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Effect of magnesium supplementation on depression status in depressed patients with magnesium deficiency: A randomized, double-blind, placebo-controlled trial

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ABSTRACT

Objectives: The aim of this study was to determine the effect of magnesium supplementation on the depression status of depressed patients suffering from magnesium deficiency.
Methods: Sixty depressed people suffering from hypomagnesemia participated in this trial. The individuals were randomly categorized into two groups of 30 members; one receiving two 250-mg tablets of magnesium oxide (MG) daily and the other receiving placebo (PG) for 8 wk. The Beck Depression Inventory-II was conducted and the concentration of serum magnesium was measured.
Results: At the end of intervention, 88.5% of the MG and 48.1% of the PG ($P = 0.002$) had a normal level of magnesium. The mean changes of serum magnesium were significantly different across the two groups. After the intervention, the mean Beck score significantly declined. However, in the MG, this reduction was more significant than in the PG ($P = 0.02$), so that the mean changes in this group experienced 15.65 ± 8.9 reduction, but in the PG, it declined by 10.40 ± 7.9.
Conclusions: Daily consumption of 500 mg magnesium oxide tablets for ≥8 wk by depressed patients suffering from magnesium deficiency leads to improvements in depression status and magnesium levels. Therefore, assessment of the magnesium serum and resolving this deficiency positively influence the treatment of depressed patients.

Introduction

Magnesium is the second intracellular cation and the fourth major element in the body [1]. Given the complex function that this element plays in our body, it is considered an important element for human health [2]. This element is an important co-enzyme for many enzymes involved in the transfer of phosphate and energy metabolism. Additionally, magnesium has major roles in stabilizing genes, DNA replication, synthesis of protein and nucleic acids, and metabolism of macronutrients [3].

Furthermore, by regulating and transferring some ions, including potassium and calcium, through pumps and channels, magnesium also is effective in neuro-transmission [4]. Accordingly, it is involved in the pathophysiology of some neurologic diseases including migraine, Alzheimer's and Parkinson's diseases, and attention-deficit/hyperactivity disorder [2,5]. In recent years, the role of this element in the incidence of depression, due to its effect on *N*-methyl-D-aspartate's (NMDA) nonselective ionotropic channels in the brain, has gained a great deal of attention [6]. These glutamate-dependent channels have important roles in neurotransmission and neuronal plasticity. Thus magnesium is involved in learning, memory, and mood of individuals [7]. NMDA channels are excited by glutamate neurotransmitter and cause entrance of sodium and calcium into the cell. Once sodium is introduced and the intracellular space is depolarized, entrance of calcium is accelerated. Calcium, then, by exciting enzymatic paths including kinase protein and synthesis of nitric oxide, plays an important role in the pathophysiology of depression [8,9]. However, magnesium is the natural antagonist

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of calcium [10], whereby inhibiting NMDA ionotropic channels, it prevents entrance of calcium into the cell, thereby inhibiting the activation of its subsequent enzymatic cascade [9,11,12].

In many studies, the level of dietary magnesium in relation to depression has been investigated. Although the obtained results are controversial, in the majority of studies a significant relationship has been observed between deficiency of the consumed magnesium and incidence of depression [13–15]. The result of a 20-y follow-up study showed that magnesium intake may have an effect on the risk for developing depression [16].

A deficiency in dietary magnesium can be accounted for by various factors such as the soil of agricultural lands and new agricultural techniques including genetic manipulation [17,18]. Another factor is the water being consumed. According to a study, given the amounts of minerals, drinking water can provide 8% of daily magnesium required by individuals [19]. Additionally, an unhealthy diet that contains a high consumption of processed foods and refined grains can result in hypomagnesemia in long term [2]. Therefore, although major sources of magnesium, including dark green leafy vegetables, grains, and nuts are available [20], hypomagnesemia is still seen in many metabolic diseases [21]. Among depressed people, incidence of hypomagnesemia has been estimated to be as high as 13.7% [22]. This figure is almost three times the value of nondepressed individuals (4.6%) [23].

