

Short Communication

Relationship between homocystein blood level and multiple sclerosis

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Multiple sclerosis which is identified by the triad of inflammation, demyelination, and gliosis, is a chronic disease beginning early in adulthood. It is a disease of time and place, meaning involves different locations in different time intervals, and results in a variability of symptoms and signs including visual complains, motor weakness, and cerebellar problems. Although the main cause of the disease is unknown, however, induced autoimmune responses, particularly in a compromised genetic background, to some environmental factors are well known causes for it. The effect of serum homocystein on this disease is the focus of many recent studies. In this study we have assessed serum homocystein level in normal and patients with multiple sclerosis in Kashan in 2007. This case controlled study has carried on 26 cases of multiple sclerosis (MS) and 26 normal cases referred to Neurology Clinics in Kashan. After obtaining informed consent form from the enrolled cases, data including age, sex, history of hypertension, cardiac or cerebral vascular attacks, TIA, and Parkinson were recorded and matched in the groups. Two cubic centimeters (cc) of venous blood obtained from each person and sent for measurement of serum homocystein with HP_LC method. The obtained data were analyzed with T test, Chi Square test, and Odds Ratio. In each group there were 21(81%) female and 5 (19%) males. The age range of 20 to 29 with 10 cases (38%) was commonest category in both groups. Mean homocystein level in MS group was $9.22 \pm 3.58 \mu\text{m/dl}$ and in normal group was $6.93 \pm 6.03 \mu\text{m/dl}$. It was $8.07 \pm 5.04 \mu\text{m/dl}$ for all of the cases. There is a significant difference between seum level of case group with that of normals ($P < 0.05$). The highest level of homocystein was $33 \mu\text{m/dl}$ in a normal 30 year old female and the least amount was zero in a diseased 39 year old female. Mean age for case group was 34.73 ± 8.46 and 34.53 ± 7.51 in controls. It was 34.62 ± 7.93 for the whole cases. There was no significant difference in age between the groups ($P > 0.005$). Higher levels of homocystein in patients with MS in comparison with their normal counterparts may be a clue to a relationship useful in control of the disease progress or flare ups.

Key words: Homocystein, multiple sclerosis.

INTRODUCTION

Multiple sclerosis is a chronic disease starting in young adulthood stage (Harrison principles of medicine, 2005), identified with the triad of inflammation, demyelination, and gliosis (Merritt's Neurology, 2005). It has a wide range of clinical manifestations including visual impairment, motor disturbances, sensory problems as burning or tingling, tremor, tiredness and so on (Harrison principles of medicine, 2005; Merritt's Neurology, 2005). More than 350,000 Americans and 1,100,000 people worldwide are involved with MS. After head injury it is the second

neurologic debilitating disease of young adults in Western countries (Merritt's Neurology, 2005).

Although no definite mechanism is determined for the disease but overt reaction of the immune system to environmental factors is a well known causing factor (Harrison principles of medicine, 2005; Merritt's Neurology, 2005). There is a relationship between increased serum level of homocystein and some neurodegenerative diseases, and such a correlation for MS is under scrutina-zation (Ramsaransing et al., 2005; Shering and Robertson, 2006; Denton and Sandare, 1999; Besler and Comoglu, 2003; Russo et al., 2003; Baig et al., 1995; Reynolds, 2006; Tajouril et al., 2006).

Ramsaransing et al. in 2006 with the concept of corre-

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Table 1. Age and sex distribution of contributors to the study.

Sex	Female		Male		Total
	MS (%)	Normal (%)	MS (%)	Normal (%)	
20 to 29	9 (35)	9 (35)	1 (3)	1 (3)	20 (38)
30 to 39	7 (27)	7 (27)	2 (8)	2 (8)	18 (35)
40 to 49	4 (16)	4 (16)	2 (8)	2 (8)	12 (24)
>50	1 (3)	1 (3)	0	0	2 (3)
Total	21 (81)	21 (81)	5 (19)	5 (19)	52 (100)

Table 2. Serum homocystein level in contributors to the study.

