Research Article

Status of serum magnesium levels in human T-cell lymphotropic virus Type 1 infected patients: A pilot study

Farnaz Zahedi Avval[1], Majid Khadem-Rezaiyan[2], Zohreh Agheltar[1], Masoud Youssefi[3,4]

[1]Department of Clinical Biochemistry, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran, [2]Department of Community Medicine and Public Health, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran, [3]Department of Microbiology and Virology, School of Medicine, Mashhad University of Medical Science, Mashhad, Iran, [4]Antimicrobial Resistance Research Center, Bu-Ali Research Institute, Mashhad University of Medical Science, Mashhad, Iran

Correspondence to: Masoud Youssefi, E-mail: youssefim@mums.ac.ir

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ABSTRACT

Background: Some mineral changes have been reported in chronic viral infections such as human immunodeficiency virus, hepatitis B virus, and hepatitis C virus. We have recently reported higher magnesium (Mg) levels in adult T-cell leukemia cases, a malignancy related to human T-cell lymphotropic virus Type 1 (HTLV-1). We expanded the study of HTLV-1 infected asymptomatic individuals as well as HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP) patients. **Objectives:** To evaluate the serum levels of Mg in HTLV-1 carriers and HAM/TSP cases. **Materials and Methods:** A cross-sectional was carried out at Mashhad blood transfusion and the Department of Neurology in Ghaem Hospital. A total of 16 symptomatic patients with HAM/TSP and 22 asymptomatic HTLV-1 carriers were enrolled. Blood samples were taken to measure serum Mg. Data analysis was performed with SPSS version 11.5. **Results:** The mean Mg in HAM/TSP was significantly higher than normal ranges. Furthermore, Mg was higher in HTLV-1 carriers than normal values. No significant difference was observed between the two groups. **Conclusion:** An increased Mg level was seen in both HTLV-1 carriers and HAM/TSP patients, though further studies should be performed with larger sample size among HTLV-1 patients.

KEY WORDS: Human T-cell Lymphotropic Virus Type 1; Magnesium; Human T-cell Lymphotropic Virus Type 1 Associated Myelopathy/tropical Spastic Paraparesis; Minerals; Serum

INTRODUCTION

It is estimated that 15-20 million people worldwide are infected with human T-cell lymphotropic virus (HTLV-1), the first identified human retrovirus.[1] However, illnesses related to the virus are manifested in only ~8% of the infected individuals, and the majority of HTLV-1 positive cases remain asymptomatic carriers. In about 3-4% of patients, the integrated proviral DNA or the virally encoded proteins cause CD4 cell or T-helper lymphocyte lymphoproliferative disease that may result in adult T-cell leukemia (ATL).[2,3] Another main complication which is seen in about 3% of infected individuals is a myelopathy known as HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP) which is believed to be mainly due to severe cytokine and cytopathic responses to the infected cells within the spinal cord.[4,5] In addition to these two most important complications, some other minor illnesses including uveitis, arthritis, and polymyositis has also been reported to be associated with the virus.[6,7]

Mineral changes have been reported in some chronic viral infections including viral hepatitis,[8,9] as well as the other retrovirus, human immunodeficiency virus (HIV).[10] Among

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various minerals, magnesium (Mg) level has been particularly shown to be depleted in HIV patients.[11]

HTLV-1 is an endemic infection and, therefore, one of the main health problems in Mashhad/Northeastern Iran[12-14] wherein this study was conducted. It is noteworthy that there is not still a global consensus guideline for the management of HTLV-1 infected patients, and any possible underlying mineral imbalance might be ignored in such patients which may affect the overall health condition of the patients. Serum Mg changes in a few cases of ATL, a malignancy related to HTLV-1 has been reported.[15] Due to the lack of studies on the mineral levels status in HTLV-1 patients, this study was performed to explore the laboratory findings in HTLV-1 asymptomatic carriers as well as HAM/TSP patients.