Although the conventional treatment of depression is administration of antidepressants including selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, and tricyclic antidepressants [24], not completing the treatment due to complications caused by these medications, such as headache and nausea, vomiting, restlessness, and drowsiness [25] as well as relapse of the depression or manic periods in about 60% of individuals, highlights the necessity of researching and investigating complementary treatments [26]. Furthermore, studying the effect of food supplements and nutrients such as magnesium on this disease can play an important role in the prevention and treatment of this problem.

The question is to what extent the condition of patients suffering from depression as well as a lack of magnesium can be improved in terms of depression mitigation by resolving the deficiency of magnesium. Accordingly, this research was designed and conducted with the aim of examining the effect of magnesium supplementation on the status of depression in those suffering from magnesium deficiency.

Materials and methods

Type of study and participants

This was a randomized, double-blind, placebo-controlled trial with 60 individuals suffering from depression and magnesium deficiency. They were selected from patients referred to Khatam-ol-Anbiya Clinic in Yazd under the supervision of a psychiatrist and through using the Beck Depression Inventory-II questionnaire. This study was designed in two phases; initially, the status of magnesium in depressed patients was investigated. Those results were published previously [22]. In the second phase, the depressed candidates suffering with magnesium deficiency who met the exclusion and inclusion criteria participated in the study. The criterion for diagnosing depression was a score >11 in the Beck Depression Inventory-II under the provision of a psychiatrist. After determining the state of each participant's depression, the magnesium status was evaluated. The criterion for deficiency was a serum magnesium level <1.8 mg/dL in men and <1.9 mg/dL in women [23].

The inclusion criteria included a serum magnesium deficiency, depression, and age between 20 and 60 y old. Exclusion criteria included the following:

- Evidence of malignancies and cancer;
- Pregnancy;
- Consumption of a multimineral/multivitamin supplement over the previous 3 mo;
- Death of a relative, loss of job, or divorce over the previous 6 mo;
- History of treatment for depression;
- Consumption of any kind of antidepressants and tranquilizers, diuretics, and laxatives over the previous 3 mo;
- Diagnosis of hypertension; diabetes; cardiovascular, hepatic, or renal disease; thyroid disorders; anemia; and cancer.

To determine the sample size, we considered $\alpha = 0.05$ and the test power of 90% for reaching a significant difference of 2 units of the mean of the total Beck score in two groups of previous studies; a sample of 25 individuals was obtained. Having accounted for the rate of attrition, this number increased to 30 individuals. Using random codes obtained from the computer, they were then categorized randomly into two 30-member groups. The first was the magnesium group (MG), and the second was the placebo group (PG). The MG received two 250-mg magnesium oxide tablets on a daily basis (21st Century® Healthcare, Inc., Arizona, USA). On the other hand, the PG received two similar tablets in terms of shape, color, and size containing starch powder (developed by Pharmacy Faculty of Shahid Sadoughi University of Medical Sciences in Yazd). The supplement and placebo were administered in two 1-mo courses. At each course, the individuals were asked to revisit the clinic after 1 mo, whereby consumption of the medication was regularly controlled by the researcher. Compliance was defined as consumption of >90% of attributed tables and was assessed by tablet count.

Measurements

To measure the depression status, the Beck Depression Inventory-II was used [27,28]. This included 21 questions for measuring the symptoms of depression, including disorders of sleep, appetite, self-confidence, hope, and feelings of sadness. Each question had four options ranging from 0 to 3. The score was based on the number of each choice. Eventually, a total score was obtained out of the 21 questions, ranging from 0 to 63. Based on this, individuals were placed in one of the following groups: 0 to 10, normal; 11 to 16, mild depression; 17 to 20, requires counseling; 21 to 30, moderately depressed; 31 to 40, severe depression; and ≥40, very severe depression.

To measure the serum magnesium, 5 mL venous blood was taken from each individual. After centrifuging the blood sample at 3000 to 4000*g* for 10 min after the sampling, the serum sample was obtained. The level of serum magnesium was measured by photometric method using blue Xylidyl (the magnesium assessment kit, Pars Azmoon Co., Iran, Tehran) with a sensitivity of 0.2 mg/dL. To investigate the intake of food, macronutrients, magnesium, and energy at the beginning and end of the study, a 24-h dietary recall questionnaire was applied. The weight of individuals was measured with an accuracy of 0.5 kg wearing lightweight clothing and using a digital balance of 100 g. Height was then measured with an accuracy of 0.5 cm, without shoes. Body mass index was obtained by dividing the weight (kg) by the square of height (m^2).

