



# Journal of Medical Sciences

ISSN 1682-4474

**science**  
alert

**ANSI***net*  
an open access publisher  
<http://ansinet.com>

**JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.**

**For further information about this article or if you need reprints, please contact:**

M. Mohammad Shirazi  
No 100, Taghdiri Street,  
Ferdos Blvd,  
Second Sadeqieh Square,  
Post Code 1481777811,  
Tehran, Iran

Tel/Fax: 98-21-88092980

J. Med. Sci., 7 (3): 413-417  
1st April, 2007

## **Dietary Supplementation in Iranian Multiple Sclerosis Patients**

M. Mohammad Shirazi, F.A. Taleban, S.M. Kimiagar and M. Ghafarpoor

The aim of this study was to determine prevalence of dietary supplements consumed by MS patients. This was a descriptive study conducted on 108 MS patients randomly selected from Iranian MS society in Tehran in 2005. Three questionnaires including personal information, disease information and supplement intake were filled out for each patient. Dosage of supplements, frequency, route of administration, regularity and the person who advised supplements were among questions. Then amount of vitamins, minerals and other nutrients ingested through supplements was calculated for each patient. Data was analyzed by SPSS software and student's t-test was used to compare dosage of nutrients with reference values. 93.5% of patients were using dietary supplements and on average each patient was consuming 3.8 types of supplements. Only 31% of the patients were using the supplements regularly and 60% of supplements used were recommended by physicians. Over-consumption of two supplements; thiamin and vitamin E, in over half of the patients were observed. Consumption of vitamins A and D, as well as iron in some patients had reached toxic levels. Frequency of supplement intake in the Iranian MS patients is higher compared to other studies. Considering large number and high dosage of trace elements ingested, it seems prescribing vitamin and mineral supplements in MS patients should be more accurately monitored. Supplementation should be based on the patients' need and amount of trace elements in food to avoid under-or over-consumption.

**Key words:** Multiple sclerosis, supplement, vitamin, mineral, nutrition, Iran

## INTRODUCTION

Multiple Sclerosis (MS) is the most prevalent autoimmune disease of central nervous system, beginning most often in late adolescence. Its clinical manifestations include fatigue, paralysis, numbness of the limbs, visual loss, bladder and bowel dysfunction, dysphagia and psychological disorder. The disease is classified as relapsing-remitting, primary progressive and secondary progressive types according to its course and progression (Victor, 2001). There are more than 40,000 diagnosed MS cases in Iran (Mohseninia, 2004) and the number is increasing. One study in Tehran (capital of Iran) revealed the average age of onset to be 27 years and female to male ratio 2.5 (Kalanie *et al.*, 2003). Another study in Isfahan (a central major city) showed a prevalence of 35.5 per 100000, average age of onset 26 and female to male ratio of 3.6 (Etemadifar *et al.*, 2006).

One well-cited assertion in the literature is that nutritional factors play a role in MS morbidity and mortality (Swank and Dugan, 1990). Nutritional interventions at early stages of the disease, when there is minimal disability, improve disease course and prognosis (Schwarz and Leweling, 2005).

Nutritional recommendations for MS patients include lower intake of total fat especially animal fat and hydrogenated oils. Consuming polyunsaturated fats especially fish oil, sufficient intake of antioxidant rich foods, calcium, cobalamin, vitamin D and dietary fiber is recommended as well (Payne, 2001). Nevertheless intake of vitamin E and other antioxidants, cobalamin, calcium, zinc and dietary fiber in many MS patients is below recommended levels (Hewson *et al.*, 1984; Timmerman and Stuijbergin, 1999).

A balanced diet is the best way to provide dietary needs, yet many MS patients are at risk of malnutrition due to physical disability which affects shopping, cooking and eating. Many of the patients also suffer from anorexia, depression, hand tremor, dysphagia and drug side effects which interfere with their dietary intake (Payne, 2001). Yet, it is doubtful whether MS patients need dietary supplements and there is no algorithm for dietary supplementation in MS patients (Bowling and Stewart, 2003).

