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The Relationship Between Serum Zinc and Magnesium Levels and Depression in Postmenopausal Women

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Abstract

Background and Objective: Depression is the most common mental disorder in different societies, and it is estimated to be the second most common disease followed by cardiovascular disease by 2020. Zinc and magnesium may play a role in the pathophysiology of depression. Therefore, the present study was designed to investigate the relationship between serum zinc, magnesium, and depression in postmenopausal women. Materials and Methods: This was a case-control study of 68 depressed women and 68 non-depressed women. At first, after completing the informed consent and demographic questionnaire and the Beck Depression Inventory, the blood samples were collected, centrifuged and frozen. Then, the zinc and magnesium levels were evaluated by the flame atomic absorption technique. Data were analyzed using SPSS-Ver22, chi-square test, independent t-test, and logistic regression. P values < 0.05 was considered significant. Results: The mean serum zinc and magnesium levels were 88.26 ± 21.21 µg/dl, 1. 82± 0/49 mg/dl in case group and 102.64 ± 24.41 µg/dl, 2.17 ± 0.57 mg/dl, in control group respectively, which showed a significant difference between mean and standard deviation of serum zinc and magnesium levels in both case and control groups. Based on logistic regression analysis, the increase in serum zinc levels is associated with a reduction in the depression risk [odds ratio: 1.027; CI 95%: 1.011 to 1.044]. Moreover, the increase in serum magnesium levels is associated with a reduction in the depression risk [odds ratio: 3/278; CI 95%: 1.62 to 6.602]. Conclusion: Based on the findings, serum zinc and magnesium levels in the case group were lower than that of the control group. This valuable information can be used in planning to prevent depression.

Keywords: Depression, Zinc, Magnesium, Postmenopausal Women, Serum.

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Introduction

Depression is the most common mental disorder in different societies, and it is estimated to be the second most common disease followed by cardiovascular disease by 2020 (WHO, 2005). Some studies show that 26 to 33 % of women experience their first depressive episode during menopause (Reed et al., 2009). Depression affects women twice more than men (Bahri et al., 2013). The prevalence of depression in postmenopausal women has been reported to be 43% (Gooneratne, 2008). The prevalence of depression among postmenopausal women in different regions of Iran has been reported differently. The prevalence of depression of postmenopausal women was 34.7% in a study conducted by Yasary et al. (2010) in Dezful, 68% in the study conducted by Tiroudi et al. in Tabriz in 2005 and 20.9% in the study conducted by Rabiei et al. in 2011. Women are at high risk for various psychological changes during menopause, and about 90% of them have some degrees of mental disorders (Sprawka et al., 2008). For example, sudden changes in mood, irritability, anxiety, the state of feeling empty and worthless, sleep disturbances, anorexia, weakness, committing suicide and death can be pointed out (Sadock, 2010; Sadock, 2009). One of the theories on the pathophysiology of depression among postmenopausal women is the role of zinc and magnesium deficiency in the pathogenesis of depression (Altura, 1991).

Zinc is considered to be one of the main elements of the body that plays a role in neuromodulatory processes of the brain-gut axis, cell proliferation, immunity, transcription, and neurological functions (Maserejian, Hall and McKinlay, 2012). Magnesium is the fourth most abundant cation in the body and is the second most prevalent intracellular cation that requires more than 300

cellular enzymatic systems for their activity (Barbagallo, Belvedere and Dominguez, 2009). Zinc and magnesium play an essential role in neurotransmitter metabolism and liberation (Etebary et al., 2010). Zinc and magnesium deficiencies in the brain cause behavioral disorders such as depression, focal epilepsy, hand and foot tremors, restlessness, irritability, fatigue, headache, learning disorder, and some nerve disorders such as epilepsy and Alzheimer (Etebary et al., 2010).