Data analysis

Data were analyzed using SPSS for Windows, version16 (SPSS Inc., Chicago, IL, USA). The Kolmogorov–Smirnov test was used to specify the distribution of data. One-way analysis of variance and Student's *t* test were used to compare the mean of the quantitative data with a normal distribution. Furthermore, paired sample *t* test was employed to compare the means of quantitative data before and after the treatment. Fisher's exact test and χ^2 test were used to compare the frequency distribution of qualitative variables. The significance level of *P* was considered to be <0.05. To analyze the data of dietary recall, Nutritionist IV software (Nutritionist IV, Bruno, CA, USA) was used.

Ethical considerations

The protocol of this clinical trial was confirmed in the commission of ethics in research at Shahid Sodughi University of Medical Sciences. Upon entering the trial, participants provided written informed consent. Patient data were kept confidentially, and participants were able to leave the study freely at any stage. Patients did not pay for the experiments or the supplement. This trial was registered in the registry of clinical trial of Health Ministry of Iran.

Results

Of 650 possible participants, 60 met the inclusion criteria and were randomly assigned to one of two groups (MG or PG). They were followed for 8 wk. At the end of the study, seven

participants were excluded due to nonattendance, pregnancy, immigration, or complications caused by consumption of the tablets. Eventually, information from 26 patients in the MG and 27 in the PG was analyzed (Fig. 1). Tablet count showed a compliance of >87% in both groups.

The age mean of the MG and PG were 32.20 ± 9.54 and 32.07 ± 7.69, respectively ($P = 0.64$). The distribution of the frequency of qualitative properties in the two groups is shown in Table 1. As can be observed, of the 26 people in the MG, 19 were women and 7 were men (73.1% and 26.9%, respectively). Similarly, of the 27 individuals in the PG, 20 were women (74.1%) and 7 were male (25.9%). The frequency of the qualitative characteristics did not show a significant difference between the two groups.

Comparison of the within- and between-group means of body mass index and daily dietary intakes are provided in Table 2. The mean of the changes in different variables, except for daily intake of carbohydrates, did not demonstrate a significant difference between the two groups.

The mean of the score of the Beck Depression Inventory-II and serum magnesium as well as their changes across the two groups are reported in Table 3. As can be seen in Table 3, the mean Beck score declined significantly in each group after the intervention. This reduction, however, was greater in the MG compared with the PG. the mean scores of changes were −15.65 ± 8.92 for MG and −10.40 ± 7.90 for PG ($P = 0.02$). As Table 3 shows, the mean serum magnesium at the end of the study increased significantly only in MG compared with the beginning of the study. Also, its mean changes were significant across the two groups. Although all of the participants had hypomagnesemia, at the end of the trial 88.5% of the MG returned to a normal state of magnesium; this was 48.1% for individuals in the PG ($P = 0.002$).

Table 1
Comparison of qualitative characteristics between the two groups at baseline

Variables	Magnesium group n (%)	Placebo group n (%)	*P* value*
Sex			0.93
Female	19 (73.1)	20 (74.1)	
Male	7 (26.9)	7 (26.9)	
Marital Status			0.28
Single	7 (26.9)	11 (40.7)	
Married	19 (73.1)	16 (59.3)	
Education			0.80
Illiterate	0 (0)	1 (3.7)	
Elementary	2 (7.7)	3 (11.1)	
Diploma	7 (26.9)	8 (29.6)	
Associate degree	2 (7.7)	2 (7.4)	
Bachelor of science	15 (57.6)	13 (48.1)	
Occupation			0.67
Unemployed	5 (19.2)	4 (14.8)	
Self-employed	1 (3.8)	3 (11.1)	
Employed	9 (34.6)	8 (29.6)	
Housewife	11 (42.3)	12 (44.4)	

* χ^2 test.