Evidence from Germany suggests that 16% of MS patients use dietary supplements (Winterholler *et al.*, 1997). Marrie *et al.* (2003) in a study conducted in Ohio found out that 24% of American MS patients used dietary supplements which had positive correlation with disease severity and duration. Pucci *et al.* (2004) showed that only 12.8% of supplements used by MS patients were recommended by health care professionals and supplement intake had positive correlation with severity of disability. According to Van Der Ploeg *et al.* (1994),

recommendations by friends and relatives were strong incentives for using supplements in MS patients.

There is no published data regarding type and dosage of dietary supplements in MS patients in Iran. The purpose of this study, therefore, was to find out the type and dosage of nutritional supplements consumed by Iranian MS patients.

## MATERIALS AND METHODS

This was a descriptive study conducted on 108 MS subjects randomly selected from Iranian MS society patients' list in Tehran in 2005. The patients were adults of both sexes who had been living in Tehran for at least 10 years. All had a definite diagnosis of relapsing-remitting type of MS for less than 10 years. None was in relapse period or undergoing steroid pulse therapy at the time of investigation. All had an EDSS equal to or less than 5.5 (Expanded Disability Status Scale (EDSS) 1: no disability, 2: minimal disability, 3: moderate disability, 4: relatively severe disability, 5: walking unaided up to 500 m, 6: needs assistance for walking, 7: wheelchair bounded, 8: restricted to bed, 9: helpless and bedridden, 10: death (Hohol *et al.*, 1997).

None was diagnosed to have any other serious medical condition including: cardiovascular diseases, renal or hepatic failure, metabolic or endocrine disorders, cancers and other neuropsychological diseases. None of the women was expecting or nursing a baby.

After the proposal was approved by the Iranian MS society regarding methodology and medical ethics, patients were admitted upon appointments. At the first visit the purpose and method of research was explained in detail and their probable questions were answered individually. Patients were asked to carry their medicines and supplements with themselves. A personal information form, a medical history questionnaire and a supplement intake questionnaire including dosage, route of administration, duration of use, regularity and people who recommended dietary supplements, were filled at the second visit. A food frequency questionnaire and three 24 h recalls were also completed for each patient. The subjects' exposure to sunlight including duration and exposure area was also recorded. Patients were asked to attend the sessions with a partner if unable to answer our questions precisely. Second session was scheduled if patients became exhausted.

To minimize inter-examiner variation, all the questionnaires were filled by the same trained medical doctor.

Data recorded in questionnaires were summarized in data sheets, converted to vitamin and mineral values using standard pharmacopoeia and entered the computer using SPSS software. Mean and standard deviation for

each vitamin and mineral were calculated and compared to Recommended Dietary Allowances (RDA) from Food and Nutrition Board using student's t-test. Pearson correlation was used to check the relationship between quantitative variables. Chi-square test was used for non parametric variables. p-values of below 0.05 were considered significant.

**RESULTS**

Average age of patients was 32 years and average age of disease onset was 27. Female to male ratio was shown to be 3 to one. Characteristics of patients are summarized in Table 1.

93.5% of MS patients who participated in the study were consuming dietary supplements. There were 50 types of dietary supplements including 22 types of vitamins, minerals, amino acids and fatty acids taken by our participants overall. The average number of dietary supplements taken by each patient was 3.80.

6.5% of the patients used no dietary supplements, 46.3% used 3 items or less, 46.3% consumed 4 types or more and 0.9% used 11 types of dietary supplements daily. Route of administration was oral in 63.8%, intramuscular in 0.9% and both in 29.4% of patients. Forty percent of dietary supplements were administered by none professionals. Only 31% of patients consumed their supplements regularly.

The most frequent supplement used by Iranian MS patients was vitamin B1 tablets which was used by 60% of them. Next were vitamin E (55%), Multivitamin (50%), calcium, vitamin D, vitamin B12, vitamin C and Iron.

Mean and standard deviation of nutrients ingested through dietary supplements are shown in Table 2. These values are compared with Recommended Dietary Allowances (RDA) in Table 3 which shows that the intake of vitamin A, thiamin, cobalamin, ascorbic acid and vitamin E through supplements was more than recommended values.

Iron intake was more than that of reference values in 16% of women and within toxic range in 13.6%. Iron consumption in 15% of male participants was more than recommended values. The average calcium intake was 10% of recommended dose in both sexes.