In similar studies, there is no single view on the relationship between serum zinc and magnesium levels and depression prevalence, in a way that some studies have shown that serum zinc and magnesium levels in depressed people, especially in postmenopausal women with depression, are lower than that in non-depressed people (Stanislawska et al., 2014; Amani et al., 2010; Barragan-Rodriguez et al., 2008). However, some other studies have found no significant relationship between serum zinc and magnesium levels with depression (Szkup et al., 2016; Imada et al., 2002). Also, studies in animals such as in mice have shown that there is a relationship between zinc and magnesium deficiencies and depressive symptoms (Nikseresht et al., 2012; Młyniec and Nowak, 2012; Whittle, Lubec and Singewald, 2009; Poleszak et al., 2004).

This study aimed to determine the association between serum zinc and magnesium level with depression in postmenopausal women. If there is a positive relation, the onset of depression in postmenopausal women can be prevented by timely education and correction of zinc and magnesium deficiencies.

Materials and Methods

This case-control study was performed on 136 postmenopausal women referring to health centers number 1 in Ahwaz in 2017. This study was approved by the ethics committee of Ahvaz Jundishapur University of Medical Sciences (IR. Ajums.RES.1396.553).

Entry criteria included: having 45-65 years, women who have had at least one year of their menstruation, having a husband, having reading and writing skills. Exit criteria included: consuming food supplements, antidepressant and diuretics drugs over the past 3 months, history of smoking cigarettes, using drugs and alcoholic beverages, having any mental disorder or systemic disease, such as diabetes, hypertension, thyroid, kidney, liver, and heart disease, malignant tumors and hemorrhagic disease, and the use of hormone therapy. After providing complete information to the participants about the study and obtaining personal satisfaction from them, a demographic questionnaire and Beck Depression Inventory were provided to the samples and completed by a researcher during an interview with the participants. Those with a Beck score of less than 10 were classified as non-depressed women and those with a score of 10-29 were classified as depressed women, and their depression was confirmed by the psychiatrist. It should be noted that the subjects of the two groups were matched for age and body mass index, and this matching was done in a group. In this study, a statistical expert has determined the sample size based on previous studies with a power of 90% and a confidence coefficient of 95% with 68 women in the case group and 68 women in the control group. Blood samples (5cc) were collected from the arterial vessels after at least 8 hours of fasting from all research samples. Then the samples were centrifuged at 3500 rpm for 10 minutes and immediately stored at -20°C, and then they delivered to the comprehensive laboratory at Ahvaz Jundishapur University of Medical Sciences. The analysis of the samples was performed using a flame atomic absorption spectroscopy instrument (AAS 5FL) at 285.2 nm wavelength for magnesium and 213.9 nm wavelength for zinc. The instrument was calibrated in the concentration of 0.1 to 1 ppm for zinc and the concentration of 0.02 to 1 ppm for magnesium. The samples were then diluted using a 5000 ppm lanthanum chloride solution with a ratio of 50 to 150 to measure magnesium, and they were diluted using a water-soluble solution of 2 to 10 ratio to measure zinc. The concentrations were determined after drawing calibration curves and calculating the equation of a line. Normal ranges of 75-130 µg/dl and 1.87-2.4 mg/dl were considered for serum zinc and magnesium levels respectively.

SPSS-Ver22 was used to analyze the data. An independent t-test was used to compare the quantitative data between the two groups. Logistic regression was also used to determine the relationship between serum zinc and magnesium levels and depression in postmenopausal women. Chi-square test was used for qualitative data analysis and P values of less than 0.05 were regarded as statistically significant.