Discussion

The findings of this study indicated that daily consumption of 500 mg magnesium oxide for 8 wk resulted in improvement of serum magnesium levels and depression in patients who were depressed and diagnosed with hypomagnesemia. Although to our knowledge, few clinical studies have been conducted in this regard, Barragán-Rodríguez et al. [29] conducted a similar study in which they investigated daily consumption of 450 mg magnesium in the form of magnesium chloride in the treatment group versus a control group. Following 12 wk of treatment, serum magnesium increased significantly in both groups, but the

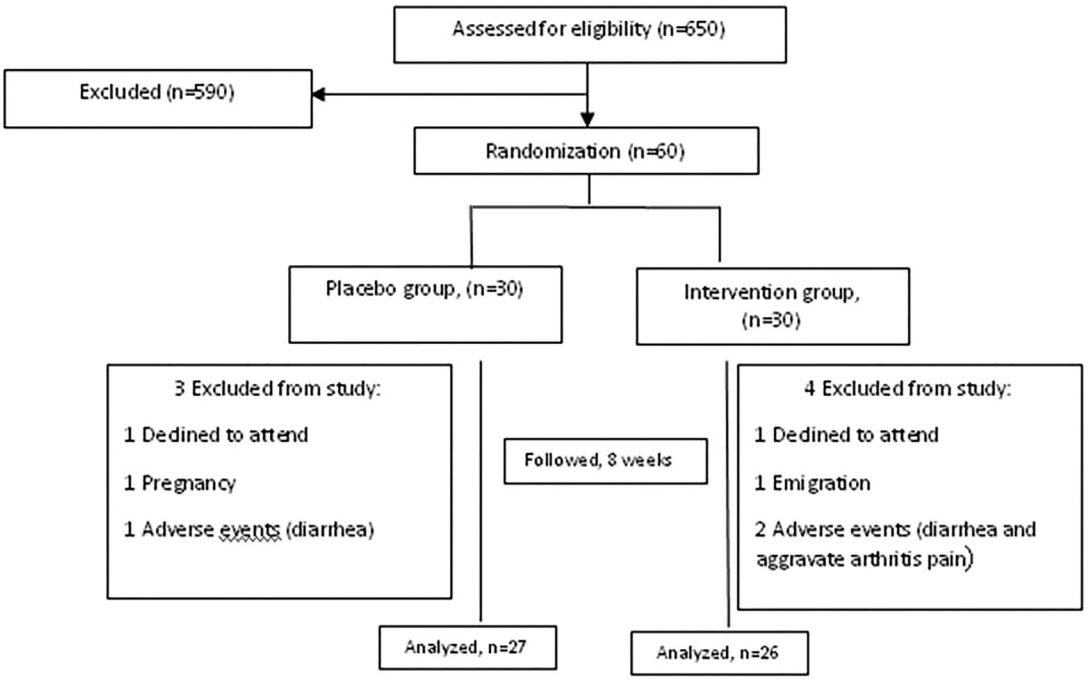

Fig. 1. Participant flow diagram throughout the study.

Table 2
Comparison of mean of anthropometric and dietary intake data between the two groups at baseline and study endpoint

Variables	n	Baseline	End	Changes	*P* value*
Body mass index (kg/m^2)					
Magnesium group	26	28.58 ± 4.5	25.89 ± 5.64	1.4 ± 0.30	0.28
Placebo group	27	25.67 ± 4.09	25.94 ± 4.31	0.46 ± 0.26	0.7
P value†		0.89	0.72	0.87	
Protein (g)					
Magnesium group	26	63.33 ± 22.83	71.51 ± 44.20	44.31 ± 8.17	0.35
Placebo group	27	75.08 ± 23.89	69.67 ± 18.43	23.45 ± −5.40	0.24
P value		0.07	0.84	0.16	
Carbohydrate (g)					
Magnesium group	26	305.1 ± 106.93	307.49 ± 101.31	87.21 ± 2.38	0.89
Placebo group	27	364.08 ± 101.04	308.19 ± 97.1	113.34 ± −55.89	0.01
P value		0.04	0.98	0.04	
Fat (g)					
Magnesium group	26	81.88 ± 37.13	75.53 ± 23.69	−6.35 ± 36.97	0.38
Placebo group	27	87.17 ± 28.87	81.60 ± 24.46	32.15 ± −5.56	0.37
P value		0.56	0.36	0.93	
Magnesium (g)					
Magnesium group	26	153.47 ± 66.71	170.83 ± 57.36	81.50 ± 17.35	0.28
Placebo group	27	162.96 ± 74.84	193.10 ± 68.83	90.29 ± 30.13	0.09
P value		0.62	0.20	0.59	