We assessed patients' exposure to sunlight and vitamin D intake was calculated as a combination of sunlight exposure and supplement intake. Seventy five percent of vitamin D was provided by supplements and 25% through sun exposure and the total value was above recommended levels in 60% of participants and within toxic range in 6.5%.

There was a negative correlation between body mass index and number of supplements used ( $r = -0.25$  and  $p = 0.01$ ). Patients' education level was correlated positively with intake of vitamin B12, omega-3 fatty acid and Iron ( $r = 0.22$  and  $p = 0.02$ ,  $r = 0.26$  and  $p = 0.00$ ,

**Table 1: Characteristics of MS patients participated in our study**

Characteristics	Women (N = 82) Mean±SD	Men (N = 26) Mean±SD	Sum Mean±SD
Age (year)	32.15±8.2	33.96±9.1	32.16±8.2
Weight (kg)	61.38±11.45	69.73±10.6	63.39±11.77
Height (m)	1.61±0.16	1.73±0.06	1.63±0.07
Body mass index	23.63±4.39	23.41±3.50	23.60±4.18
Disease duration (year)	4.45±2.7	3.85±2.5	4.31±2.65

**Table 2: Mean, SD, minimum and maximum of nutrients taken through supplements**

Nutrients	Mean	Standard deviation	Minimum	Maximum
Vitamin A (IU)	1214.17	3063.73	0	30916.67
Thiamin (mg)	82.94	131.58	0	600.00
Riboflavin (mg)	0.67	1.33	0	8.63
Pyridoxine (mg)	1.64	4.60	0	40.00
Folic acid (mcg)	190.43	417.31	0	2200.00
Cobalamin (mcg)	3.58	6.74	0	33.33
Nicotinamide (mg)	5.33	9.31	0	50.00
Biotin (mcg)	2.32	9.70	0	45.00
Pantothenic acid (mg)	0.58	2.24	0	11.00
Ascorbic acid (mg)	91.63	225.00	0	1400.00
Vitamin D (IU)	637.34	2158.00	0	14285.70
Vitamin E (IU)	69.44	115.58	0	475.00
Calcium (mg)	111.27	183.93	0	675.00
Magnesium (mg)	7.67	23.14	0	100.00
Iron (mg)	10.14	25.26	0	120.00
Copper (mg)	0.12	0.44	0	2.00
Zinc (mg)	0.0093	0.067	0	0.50
Phosphorus (mg)	6.80	27.09	0	125.00
Iodine (mcg)	11.02	37.66	0	150.00
Omega 3 fatty acid (mg)	38.55	129.71	0	875.00
Dietary fiber (g)	0.56	3.51	0	35.00

Table 3: Comparison of nutrient intake only through dietary supplements with recommended values

Nutrients	Less than recommended (%)	More than recommended (%)	In toxic level (%)
Vitamin A*	83.8	15.29	0.9
Thiamin*	38.9	61.10	0.0
Pyridoxine*	74.1	25.90	0.0
Folic acid*	88.9	4.60	6.5
Cobalamin*	69.4	30.60	0.0
Ascorbic acid*	73.1	26.90	0.0
Vitamin D <sup>+</sup>	70.4	23.10	6.5
Vitamin E*	50.0	50.00	0.0
Calcium <sup>++</sup>	100.0	0.00	0.0
Iron in women <sup>++</sup>	84.0	2.50	13.6
Iron in men <sup>++</sup>	85.2	14.80	0.0

\* values are compared with RDA; + values are compared with AI; ++ values are compared with DRI

r = 0.22 and p = 0.02, respectively). No relationship was found between regularity of supplement intake and disease severity or patients characteristics.

Patients who consumed less supplements and who were suggested to use it by professionals, ingested their dietary supplements more regularly (p = 0.000 and p = 0.000, respectively).

### DISCUSSION

This study showed that over 90% of the MS patients take at least one form of supplements. Winterholler *et al.* (1997) reported that 16% of MS patients in Germany consumed dietary supplements while Marrie *et al.* (2003) reported less than a quarter of patients taking supplements in the United States. Sixty percent of the supplements in present study were recommended by health care workers versus 12.8% in Pucci *et al.* (2004) study. Our data shows that frequency of supplement intake in Iranian MS patients is relatively high and that patients prefer to be advised by a professional.