Findings

In this study, the two groups did not have a significant difference in terms of demographic characteristics (P> 0.05). According to Table 1, the average age was 55.05 ± 5.12 in the case group and 54.89 ± 5.07 in the control group. The average age of menopause in the case group was 48. 92 ± 3.16 and 48.98 ± 3.46 in the control group. The average Body Mass Index (BMI) was 25.84 ± 4.80 in the case group and 26.19 ± 5.12 in the control group, which did not show any significant difference between the two groups (P = 0.68). Most of the research units (86%) were housewives. The level of literacy in most of the research units (83.1%) was lower in high school. The majority of women (88.2%) were satisfied with their marital relationship. 52.9% of the subjects in the case group and 57.4% of the subjects in the control group were in a moderate economic situation. The averages of serum zinc and magnesium levels were 88.26 ±21.02 µg/dl, 1.82 ± 0.49 mg/dl respectively in the case group, and 102.64 ± 24.41 µg/dl and, 2.17 ± 0.57 mg/dl respectively in the control group. The results of the independent t-test showed that there was a significant difference between serum zinc and magnesium levels in the two groups so that in depressed women (case group), serum zinc and magnesium levels were significantly lower than that in non-depressed women (control group) (P<0.001). Based on this analysis, an increase in serum levels decreases the risk of depression (odds ratio: 1.027; confidence interval 95%: 1.011 to 1.044). Further, an increase in serum magnesium levels is also associated with a reduction in the risk of depression (odds ratio: 3.278; confidence interval 95%: 1.62 to 6.602) (Table 3).

Discussion

The results showed that there is a significant relationship between serum zinc and magnesium level and depression in postmenopausal women. Serum zinc and magnesium levels are associated with a decrease in the risk of depression in postmenopausal women. According to recent studies, the main elements such as zinc and magnesium apply their antidepressant effects through neurotransmitters such as monoamine (Szewczyk et al., 2008; Szewczyk et al., 2009; Ruljancic et al., 2013).

Zinc applies its antidepressant effects by inhibiting glutamate receptors (NMDA = N-methyl-d-aspartate) and nitric oxide synthase (NOS), which are targets for antidepressants. On the other hand, the mechanism of the effect of magnesium on depression is that magnesium ions reduce the nitric oxide production by inhibiting calcium channels through NMDA receptors (Eby and Eby, 2006; Lobato et al., 2008; Paul et al., 2001). Magnesium also prevents the overactivation of the HPA (Hypothalamic-Pituitary-Adrenal) axis by reducing the level of Corticotropin-Releasing Hormone (CRH), thereby applies its antidepressant effect (Sartori et al., 2012). In a study by Szkup et al. on postmenopausal women with depression, there was no significant relationship between serum zinc level and depression in postmenopausal women. Also, zinc concentrations in depressed women were higher than those in non-depressed women (Szkup et al., 2016). Moreover, in a cross-sectional study among women with postpartum depression, there was no significant relationship between serum zinc level and depression (Edalati-Fard et al., 2016). In the present study, although serum zinc level was normal in both case and control groups, average and standard deviation of serum zinc level were significantly lower in the case group than the control group ($P<0.001$). The results of the abovementioned studies are not consistent with the present study. The relationship between zinc and depression on rodents has shown that there is a relationship between zinc deficiency and depressive symptoms. (Młyniec and Nowak, 2012; Whittle, Lubec and Singewald, 2009; Tamano et al., 2009). Cross-Sectional studies among adolescents (Kim et al., 2015) and postmenopausal women (Stanislawska et al., 2014) reported a positive relationship between zinc deficiency and depression severity. In a study conducted by Islam et al. among 50 generalized anxiety disorder patients and 51 healthy volunteers, there was a significant difference in serum zinc level between the case and control groups. The serum zinc level in the case group was significantly lower than that of the control group (Islam et al., 2013). In a study conducted by Ranjbar et al., 39 patients with treatment-resistant depression took 27mg of zinc supplement with antidepressants at the same time for 12 weeks. Their depression scores were significantly lower than that of the placebo group (Ranjbar et al., 2013). The results of the above-mentioned studies are in line with the present study.

According to some studies, the same as zinc, magnesium deficiency induces depression-like symptoms in mice. On the other hand, antidepressant and antianxiety activity of these ions have been tested in animals (Nikseresht et al., 2012; Poleszak et al., 2004; Singewald et al., 2004; Winther et al., 2015). In cross-sectional studies among postmenopausal women (Stanislawska et al., 2014; Szkup et al., 2016) and women with postpartum depression (Edalati-Fard et al., 2016), there were fewer depressive symptoms in women with higher levels of magnesium. The results obtained by Abbasi et al. (2013) revealed that magnesium supplementation reduced the score of depressive symptoms in the magnesium supplement group compared to the placebo group.

