Assessment of serum magnesium, copper, and zinc levels in multiple sclerosis (MS) patients

Seyed Ali Masoud MD•* , Esmail Fakharian MD*

Objective: multiple sclerosis (MS) is a chronic disease with prominent neurological and behavioral and psychiatric manifestations and unknown etiology which is demarcated with inflammation and destruction of white matter of brain and spinal cord and its replacement with gliotic tissue in young aged people and particularly females. The role of trace elements in multiple sclerosis is set forth in several studies and we are going to evaluate it in these patients in Kashan-Iran.

Methods: Serum magnesium, zinc, and copper levels from 35 MS patients (28 female and 7 male) were measured by an ELIZA method and results were compared with data from healthy matched controls, and data analyzed using T test.

Results: Mean age of patients in this study was 32.3± 6.4 years and 28 (80%) were in age range of 20 to 40. The incidence of MS was found to be 11.6 in 100,000 populations in Kashan district which is a moderate incidence. Muscle weakness (80%), visual disturbances (57.1%), and paresthesia (34.2%) were the most common clinical presentations. Mean serum level of magnesium was 1.87 ± 0.37, copper 110.7 ± 19.5, and zinc 85.4 ± 13.5 in patients (control group), and 2.22 ± 0.24, 133.7 ± 13.4, and 110 ± 8.3 respectively in case group. This difference is statistically significant (P< 0.001). The most common clinical pattern of the disease was recurrent MS in 54.2% of cases.

Conclusion: We found that serum level of magnesium, copper, and zinc is significantly decreased in patients inflicted with MS. This is shown in some other studies and may result in use of supplemental use of trace elements for MS patients to either decrease symptoms or complications.

Iranian Journal of Psychiatry and Behavioral Sciences (IJPBS), Volume 1, Number 2, Autumn and Winter 2007: 38-42.

Keywords: Copper • Magnesium •Zinc • Multiple sclerosis

Introduction

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system which is marked by motor, psychiatric and cognitive abnormalities (1, 2). In European countries it is the second neurologic debilitating disease after trauma among young aged and middle aged people. Its peak incidence is between 20 and 30 and is rare before 10 and after 60 years old (3,4). Multiple sclerosis (MS) is more common in women with a female to male ratio of 2:1 (3,5). The incidence of MS varies in different races and is more frequent in whites. Generally its prevalence increases from equator to the poles. Its highest incidence is 30 in 10,000 populations (1,5). MS causes inflammation and destruction of myelinated tracts (1), and produces plaques in white matter of such areas as optic nerve, periventricular regions, corpus callosum, brain stem, and spinal cord (5,6). There are three broad groups of mental symptoms that affect patients with MS. These include fatigue, psychiatric symptoms and cognitive impairment (7). Some psychiatric disturbances were noted in 75% of patients (8). Depression is common; it affects 6 to 57 percent of patients and results in a higher rate of suicide than is seen in general population (9-11). Common neurological signs and symptoms of the disease are fatigue (50-60%), and paraparesis (45-79%), sensory disturbances (10-40%), visual blurring secondary to optic neuritis (14.29%), diplopia (8-13%), ataxia (2-18%), urinary disturbances (0-13%), vertigo (2-9%), and convulsion (3-4%) (1,4). This disease is characterized by its recurrences, and involvement of multiple

Authors' affiliation : * Kashan University of Medical Sciences, Kashan, Iran

•**Corresponding author :** Seyed Ali Masoud MD, Associate professor of Neurology, Kashan University of Medical Sciences, Kashan, Iran
Tel : +98 361 5550026-9
Fax : +98 361 5558900
E-mail: masoud_s_a@yahoo.com

areas of the nervous system. Although there is no well known underlying cause for the disease, however, many different factors including genetic background, autoimmune mechanisms, environmental factors, especially viral infections, and nutritional deficiencies of minerals, and trace elements are involved in the appearance, exacerbation, or recurrence of the disease (1, 3, 4, 12-15).

Many studies have shown persistent low levels of zinc in MS patients. Zinc has an important role in inhibition of potentially destructive immune reactions against T lymphocytes, and predisposing inflammatory responses of MS. It is also an antioxidant protecting cell membranes and myelin (16). Copper level also changes in MS. Copper is needed for basal metabolic activities of bone, skin, and nervous system, more importantly it is needed for enzyme reactions involved in the production of ATP, and transmission of impulses in nerves and muscles. In a study on 50 patients with MS it has shown that serum zinc level was lower than control group, and low cupper level was considerable in young patients (12). In another study on 27 patients RBC's gluthation peroxidase copper concentration was significantly lower than controls, but zinc serum level was normal (16).