Forty seven percent of patients consumed 4 or more items of dietary supplements daily. By adding different types of medications used to control MS complications, it becomes a high number of medications. Only 31% of our patients consumed their supplements regularly. Polypharmacy is a known reason for decreased compliance of patient and irregularity in medication usage (McFrath, 1999).

The intake of vitamin A, thiamin, cobalamin, ascorbic acid and vitamin E from supplements alone was more than recommended. The most frequent supplement used by our patients was thiamin which enjoys the least scientific documents to be beneficial in MS patients (Geny *et al.*, 1992). There is evidence that excessive intake of vitamin A may lead to limb pain, anorexia and fatigue. High intake of ascorbic acid leads to gastrointestinal disturbances and diarrhea (Gallagher, 2004). It seems that overdosing some micronutrients can mimic MS symptoms.

Iron intake was more than recommended in 16% of women and 15% of men. Excessive intake of iron leads to

oxidative stress which has a known role in pathogenesis of autoimmune diseases specially MS (Koch *et al.*, 2005; Zhang *et al.*, 2005). Average calcium intake by our patients was 10% of recommended dose; MS patients are more susceptible to osteoporosis due to low physical activity, steroid therapy and other factors (Shabas and Weinreb, 2000; Weinstock *et al.*, 2004), therefore sufficient consumption of calcium through diet or supplements is justified.

Only 17% of our patients consume omega-3 fatty acids. Some research suggests that omega-3 fatty acids are beneficial in MS patients as they stimulate production of anti inflammatory cytokines (Nordvik, 2000; Warner, 1997). Therefore it seems prudent to take more omega-3 fatty acids through diet or dietary supplements.

Regularity of supplement intake was related to the number of supplements and also to the person who advised them, i.e., patients who consumed less supplements and were advised by a physician, used it more regularly. It seems the best course would be to educate the patients to take supplements only on the advice of professionals while the physicians should be encouraged to prescribe supplements only when needed and preferably in combination rather than several separate supplements. Certain nutrients should be assessed before prescribing dietary supplements to avoid under- or over-dosage.

### RECOMMENDATIONS

In summary, as MS patients are susceptible to inadequate intake of nutrients due to physical disability, dysphagia, hand tremor, anorexia and side effects of medications, they may take advantage of dietary supplements. However supplements used by these patients should be monitored. We recommend that supplements be prescribed by professionals and according to scientific documents. Also the patients' personal need should be estimated according to their nutritional intake and disease condition so that both malnutrition and over-dosage be prevented. It seems some kind of supplements which provide various types of vitamins and minerals are justified in order to avoid polypharmacy which can reduce compliance. Patients should be encouraged to take professional advice and to take their supplements exactly as prescribed. Further research is necessary to assess efficacy and long term effects of dietary supplementation in MS patients.

### ACKNOWLEDGMENT

The authors would like to thank Iranian MS Society staff for their assistance and support and MS patients for their active participation.

