seen in people who have a dry and warm brain state, and thus the treatment should include some food to replenish the brain's moisture. Horse milk (affectionately referred to as "Leban Al-Ramak" or "Leban al-Khayil") is typically marketed as a cold, moist beverage [53]; as such, it alleviates symptoms of dryness and discomfort in similar situations. Horse milk has been described in these books as appetizing, mood-enhancing, easily digestible, and curative of diseases caused by heat and drought [54]. On the other hand, one of the suitable ingredients for treating dryness is whey protein (roughly equivalent to Ma'al-jobon), the amount of this protein is higher in horse milk than cow's milk [55-57].

Horse milk may be used to alleviate the symptoms of patients with ADHD due to these properties. This effect is more pronounced in mare milk than in other types of milk. Although the time period for prescribing horse milk and monitoring patients was limited in our study, ADHD is a chronic disease, and long-term follow-up is necessary to determine the effects and possible side effects of horse milk. Additionally, the changes in CS were not re-examined following the cessation of horse milk to determine how long the desired effects of horse milk may persist following milk cessation. Due to the high cost of horse milk in some countries, some families may not be economically feasible to use it in the community.

## Conclusion

Mare milk was effective at alleviating ADHD symptoms in our study, which may be attributed to its high essential protein content, which is comparable to human milk, or to its high poly unsaturated fatty acid lipid content. Additionally, due to mare milk's moistening effect, Persian medicine recommended it for the treatment of diseases with similar symptoms. This is the first study to demonstrate that this result can be extrapolated through mare milk consumption. Additional trials are needed to confirm this result.

The time period for prescribing horse milk and monitoring patients was limited in our study, ADHD is a chronic disease, and long-term follow-up is necessary to determine the effects and possible side effects of horse milk. Additionally, the changes in CS were not re-examined following the cessation of horse milk to determine how long the desired effects of horse milk may persist following milk cessation. Due to the high cost of horse milk in some countries, some families may not be economically feasible to use it in the community.

## Data Availability

The data supporting the findings of this study are available upon request from the corresponding author.

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## Conflict of Interests

None of the authors have disclosed any potential conflicts of interest.

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## References

[1] Wilens TE, Biederman J, Spencer TJ. Attention deficit/hyperactivity disorder across the lifespan. Annu Rev Med 2002;53:113-131.

[2] Biederman J, Newcorn J, Sprich S. Comorbidity of attention deficit hyperactivity disorder. Am J Psychiatry 1991;148:564-577.

[3] Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. Am J Psychiatry 2007;164:942-948.

[4] Cuffe SP, Moore CG, McKeown RE. Prevalence and correlates of ADHD symptoms in the national health interview survey. J Atten Disord 2005;9:392-401.

[5] Faraone SV, Sergeant J, Gillberg C, Biederman J. The worldwide prevalence of ADHD: is it an American condition? World Psychiatry 2003;2:104-113.

[6] Azadbakht L, Esmaillzadeh A. Dietary patterns and attention deficit hyperactivity disorder among Iranian children. Nutrition 2012;28:242-249.

[7] Egger HL, Angold A. Common emotional and behavioral disorders in preschool children: presentation, nosology, and epidemiology. J Child Psychol Psychiatry 2006;47:313-337.

[8] Connor DF. Preschool attention deficit hyperactivity disorder: a review of prevalence, diagnosis, neurobiology, and stimulant treatment. J Dev Behav Pediatr 2002;23:S1-9.

[9] Biederman J. Attention-deficit/hyperactivity disorder: a selective overview. Biol Psychiatry 2005;57:1215-1220.

[10] Ghanizadeh A, Haddad B. The effect of dietary education on ADHD, a randomized controlled clinical trial. Ann Gen Psychiatry 2015;14:12.

[11] Li Z, Chang SH, Zhang LY, Gao L, Wang J. Molecular genetic studies of ADHD and its candidate genes: a review. Psychiatry Res 2014;219:10-24.