* Paired *t* test.
† Student *t* test.

difference of depression status between the two groups was not significant [29]. Eby et al. also investigated the effect of magnesium supplement (125–300 mg in the form of turinate or glicinate) on three depressed individuals, observing rapid improvement of major depression in all [11]. Although in the mentioned study the status of serum magnesium was not examined in individuals at the prescribed dosage, the results were in line with those of the present study.

Evaluation of the serum magnesium levels of the participants indicated that more patients in the MG responded to the magnesium supplement treatment (88.5% versus 48.1%), and reached the normal state. Nevertheless, after the intervention ~11.5% of the individuals in the MG were still below the normal level of serum magnesium. This might be due to insufficient magnesium dose, insufficient duration of the treatment, insufficient intake of magnesium from the diet, and so on. Abbasi et al. [30] examined the effect of 8 wk of daily consumption of 500 mg magnesium oxide tablet on the sleep status of the elderly. They observed that at the end of the 8-wk period, the serum magnesium level was not significantly different between the magnesium group and the placebo group [30]. Reasons for the insignificant change vary. One factor could be the sensitivity of serum magnesium as an index for evaluation of magnesium status (i.e., it appears that it did not have the necessary sensitivity) [31]. According to these studies, there is equilibrium between the concentration of serum magnesium and bone, thus when magnesium is deficient, this element is released into the blood from the degradable part of the bone. This can then falsely show the serum magnesium levels to be high [32]. Additionally, because the equilibrium of magnesium changes slowly in the body, consumption of oral supplements of magnesium might not affect the serum magnesium even within several weeks or months. However, despite all of these problems, serum magnesium is still one of the widely used indices when measuring the status of magnesium in the body. Because indices like magnesium erythrocyte and urine magnesium are not very accurate, determination of an accurate method remains a challenge [33].

In addition to what has been mentioned here, determination of the magnesium dose and the duration of treatment for individuals suffering from hypomagnesemia also are important. Based on previous studies, the dose prescribed for treating depression has ranged from 125 to 450 mg [11,29,34]. Furthermore, the course of therapeutic supplement also has varied from 7 to 20 mo [11,29,35]. One review study recommended daily consumption of magnesium oxide for treating hypomagnesemia to be 800 mg/d. Side effects associated with this tablet include gastrointestinal disorders and diarrhea, thus it is difficult to prescribe an amount of the supplement that will not result in undesirable complications and will be effective [36]. However, it seems that an increase in daily consumption leads to better results.

Considering the mechanism of the effect of magnesium in brain and mental functions, various speculations have been presented. According to these studies, magnesium has a pivotal role in synaptic function, especially in the brain's hippocampus neurons [24]. In addition to being an inhibitory regulator in NMDA channels, magnesium has also an excitatory effect on production of brain-derived neurotrophic factor (BDNF) and cyclic adenosine monophosphate response element-binding protein in the brain. Cyclic adenosine monophosphate response element-binding protein is a protein that regulates the activity of the genes affecting the function of human brain, especially the genes involved in the production of dopamine. BDNF is a neurotropic factor widely expressed in the central nervous system, playing an important role in the evolution of brain, survival, and maintenance of neurons. Furthermore, BDNF also has a role

Table 3
Comparing the mean of Beck Depression Inventory-II score and serum magnesium between and within the two groups

Variables	n	Baseline	End	Changes	*P* value*
Beck score					
Magnesium group	26	26.9 ± 7.1	11.26 ± 6.9	−15.65 ± 8.92	0.001
Placebo group	27	25.6 ± 6.1	15.2 ± 9.3	−10.40 ± 7.90	0.001
P value†		0.49	0.08	0.02	
Serum magnesium (mg/dL)					
Magnesium group	26	1.77 ± 0.19	2.08 ± 0.19	0.31 ± 0.29	0.001
Placebo group	27	1.82 ± 0.13	1.91 ± 0.27	0.09 ± 0.03	0.110
P value		0.27	0.01	0.01	

* Paired *t* test.
† Student *t* test.

in inhibition of NMDA channels. In some studies, increased expression of the *BDNF* gene has been observed after treatment with electric shock and some antidepressants [24,37]. Therefore, magnesium can be effective in improving depression.