**REFERENCES**

- Bowling, A.C. and T.M. Stewart, 2003. Current complementary and alternative therapies for multiple sclerosis. *Curr. Treat Options Neurol.*, 5: 55-68.
- Etemadifar, M., M. Janghorbani, V. Shaygannejad and F. Ashtari, 2006. Prevalence of multiple sclerosis in Isfahan, Iran. *Neuroepidemiology*, 27: 39-44.
- Food and Nutrition Board, Institute of Medicine, National Academies. <http://www.iom.edu/CMS/3788/21370.aspx>
- Gallagher, M.L., 2004. Vitamins. In: *Nutrition and Diet Therapy*. L.K., Mahan Escott-Stump, S. Krause's Food, 11th Edn., Philadelphia. Saunders, pp: 75-120.
- Geny, C., P.F. Poradat, J. Yulis, S. Walter, D. Cesaro and J.D. Degos, 1992. Hypothermia, multiple sclerosis, wernicke encephalopathy. *Acta Neurol. Scand*, 86: 632-634.
- Hewson, D.C., M.A. Philips, K.E. Simpson, P. Drury and M.A. Crawford, 1984. Food intake in multiple sclerosis. *Hum. Nutr. Applied Nutr.*, 38A: 355-367.
- Hohol, M.J., C.R. Guttmann, J. Orav, G.A. Mackin, R. Kikinis, S.J. Khoury, F.A. Jolesz and H.L. Weiner, 1997. Serial neuropsychological assessment and magnetic resonance imaging analysis in multiple sclerosis. *Arch. Neurol.*, 54: 1018-1025.
- Kalanie, H., K. Gharagozli and A.R. Kalani, 2003. Multiple Sclerosis: Report on 200 cases from Iran, 2003. *Mult. Scler.*, 9: 36-38.
- Koch, M.W., G.S. Ramsaransing, A.V. Arutjunyan, M. Stepanov, A. Teelken, D.J. Heersema and J. De Keyser, 2005. Oxidative stress in serum and peripheral blood leukocytes in patients with different disease courses of multiple sclerosis. *J. Neurol.*, 14: 120-126.
- Marrie, R.A., O. Hadjimichael and T. Vollmer, 2003. Predictors of alternative medicine use by multiple sclerosis patients. *Mult. Scler.*, 9: 461-466.
- McFrath, 1999. Physicians' perspectives on communicating prescription drug information. *Qual. Health Res.*, 9: 731-745.
- Mohseninia, M., 2004. Multiple sclerosis in Iran. *J. Iranian MS Soc.*, 2: 47-50.
- Nordvik, I., 2000. Effect of dietary advice and N-3 supplementation in newly diagnosed MS patients. *Acta Neurol. Scand*, 102: 143-149.
- Payne, A., 2001. Nutrition and diet in clinical management of M.S. *J. Hum. Nutr. Diet.*, 14: 349-360.
- Pucci, E., E. Cartechini, C. Taus and G. Giuliani, 2004. Why physicians need to look more closely at the use of complementary and alternative medicine by multiple sclerosis patients. *Eur. J. Neur.*, 11: 263-267.
- Schwarz, S. and H. Leweling, 2005. Multiple sclerosis and nutrition. *Mult. Scler.*, 11: 24-32.
- Shabas, D. and H. Weinreb, 2000. Preventive healthcare in women with multiple sclerosis. *J. Womens Health Gend Based Med.*, 9: 389-395.
- Swank, R.L. and B.B. Dugan, 1990. Effect of low saturated fat diet in early and late cases of multiple sclerosis. *Lancet*, 336: 37-39.
- Timmerman, G.M. and A.K. Stuijbergin, 1999. Eating patterns in women with multiple sclerosis. *J. Neur. Nurs.*, 31: 152-158.
- Van der Ploeg, H.M., M.J. Molennar and C.W. Van Tiggelen, 1994. Use of alternative treatments by patients with multiple sclerosis. *Ned. Tijdschr Geneesk.*, 138: 296-299.
- Victor, M., 2001. Multiple Sclerosis and Related Demyelinative Diseases. In: *Adams and Victor's Manual of Neurol.* Victor, M., A.H. Ropper. 7th Edn., USA. Mcgraw-Hill, pp: 332-335.
- Warner, R., 1997. The ratio of dietary N-6 to N-3 fatty acids influences immune system function, eicosanoid metabolism. *J. Nutr.*, 127: 1198-1205.
- Weinstock-Guttman, B., E. Gallagher, M. Baier, L. Green, J. Feichter, K. Patrick, C. Miller, K. Wrest and M. Ramanathan, 2004. Risk of bone loss in men with multiple sclerosis. *Mult. Scler.*, 10: 170-175.
- Winterholler, M., F. Erbguth and B. Neundoerfer, 1997. The use of alternative medicine by multiple sclerosis patients-patient characteristics and patterns of use. *Fortschr Neurol. Psychiatr.*, 65: 555-561.
- Zhang, X., M. Haaf, B. Todorich, E. Grosstephan, H. Schieremberg, N. Surguladze and J.R. Connor, 2005. Cytokine toxicity to oligodendrocyte precursors is mediated by Iron. *Glia*, 52: 199-208.