[12] Faraone SV, Khan SA. Candidate gene studies of attention-deficit/hyperactivity disorder. J Clin Psychiatry 2006;67:13-20.
[13] Zametkin AJ, Rapoport JL. Neurobiology of attention deficit disorder with hyperactivity: where have we come in 50 years? J Am Acad Child Adolesc Psychiatry 1987;26:676-686.
[14] Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 1999;341:549-555.
[15] Hauser P, Zametkin AJ, Martinez P, Vitiello B, Matochik JA, et al. Attention deficit-hyperactivity disorder in people with generalized resistance to thyroid hormone. N Engl J Med 1993;328:997-1001.
[16] Matochik JA, Zametkin AJ, Cohen RM, Hauser P, Weintraub BD. Abnormalities in sustained attention and anterior cingulate metabolism in subjects with resistance to thyroid hormone. Brain Res 1996;723:23-28.
[17] Weiss RE, Stein MA, Trommer B, Refetoff S. Attention-deficit hyperactivity disorder and thyroid function. J Pediatr 1993;123:539-545.
[18] Nigg JT, Holton K. Restriction and elimination diets in ADHD treatment. Child Adolesc Psychiatr Clin N Am 2014;23:937-953.
[19] Stevenson J. Dietary influences on cognitive development and behaviour in children. Proc Nutr Soc 2006;65:361-365.
[20] Konikowska K, Regulska-Ilow B, Rozanska D. The influence of components of diet on the symptoms of ADHD in children. Rocz Panstw Zakl Hig 2012;63:127-134.
[21] Findling RL. Evolution of the treatment of attention-deficit/hyperactivity disorder in children: a review. Clin Ther 2008;30:942-957.
[22] Biederman J. Attention-deficit/hyperactivity disorder: a selective overview. Biol Psychiatry 2005;57:1215-1220.
[23] Mohammadi M, Akhondzadeh S. Advances and considerations in attention-deficit/hyperactivity disorder pharmacotherapy. Acta Med Iran 2011;49:487-498.
[24] Findling RL. Evolution of the treatment of attention-deficit/hyperactivity disorder in children: a review. Clin Ther 2008;30:942-957.
[25] Mohammadi MR, Akhondzadeh S. Pharmacotherapy of attention-deficit/hyperactivity disorder: nonstimulant medication approaches. Expert Rev Neurother 2007;7:195-201.
[26] Molina BS, Hinshaw SP, Swanson JM, Arnold LE, Vitiello B, et al. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. J Am Acad Child Adolesc Psychiatry 2009;48:484-500.
[27] Klein RG, Mannuzza S, Olazagasti MAR, Roizen E, Hutchison JA, et al. Clinical and functional outcome of childhood attention-deficit/hyperactivity disorder 33 years later, Arch Gen Psychiatry 2012;69:1295-1303.
[28] Mohammadi MR, Kazemi MR, Zia E, Rezazadeh SA, Tabrizi M, et al. Amantadine versus methylphenidate in children and adolescents with attention deficit/hyperactivity disorder: a randomized, double-blind trial. Hum Psychopharmacol 2010;25:560-565.
[29] Mohammadi M, Kashani L, Akhondzadeh S, Izadian E, Ohadinia S. Efficacy of theophylline compared to methylphenidate for the treatment of attention-deficit hyperactivity disorder in children and adolescents: a pilot double-blind randomized trial. J Clin Pharm Ther 2004;29:139-144.
[30] Salehi B, Imani R, Mohammadi MR, Fallah J, Mohammadi M, et al. Ginkgo biloba for attention-deficit/hyperactivity disorder in children and adolescents: a double blind, randomized controlled trial. Prog Neuropsychopharmacol Biol Psychiatry 2010;34:76-80.
[31] Akhondzadeh S, Mohammadi M, Momeni F. Passiflora incarnata in the treatment of attention-deficit hyperactivity disorder in children and adolescents. Clin Pract 2005;2:609.
[32] Akhondzadeh S, Mohammadi MR, Khademi M. Zinc sulfate as an adjunct to methylphenidate for the treatment of attention deficit hyperactivity disorder in children: a double blind and randomized trial. BMC Psychiatry 2004;4:9.
[33] Abbasi SH, Heidari S, Mohammadi MR, Tabrizi M, Ghaleiha A, et al. Acetyl-L-carnitine as an adjunctive therapy in the treatment of attention-deficit/hyperactivity disorder in children and adolescents: a placebo-controlled trial. Child Psychiatry Hum Dev 2011;42:367-375.
[34] Konofal E, Lecendreux M, Deron J, Marchand M, Cortese S, et al. Effects of iron supplementation on attention deficit hyperactivity disorder in children. Pediatr Neurol 2008; 38:20-26.
[35] Konikowska K, Regulska-Ilow B, Rozanska D. The influence of components of diet on the symptoms of ADHD in children. Rocz Państw Zakł Hig 2012;63:2.
[36] Salimei E, Fantuz F. Equid milk for human consumption. Int Dairy J 2012;24:130-142.
[37] Malacarne M, Martuzzi F, Summer A, Mariani P. Protein and fat composition of mare's milk: some nutritional remarks with reference to human and cow's milk. Int Dairy J 2002;12:869-877.
[38] Nikkhah A. Equidae, camel, and yak milks as functional foods: a review. J Nutr Food Sci 2011;1:5.
[39] Iacono G, Carroccio A, Cavataio F, Montalto G, Soresi M, et al. Use of ass' milk in multiple food allergy. J Pediatr Gastroenterol Nutr 1992;14:177-181.
[40] Businco L, Giampietro PG, Lucenti P, Lucaroni F, Pini C, et al. Allergenicity of mare's milk in children with cow's milk allergy. J Allergy Clin Immunol 2000;105:1031-1034.
[41] Pieszka M, Łuszczyński J, Zamachowska M, Augustyn R, Długosz B, et al. Is mare milk an appropriate food for people?–a review. Ann Anim Sci 2016;16:33-51.
[42] Daley CA, Abbott A, Doyle PS, Nader GA, Larson S. A review of fatty acid profiles and antioxidant content in grass-fed and grain-fed beef. Nutrition J 2010;9:10.
[43] Bekaroğlu M, Aslan Y, Gedik Y, Değer O, Mocan H, et al. Relationships between serum free fatty acids and zinc, and attention deficit hyperactivity disorder: a research note. J Child Psychol Psychiatry 1996;37:225-227.
[44] Csapó-Kiss Z, Stefler J, Martin T, Makray S, Csapó J. Composition of mares' colostrum and milk. Protein content, amino acid composition and contents of macro and micro-elements. Int Dairy J 1995;5:403-415.
[45] Belanger SA, Vanasse M, Spahis S, Sylvestre MP, Lippé