Measurement of serum calcium and magnesium levels in 50 patients with a mean age of 31.8 showed lower magnesium levels (13).

If the hypothesis of decreased levels of trace elements is right then supplementation therapy for MS patients may be a serious future consideration. In this study we measured serum level of trace elements in MS patients referring to neurology clinics of Kashan University of Medical Sciences (KAUMS) in 2004- 2005, and compare it with control group.

Materials and Methods

Thirty-five MS patients with definite diagnosis of MS on the base of clinical examination and MRI guideline and attending at the neurology clinics of Kashan participated in the study after giving written informed consent. Control group was selected from matched people of the same age and sex without diseases affecting serum copper, zinc, and magnesium levels.

Blood samples (2 ml) were taken using a butterfly cannula and were transferred into sterile glass tubes. After centrifugation the serum was transferred into sterile polypropylene tubes. Serum level of the zinc, copper, and magnesium were assayed by autoanalyzer (Zist shimi kit, Tehran).

Statistical analysis was performed using SPSS for Windows (ver.98). For comparing paired clinical data, a paired sample t-test or 2-tailed Wilcox on matched pairs signed-rank test was used. For comparing non-paired clinical data, either an independent samples t-test or a Mann-Whitney U test was used. In all cases $p< 0.05$ was taken as statistically significant.

Results

A cohort of thirty-five MS patients was studied. In this study the most common age group was 20-40, including 22 females (78.5%), and 6 males (21.5%) figure 1. There were 28 females and 7 males. The youngest female patient was 17 years and the oldest 41, the youngest man 28, and the oldest 42, and the mean was 31.6 ± 6.6, and 35.1 ± 4.5 respectively, and the whole mean was 32.3 ± 6.4. There were no significant sex differences in the characteristics of the subjects (independent sample t-test) (p= 0.01).

However, females are involved earlier.

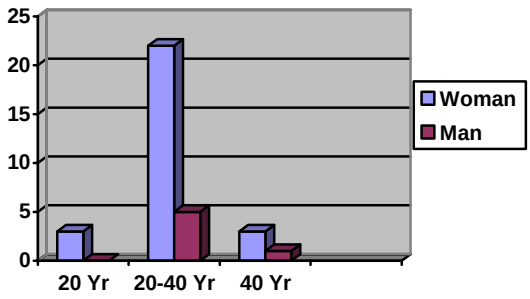

Figure 1: Distribution Of MS patients according to sex and age in MS patients referred to neurology clinics of Kashan 2004-2005

Muscle weakness was found as the most common clinical finding in our patients (80%). Other findings included visual problems in 57.1%, urinary problems in 51.4%, paresthesis in 34.2%, depression in 31.4%, and tremor in 22.8%.

The most common clinical pattern in females was recurrent-remitting MS (60.7%), and in males it was secondarily progressive (42.8%), and as a whole recurrent-remitting pattern was the most common clinical presentation (54.2%).

Table-1: serum magnesium level differences according to sex in MS patients referred to neurology clinics of Kashan 2004-2005

Statistical Characters / Groups Characters		Number	Mean mg X ± SD	P Value
Female	MS Patient	28	1.83 ± 0.36	0.0001
	Healthy	28	2.17 ± 0.23	
Male	MS Patient	7	2.01 ± 0.41	0.0001
	Healthy	7	2.42 ± 0.16	
Total	MS Patient	35	1.87 ± 0.37	0.0001
	Healthy	35	2.22 ± 0.24	

Table-2: serum copper level differences according to sex in MS patients referred to neurology clinics of Kashan 2004-2005

Statistical Characters / Groups Characters		Number	Mean mg X ± SD	P Value
Female	MS Patient	28	111.7± 18.9	0.001
	Healthy	28	136.7 ±13.1	
Male	MS Patient	7	106.2± 20.4	0.001
	Healthy	7	122.1 ±5.7	
Total	MS Patient	35	110.6 ±19.5	0.001
	Healthy	35	133.7±13.4	

Table-3: serum Zinc level differences according to sex in MS patients referred to neurology clinics of Kashan 2004-2005