In the study conducted by Rodríguez et al., the positive effect of magnesium supplements as a treatment for depression in older adults with type 2 diabetes is 50 mg of imipramine (Barragan-Rodriguez et al., 2008). The results of this study are consistent with the results of the abovementioned studies.

In the study conducted by Islam et al. (2013), there was no significant difference in serum magnesium levels between patients with a generalized anxiety disorder in both case and control groups. Also, Imado et al. evaluated serum magnesium levels in 71 patients with mental disorders and 30 healthy people. The findings showed that the level of magnesium in patients with mental disorders was significantly more than that of the control group (Imada et al., 2002). One of the reasons for the discrepancy between the present study and some of the abovementioned studies is that most of them have been conducted among patients with mental disorders.

The strengths of the present study were that, unlike most previous studies that were cross-sectional, this study was a case-control study. It should be noted that in case-control studies, more reliable results are obtained than cross-sectional studies. In this study, it has been tried to consider some of the factors as an exit criterion to control the confounding effect of factors affecting depression. For example, to control the confounding effect of demographic factors, samples were matched according to age and BMI. Trusting participants' statements that were outside the researcher's control is one of this study's limitations.

Conclusion

According to the results of this study, there is a significant relationship between serum zinc and magnesium levels and depression in postmenopausal women. Menopausal women with zinc and magnesium deficiency are at greater risk of depression. This valuable information can be used in planning to prevent depression.

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Table 1. Frequency distribution of demographic characteristics of research units in two groups

variable		Case (n=68)	Control (n=68)	P
Age (years)		55.05±5.12	54.89±5.07	0.86
Age of menopause (years)		48.92±3.16	48.98±3.46	0.91
Duration of menopause		6.11±4.33	5.91±4.25	0.78
Duration of living with husband		36.63±7.25	36.67±7.32	0.97
BMI ($kg/m^{2)}$		25.84±4.80	26.19±5.12	0.68
Number of children		5.44±2.03	5.77±2.06	0.34
Monthly income		1414705.88± 636692.64	1591176.47± 586600.44	0.09
Number of people living at home		3.66±1/61	3/48±1/05	0.45
Education	Elementary	(50)34	(39.7)27	0.35
	Guidance	(36.8)25	(39.7)27	
	Diploma	(7.4)5	(16.2)11	
	Academic	(5.9)4	(4.4)3	
Husband's education	Elementary	(54.4)37	(51.5)35	0.25
	Guidance	(20.6)14	(33.8)23	
	Diploma	(17.6)12	(10.3)7	
	Academic	(7.4)5	(4.4)3	
Job	Housewife	(86.8)59	(85.3)58	
	Employed	(13.2)9	(14.7)10	
The economic situation	Weak	(38.2)26	(29.4)20	0.47
	Medium	(52.9)36	(57.4)39	
	Good	(8.8)6	(13.2)9	
Satisfaction with marital life	Completely satisfied	(19.1)13	(32.4)22	0.47
	Satisfied	(66.2)45	(58.8)40	
	Fairly satisfied	(11.8)8	(8.8)6	
	Dissatisfied	(2.9)2	(0)0	

Table 2. Comparing mean and standard deviation of serum zinc and magnesium levels in research units

Variable	Case		Control		P
	Average	Standard Deviation	Average	Standard Deviation	
Zinc $\mu g/dl$	88.26	21.02	101.64	24.41	p<0.001
Magnesium mg/dl	1.82	0.49	2.17	0.57	p<0.001

Table 3. Logistic regression to determine the relationship between serum zinc and magnesium levels and depression in postmenopausal women

Variable	Beta	$OR(CI\ 95\%)^{¥}$	P
Zinc $\mu g/dl$	0.027	1.027(1.011 to 1.044)	0.001
Magnesium mg/dl	1.187	3.278(1.628 to 6.602)	0.001

¥ Odd ratio (95% Confidence Interval)