S, et al. Omega-3 fatty acid treatment of children with attention-deficit hyperactivity disorder: A randomized, double-blind, placebo-controlled study. Paediatr Child Health 2009;14:89-98.

[46] Bloch MH, Qawasmi A. Omega-3 fatty acid supplementation for the treatment of children with attention-deficit/hyperactivity disorder symptomatology: systematic review and meta-analysis. J Am Acad Child Adolesc Psychiatry 2011;50:991-1000.

[47] Carabotti M, Scirocco A, Maselli MA, Severi C. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. Ann Gastroenterol 2015;28:203-209.

[48] Jianqin S, Leiming X, Lu X, Yelland GW, Ni J, et al. Erratum to: 'Effects of milk containing only A2 beta casein versus milk containing both A1 and A2 beta casein proteins on gastrointestinal physiology, symptoms of discomfort, and cognitive behavior of people with self-reported intolerance to traditional cows' milk'. Nutrition J 2016;15:45-45.

[49] Pelsser LM, Frankena K, Toorman J, Savelkoul HF, Dubois AE, et al. Effects of a restricted elimination diet on the behaviour of children with attention-deficit hyperactivity disorder (INCA study): a randomised controlled trial. The Lancet 2011;377:494-503.

[50] Karababa İF, Savas SN, Selek S, Cicek E, Cicek EI, et al. Homocysteine levels and oxidative stress parameters in patients with adult ADHD. J Atten Disord 2017;21:487-93.

[51] Lee JY, Hwang IW, Lim MH, Kwon HJ, Jin HJ. Association of glutathione S-transferases M1, T1 and P1 gene polymorphisms with attention deficit and hyperactivity disorder in Korean children. Gene 2016;25:228-33.

[52] Joshi K, Lad S, Kale M, Patwardhan B, Mahadik SP, et al. Supplementation with flax oil and vitamin C improves the outcome of Attention Deficit Hyperactivity Disorder (ADHD). Prostaglandins Leukot Essent Fatty Acids 2006;74:17-21.

[53] Aghili MH. Makhzan-al-Advia. Tehran University of Medical Sciences. Tehran 2009; p 695.

[54] Jorjani S. Zakhireh Kharazmshahi (persian). 2nd ed. Ehya'e tibbe tabiee. Qom; p 416.

[55] Aghili Khorasani MH. Gharabadin e kabir (persian). Noor e vahy. Qom 2011; p 308.

[56] Mostajeran Z, Mosavat H, Najafi M, Emtiazy M, Hashempur MH. Whey Protein (Ma'aljobon) as a Complementary Therapy for Treatment of Attention-deficit/ Hyperactivity Disorder (ADHD): A Randomized Open-label Controlled Clinical Trial. Galen M J 2020;9:e1690.

[57] Potočnik KH, Gantner V, Kuterovac K, Cividini A. Mare's milk: composition and protein fraction in comparison with different milk species. Mljekarstvo 2011;61:107-113.