Among the limitations of this study is its relatively short duration of treatment. Not measuring and specifying the status of some other nutrients involved in the metabolism of magnesium such as vitamin D and calcium and not using some other sensitive indices indicating the status of magnesium in the body are other limitations. As a strong point of this trial, one can mention the high rate of patient compliance in consuming the supplements and the consistency of follow-up in the treatment.

Based on the results obtained from this study, it is suggested that in future investigations, different doses of magnesium supplements or different courses of treatment be evaluated. Furthermore, because the status of vitamin D, parathormone, and calcium is associated with depression and serum magnesium, measurement of these indices in future studies is suggested for better evaluation of the effect of magnesium supplements on depression.

Conclusion

This study indicated that daily consumption of 500 mg magnesium oxide tablet for ≥8 wk by individuals with depression and hypomagnesemia results in improvement in both the depression and the status of magnesium in their bodies. Therefore, when evaluating patients with depression, evaluation of the serum magnesium status and resolving this deficiency, if present, contribute to better treatment outcomes and thus are recommended.

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References

[1] Volpe SL. Magnesium and the athlete. Curr Sports Med Rep 2015;14:279–83.
[2] Gröber U, Schmidt J, Kisters K. Magnesium in prevention and therapy. Nutrients 2015;7:8199–226.
[3] Pasternak K, Kocot J, Horecka A. Biochemistry of magnesium. J Elementol 2010;15:601–16.
[4] Romani A. Regulation of magnesium homeostasis and transport in mammalian cells. Arch Biochem Biophys 2007;458:90–102.
[5] de Baaij JH, Hoenderop JG, Bindels RJ. Magnesium in man: implications for health and disease. Physiol Rev 2015;95:1–46.
[6] Haddad JJ. N-methyl-D-aspartate (NMDA) and the regulation of mitogen-activated protein kinase (MAPK) signaling pathways: a revolving neurochemical axis for therapeutic intervention? Prog Neurobiol 2005;77:252–82.
[7] Paoletti P, Bellone C, Zhou Q. NMDA receptor subunit diversity: Impact on receptor properties, synaptic plasticity and disease. Nat Rev Neurosci 2013;14:383–400.
[8] Jin DZ, Xue B, Mao LM, Wang JQ. Metabotropic glutamate receptor 5 upregulates surface NMDA receptor expression in striatal neurons via CaMKII. Brain Res 2015;1624:414–23.
[9] Whittle N, Li L, Chen WQ, Yang JW, Sartori SB, Lubec G, et al. Changes in brain protein expression are linked to magnesium restriction-induced depression-like behavior. Amino Acids 2011;40:1231–48.
[10] Iseri LT, French JH. Magnesium: nature's physiologic calcium blocker. Am Heart J 1984;108:188–93.
[11] Eby GA, Eby KL. Rapid recovery from major depression using magnesium treatment. Med Hypotheses 2006;67:362–70.
[12] Eby GA, Eby KL. Magnesium for treatment-resistant depression: a review and hypothesis. Med Hypotheses 2010;74:649.
[13] Derom ML, Martínez-González MA, del Carmen Sayón-Orea M, Bes-Rastrollo M, Beunza JJ, Sánchez-Villegas A. Magnesium intake is not related to depression risk in Spanish university graduates. J Nutr 2012;142:1053–9.
[14] Tarleton EK, Littenberg B. Magnesium intake and depression in adults. J Am Board Fam Med 2015;28:249–56.
[15] Yary T, Aazami S, Soleimannejad K. Dietary intake of magnesium may modulate depression. Biol Trace Elem Res 2013;151:324–9.