Statistical Characters / Groups Characters		Number	Mean mg X ± SD	P Value
Female	MS Patient	28	87.2 ±13.6	0.0001
	Healthy	28	110.2 ±7.5	
Male	MS Patient	7	78.5 ±10.5	0.0001
	Healthy	7	109.2 ±10.7	
Total	MS Patient	35	85.4 ±13.5	0.0001
	Healthy	35	110 ± 8.3	

A comparison of the serum magnesium, copper, and zinc levels in control group and MS patient are shown in Tables 1,2,3. Statistical analysis using t-test revealed that the serum magnesium, copper, and zinc levels were significantly lower in MS patients compared to control group ($p<0.001$). The mean serum levels of copper and zinc in female subjects for both groups was significantly higher compared to male ($p<0.001$), but the mean serum levels of magnesium in females for both groups was lower than males ($P<0.0001$).

Discussion

In this study on 35 patients 28 (80%) were female and 7 (20%) male, which shows a 4:1 ratio. In a study by Capston and et al in 1998 in London this ratio was more than 2 (17). In another study by Lotfi and Sanati on 318 MS patients the ratio was 1.5 (18) which different from our findings.

Total mean age of our patients was 32.3 ± 6.4. The mean for females was 31.6 ± 6.6 and for males 35.1 ± 4.5. Twenty eight (80%) of patients were between 20 and 40.

In Capstan's study female patients were 1-2 years younger than males (17). Lotfi and Sanati reported mean age of MS patients 26.6 ± 8.1 (18), and Motamedi and Sahraian reported it 31.8 (13).

In our study muscle weakness was the most common finding found in 80% of cases. Paresthesia (34.2%) among sensory findings, tremor (22.8%) among cerebellar signs, ocular disturbances (57.1%) among brain stem findings, urinary problems (51.4%) among autonomic disturbances, and depression (31.4%) among psychologic presentations were the most common clinical presentations in the patients. Other clinical signs were spasticity in 20%, hyper reflexia in 25.7%, Babinski sign in 22.8%, Hermit's sign in 8.5%, ataxia in 20%, nystagmus in 14.2%, dysarthria in 5.7%, dizziness in 17.1%, and gastrointestinal problems in 37.1%.

Miller in his study reported muscle weakness in 61 to 100 per cent, spasticity in 73 to 100 percent, hyper reflexia in 62 to 95

per cent, visual problems in 27 to 55 per cent, and dizziness in 7 to 27 per cent of cases (19).

Barnes in his study reported ataxia in 37-78%, nystagmus in 54-73%, dysarthria in 29-62%, and tremor in 36- 81% (20). In these studies muscle weakness, visual disturbances, and dizziness are in accord with each other.

In the present study the most common disease pattern is recurrent remitting one in 19 (54.2%) patients which is in accordance with previous studies (1).

In our study the difference of total serum magnesium, copper, and zinc levels between case and control groups were statistically significant as was in both females and males.

Palm et al in their study on 50 MS patients showed that serum zinc and copper levels were lower than their control group (12). In another study Smith et al studied trace elements level in 27 MS patients with and without glucocorticosteroid treatment and compared it with normal persons. Serum zinc level was equal in all groups but red blood cell glutathione peroxidase copper concentration was significantly decreased in MS patients. They concluded that disturbance in zinc and copper homeostasis may be due to the use of steroids in the course of disease, and their replacement may be effective in its treatment (16).

Kapaki and et al in their study measured serum levels of copper, zinc, and magnesium in CSF with atomic absorption spectrophotometry in 74 patients with different neurological diseases and compared it with 28 normal people, and concluded that copper and zinc levels are increased in CSF which may be due to impaired blood brain barrier. Serum level of copper was decreased which is compatible with our findings (15).

Smith et al in their study have stated that deficiency of essential minerals and heavy metals can be dangerous for the health of MS patients. Many different studies have shown low zinc levels and changing copper levels in MS patients (16).

Janson in his study showed that considering higher incidence of MS in females, appearance of MS in adolescence, increased demand of females to copper during menstruation, decreased level of magnesium during menstruation, and need for higher amounts of zinc during rapid growth of girls in adolescence, supplementation of diet with zinc and copper during their adolescence and early young hood may prevent infliction with MS (14).

Motamedi and Sahraian in their 50 patients showed decreased serum level of magnesium compared with control group (13). These are in accord with our findings.

In conclusion the findings of this study and some other previous ones supposes that decreased serum magnesium, cupper, and zinc levels in MS patients may be an important indicator of the disease, and the use of dietary supplements of these trace elements may result in improvement or even prevention of the disease.