Homocystein level groups	<5 $\mu\text{m/dl}$ (%)	5 to 15 $\mu\text{m/dl}$ (%)	15 $\mu\text{m/dl}$ (%)	Total (%)
MS Group	3 (12)	23 (88)	0	26 (100)
Normal Group	10 (38)	15 (58)	1 (4)	26 (100)
Total	13 (25)	38 (73)	1 (2)	52 (100)

lation between high homocystein level and neurodegenerative diseases tried to find the cause of increased homocystein level and its effect on MS by measurement of serum homocystein in 88 patients with the disease and 57 normal cases. It was found that mean plasma level of homocystein was higher in MS patients in comparison with normal cases. There was no difference between the patients with silent disease, primary or secondary progression (Ramsaransing et al., 2005).

Denton and Sandare in 1999 showed a relationship between serum homocystein level and MS (Denton and Sandare, 1999).

Besler and Comoglu in 1993 showed increased serum homocystein level in active phase of the disease in those with low level of serum folate and vitamin B12 although it was not significant in comparison with normal cases (Besler and Comoglu, 2003).

Russo et al. in 2003 showed hypercysteinemia in 60% of patients with MS (Russo et al., 2003). In their study Baig et al. (1995) found increased plasma level of cobalamin and homocystein in MS patients. The increased homocystein plasma level was associated with significantly decreased vitamin B12 level both in serum and CSF ($P < 0.001$). It was concluded that decreased serum B12 level will result in elevated plasma homocystein (Baig et al., 1995).

These controversial findings made us to carry a study about the possible role of homocystein in prevention, diagnosis, and even treatment of multiple sclerosis patients in Kashan.

MATERIALS AND METHODS

In this case controlled study all the patients referring to neurology clinics of Shahid Beheshti university hospital and private clinics and had the diagnosis of multiple sclerosis (MS) enrolled to the study as case group and matched normal people without history of cerebrovascular accidents, TIAs, hypertension, myocardial infarction, Par-

kinson, as well as those without history of use of drugs that increase serum homocystein level e.g., anti-epileptic drugs, isoniazide, methotrexate, and nitrous oxide were enrolled and assigned as control group from 2007 - 2008. After completion and signing of an informed consent form including age and sex, 2cc clotted venous blood from each person was obtained and assessed with HPLC technique for its homocystein level. Homocystein level was considered normal between 5 and 15 $\mu\text{m/dl}$, and those above or below this range were considered abnormal. Data were analyzed using chi square and T tests, and confidence interval was determined with the use of Odds ratio.

RESULTS

Twenty one (81%) out of 26 patients with MS was female, and most of the patients (38%) were in range of 20 - 29 year old. Age and sex distribution of both groups is brought in Table 1. Mean age of MS patients was 34.73 ± 8.46 and that of control group 34.53 ± 7.51 . There was no difference between the groups ($P = 1$). Table 2 shows concentration of serum homocystein in the two groups. The mean serum level of homocystein in MS group was 9.22 ± 3.58 $\mu\text{m/dl}$, and in control group 6.93 ± 6.03 $\mu\text{m/dl}$. This difference was statistically significant ($P < 0.05$).

DISCUSSION AND CONCLUSION

In this study serum homocystein level was significantly higher than the normal group (9.22 ± 3.58 $\mu\text{m/dl}$ in comparison with 6.93 ± 6.03 $\mu\text{m/dl}$). Ramsaransing et al. (2006) and Russo et al. (2003) have shown the same difference in their study. In the former study the difference was not significant in active phase of the disease. In Besler study in spite of higher level of homocystein in MS patients and its correlation with lower levels of vitamin B12 and folate the difference in the groups was not statically significant (Besler and Comoglu, 2003). Baig in his study showed higher levels of homocystein both in CSF and plasma in MS patients (Baig et al., 1995).

In conclusion, although there are clues in favor of a correlation between serum level of homocystein and multiple

sclerosis which may hopefully be used for prediction and even treatment of the disease, however the scanty number of patients in the available studies, and weak difference in the groups in some of them mandates cautious approach to this finding and the need for more scrutinized researches with larger number of patients allocated to them.

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