MATERIALS AND METHODS

Samples

This cross-sectional study was done in 2014. Convenience/availability sampling was performed from patients with the positive HTLV-1 test in Mashhad blood transfusion center who accepted to participate in the study. All HTLV-1 positive patients were confirmed by western blot analysis. Furthermore, HAM/TSP patients referred to the Department of Neurology in Ghaem University Hospital were included. A total of 16 symptomatic patients with HAM/TSP and 22 asymptomatic HTLV-1 carriers were finally enrolled into the study. Blood samples were taken to measure Mg. Mg was measured with usual photometric methods.

Ethical Considerations

Written informed consent was obtained from all participants. The study was reviewed and approved by Ethical Committee of Mashhad University of Medical Sciences (Ref. No.: 900796).

Statistics

Data analysis was performed with SPSS version 11.5. The comparison between the HAM/TSP and carrier groups was performed using Student's *t*-test. The significance level as <0.05 was considered in all calculations.

RESULTS

Among all participants, 69% (11 out of 16) of HAM/TSP patients, and 14% (3 out of 22) of carriers were females ($P = 0.001$). The mean age of patients with HAM/TSP and carriers were 48.5 ± 11 and 39.1 ± 7.7 years, respectively ($P = 0.007$).

The mean levels of Mg (mg/dl) in HAM/TSP (2.28 ± 0.22) was significantly higher than normal range announced by UpToDate (1.7-2.2) ($P < 0.001$). Furthermore, Mg was higher in HTLV-1 carriers (2.39 ± 0.25) than normal range ($P < 0.001$). We did not observe any significant difference in Mg between HAM/TSP and HTLV-1 carriers.

DISCUSSION

This study was performed on 38 individuals infected with HTLV-1 of which 16 were HAM/TSP patients. The proportion of females was higher in HAM/TSP patients than carriers which are consistent with previous reports.[16] The mean age of patients with HAM/TSP was higher than the carriers which might be due to the time interval between infection and initiation of neurologic complication.

The amount of Mg in HAM/TSP and HTLV-1 carriers was significantly higher than the normal population although Mg level was not significantly different in the two groups. We cannot comment on higher Mg in these patients, though one might assume whether higher intracellular Mg might affect the serum levels, though it seems unlikely that such intracellular accumulation could entirely explain the higher observed Mg serum level.

In vitro studies have shown intracellular accumulation of another mineral, Ca in HTLV-1 infected lymphocytes.[17] Studies on the levels of minerals and some related hormones during HIV infections have shown that the concentration of free Mg in lymphocytes is linked with proper activity of the viral reverse transcriptase enzyme.[18] Moreover, some other mineral changes including depleted Ca and increased parathyroid hormone (PTH) have been reported among HIV-infected individuals.[11] It has been proposed that vitamin D depletion in HIV patients may play a major role in Ca deficiency and thereby PTH increase but the mechanism of vitamin D depletion *per se* among HIV patients remains unclear.[11,19] Although the exact mechanism behind such mineral changes in HIV patients, still is not entirely understood, it has been proposed that cytokines and inflammatory responses may contribute to such observed mineral changes.[20] During HTLV-1 infection particularly in HAM/TSP patients, a notable immune response is observed.[21-23] Furthermore, changes in serum levels of selenium, zinc, and Mg minerals in HIV-infected patients have been previously reported.[24] We observed higher Mg concentrations in both HTLV-1 carriers and HAM/TSP patients. Although, the exact mechanism of such observed mineral changes remains to be fully explored.

The main limitation of this study that should be noted is that the study was performed on a rather small number of included patients and further studies with preferably larger sample size should be carried out to establish these findings.

CONCLUSION

Mg was significantly higher in HAM/TSP and HTLV-1 carriers than normal ranges. Such accumulating reports

might indicate a diagnostic or management protocol considering possible minerals changes in such patients. Furthermore, additional investigations are needed to explore possible mechanism behind higher Mg levels during HTLV-1 infection.

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