Acknowledgments

The authors give their thanks and best regards to Mr. Moosavi, and Mohammad-Yavar, and Dr Mohammad-Yashar Manhoobi for their support for this study.

References

1. Hause SL, Goodlin DE. MS and demyelinating disease. In: Harrison TR, Brawn E, Fauci AS, Kasplel DL, Hauser SL, Longe DL, editors. Harrison`s Principles of Internal Medicine. New York, Mc Craw-Hill; 2005. Vol. 4. p. 2452- 2460.
2. Murphy C, Wetter S. Psychophysiology: Event- related potentials and psychophysics in dementia. In: Hugo AH D,haenen, Johan A den Boer, and Paul Willner, editors. Biological psychiatry. England: Wiley; 2002. p. 295-308.
3. Victor M, Ropper AH. Adam`s and Victor`s Principles of Neurology. New York: Mc Graw- Hill; 2005. p. 954-979.
4. Miller JR. Multiple Sclerosis. In: Rowland LP editor. Merrit`s textbook of neurology. Philadelphia: Lippincott Williams and Wilkins; 2005. p. 773-791.
5. Compston A, Eber G, Lassmann H, Mc Donald I, Wakerle H. Mcalpine`s Multiple

Sclerosis, London: Cherchil Livingstone; 1998. p. 145-495.
6. Killestein J, Rep MHG, Meil JF. Seasonal variations in immune measurements and MRI markers of disease activity in MS. Neurology 2002; 58(7): 1077 – 80.
7. Joffe RT. Neuropsychiatric aspects of multiple sclerosis and other demyelinating disorders. In: Sadock BJ, and Sadock VA, editors. Kaplan and Sadock's Comprehensive textbook of psychiatry. Philadeiphia: Lippincott Williams and Wilkins; 2005. p. 423-425.
8. Fricchion G, El-Chemali, Weilburg JB and Murray GB. Neurology and neurosurgery. In: Wise MG, and Rundell JR, editors. Textbook of consultation-liaison psychiatry. Psychiatry in the medically ill. Washington: American Psychiatric Publishing; 2002. p. 670-700.
9. Sadock BJ, Sadock VA. Concise textbook of clinical psychiatry. Philladelphia: Lippincott Williams and Wilkins; 2004. P 69.
10. Rouchel AM, Pounds R, Tierney JG. Depression. In: Wise MG, and Rundell JR, editors. Textbook of consultation-liaison psychiatry. Psychiatry in the medically ill. Washington: American Psychiatric Publishing; 2002. p. 307-38.
11. Ron MA. Psychiatric aspects of neurological disease. In: Gelder MG, Lopez-Ibor Jr JJ, and Andreasen NC, editors. New Oxford textbook of psychiatry. Oxford: Oxford University Press; 2000. p. 1147-1153.
12. Palm R , Halmans G. Zinc and copper in multiple sclerosis. J Neurol Neurosurg Psychiatry 1982; 45(8): 691-8.
13. Moatamedi M, Sahraian M. Evaluation of serum calcium and magnesium in 50 patients with multiple sclerosis. Iranian journal of Neurology 2003; 3(7): 7-9.
14. Johnson S. The possible role of gradual accumulation of copper , cadmium , lead and Iron and gradual depletion of Zn, Mg, Se, Vit B2, B12, D and E in multiple sclerosis . Am J Forensic Med Pathol 2000; 55(3): 239-41.
15. Kapaki E, Segdista J, Papageorgiou C. Zinc, copper and magnesium concentration in serum and CSF of patients with neurological disorders. Acta Neurol Scand 1989; 79(5):373-8.
16. Smith DK, Feldman EB, Feldman DS. Trace element status in multiple sclerosis. Am J Clin Nutr 1989; 50(1): 136-40.
17. Capston A, Eber SG, Iassman H, Mc Donald I, Mathews B, Wakerle H. Macapline's multiple sclerosis. London: Churchill Livingstone; 1998. p. 145-495.
18. Lotfi J, Sanati MH. Epidemiology of multiple sclerosis . Iranian journal of Neurology 2003; 3(7): 12.
19. Miller JR. Common symptoms and signs in multiple sclerosis. Philadelphia: Black Stone; 1997. p.778-779.
20. Barnes NP, Kent RM, Semlyn JK, Macmullen KM. Spasticity in multiple sclerosis. New Castle: New Castle Academic Unit of Neurological Rehabilitation; 2000-2001.