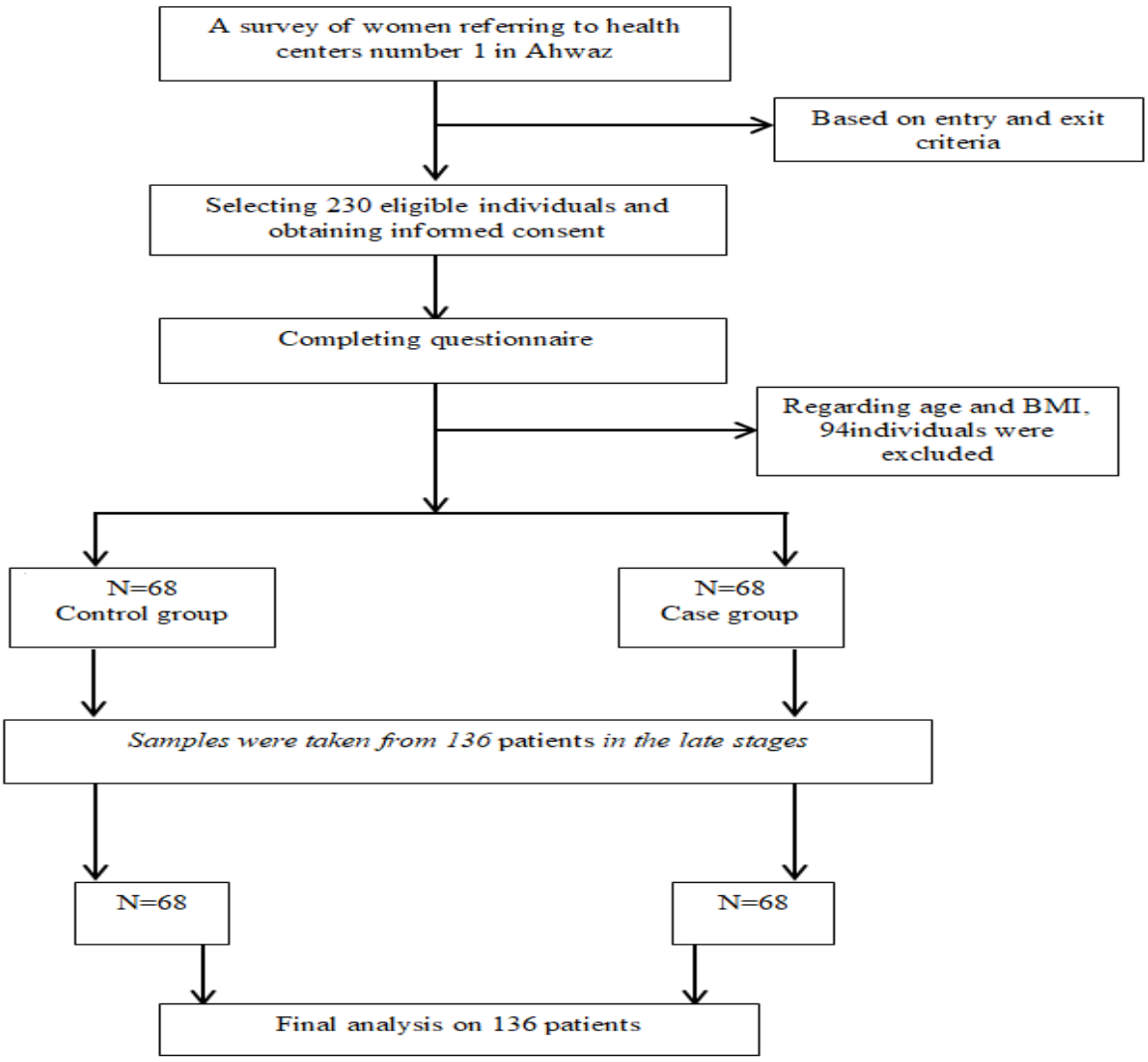

Diagram 1: Participants and excluded individuals from the study.