[16] Yary T, Lehto SM, Tolmunen T, Tuomainen TP, Kauhanen J, Voutilainen S, et al. Dietary magnesium intake and the incidence of depression: a 20-year follow-up study. J Affect Disord 2016;193:94–8.
[17] Davis DR. Declining fruit and vegetable nutrient composition: what is the evidence? HortScience 2009;44:15–9.
[18] Grzebisz W. Magnesium-food and human health. J Elementol 2011;16:300–7.
[19] Drywien ME, Nadolna A. Assessment of mineral bottled water as a source of selected minerals among students. Roca Panstw Zakl Hig 2011;63:347–52.
[20] Volpe SL. Magnesium in disease prevention and overall health. Adv Nutr 2013;4:378S–83S.
[21] Blaszczyk U, Duda-Chodak A. Magnesium: its role in nutrition and carcinogenesis. Roca Panstw Zakl Hig 2013;64:165–71.
[22] Rajizadeh A, Mozaffari-Khosravi H, Yassini-Ardakani M, Dehghani A. Serum magnesium status in patients subjects with depression in the City of Yazd in Iran 2013–2014. Biol Trace Elem Res 2016;171:275–82.
[23] Syedmoradi L, Ghasemi A, Zahediasl S, Azizi F. Prevalence of hypo-and hypermagnesemia in an Iranian urban population. Ann Hum Biol 2011;38:150–5.
[24] Szewczyk B, Poleszak E, Sowa-Kucma M, Siwek M, Dudek D, Ryszewska-Pokrasniewicz B, et al. Antidepressant activity of zinc and magnesium in view of the current hypotheses of antidepressant action. Pharmacol Rep 2008;60:588–9.
[25] Anderson HD, Pace WD, Libby AM, West DR, Valuck RJ. Rates of 5 common antidepressant side effects among new adult and adolescent cases of depression: a retrospective US claims study. Clin Ther 2012;34:113–23.
[26] Culver JL, Arnow BA, Ketter TA. Bipolar disorder: improving diagnosis and optimizing integrated care. Clin Psychol 2007;63:73–92.
[27] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th text revision. Washington, DC: Author; 2000.
[28] Dabson K, Mohammadkhani P. Psychometrics characteristic of Beck Depression Inventory-II in patients with major depressive disorder. J Rehabil 2007;8:82–6.
[29] Barragán-Rodríguez L, Rodríguez-Morán M, Guerrero-Romero F. Efficacy and safety of oral magnesium supplementation in the treatment of depression in the elderly with type 2 diabetes: a randomized, equivalent trial. Magnes Res 2008;21:218–23.
[30] Abbasi B, Kimiagar M, Sadeghniiat K, Shirazi MM, Hedayati M, Rashidkhani B. The effect of magnesium supplementation on primary insomnia in elderly: a double blind placebo-controlled clinical trial. J Res Med Sci 2012;17:1161–9.
[31] Witkowski M, Hubert J, Mazur A. Methods of assessment of magnesium status in humans: a systematic review. Magnes Res 2012;24:163–80.
[32] Elin RJ. Assessment of magnesium status for diagnosis and therapy. Magnes Res 2010;23:194–8.
[33] Arnaud MJ. Update on the assessment of magnesium status. Br J Nutr 2008;99:S24–36.
[34] Walker AF, De Souza MC, Vickers MF, Abeyasekera S, Collins ML, Trinca LA. Magnesium supplementation alleviates premenstrual symptoms of fluid retention. J Womens Health 1998;7:1157–65.
[35] Bhudia SK, Cosgrove DM, Naugle RI, Rajeswaran J, Lam BK, Walton E, et al. Magnesium as a neuroprotectant in cardiac surgery: a randomized clinical trial. J Thorac Cardiovasc Surg 2006;131:853–61.
[36] Guerrera MP, Volpe SL, Mao JJ. Therapeutic uses of magnesium. Am Fam Physician 2009;80:157–62.
[37] Bocchio-Chiavetto L, Zanardini R, Bortolomasi M, Abate M, Segala M, Giacopuzzi M, et al. Electroconvulsive therapy (ECT) increases serum brain derived neurotrophic factor (BDNF) in drug resistant depressed patients. Eur Neuropsychopharmacol 2006;16:620–4.