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Original Article

Investigation of Biochemical Factors in Multiple Sclerosis Patients With Fingolimod and Natalizumab Drugs

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Abstract

Background: Multiple sclerosis (MS) is a chronic inflammatory disease that demyelinates the central nervous system. Myelin, a two-layer lipid membrane around axons, is responsible for signaling and nerve impulse transmission. Fingolimod as the first oral treatment for MS patients is fingolimod. This drug reduces magnetic resonance imaging (MRI) activity and relapse rate by preventing the migration of T cells from the secondary lymphoid organs into the blood circulation. This study aimed to evaluate biochemical factors in MS patients.

Methods: A total of 30 MS patients who applied for the MS clinic of Imam Reza hospital (Tabriz-Iran) were chosen for this study. The patients were divided into three groups, including the MS group, MS + Fingolimod, and MS + Natalizumab. For measuring the erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hs-CRP), and neurofilament light chain (NfL) factors, all samples were thawed, processed, and assayed with immunoassay kits.

Results: The NfL level decreased for both natalizumab and fingolimod groups compared with the MS group ($P<0.0001$). Likewise, the ESR level decreased in the fingolimod group more than in the natalizumab group ($P<0.0001$). In addition, the CRP level decreased in the fingolimod and natalizumab group compared with the MS group ($P<0.0001$).

Conclusion: Based on the obtained results it can be concluded that the level of ESR and NfL is high in MS patients, but natalizumab and fingolimod decrease these biochemical factors in MS patients.

Keywords: Multiple sclerosis, Natalizumab, Fingolimod

Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease that demyelinates the central nervous system. Myelin, a two-layer lipid membrane around axons, is responsible for signaling and nerve impulse transmission. Myelin protects the axon from harmful external factors and enhances the transmission of electrical impulses. Optic nerves, brain, and spinal cord are involved in MS patients. The most important symptoms of MS include fatigue, numbness, muscle spasms, mobility and vision problems, loss of balance, acute paralysis, tremor, as well as thinking, learning, and planning problems. The first symptoms of MS appear between the ages of 20 and 40. Diagnosing MS is difficult due to the wide variety of its symptoms. Studies show that major histocompatibility complex genes play a role in MS along with environmental factors. The prevalence of MS is increasing in developed and developing countries.[1-4] Previously, the only drugs available to treat MS were steroids, but today new compounds have been approved to deal with the course of the disease and improve the individual's condition. Identifying the best treatment and drug for MS patients can be difficult; accordingly, the clinical presentation of the patient is extremely important for choosing the right treatment. For the relapsing-remitting form of MS, three types of drugs are recommended such as selective immunosuppressive agents, disease-modifying agents, and recently approved drugs.[5-7] Natalizumab is the first monoclonal antibody approved for the treatment of MS.[8-10] This drug reduces the relapse rate of the disease by preventing lymphocytes from entering the central nervous system.[11-15] Progressive multifocal leukoencephalopathy is the main complication of natalizumab treatment.[16-19] Moreover, the first oral treatment for MS patients is fingolimod. This drug reduces magnetic resonance imaging (MRI) activity and relapse rate by preventing the migration of T cells from the secondary lymphoid organs into the blood circulation.[20-22] Bradycardia, increased risk of infection, leukopenia, increased risk of skin cancer, macular edema, and liver dysfunction are some of the side effects of fingolimod.[23] Furthermore, in one clinical trial, a decrease in brain volume was observed in patients who received the drug compared to the placebo.[24-28] This study aimed to investigate the expression of the biochemical

factors in patients who take MS drugs.

Materials and Methods

Patients and Samples

A total of 30 MS patients who applied for the MS clinic of Imam Reza hospital in Tabriz, Iran, were chosen for this study. The patients were allocated into three groups (n = 10), including the MS group, MS + Fingolimod, and MS + Natalizumab. The 10 cc of whole blood was taken and centrifuged. For measuring the erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hs-CRP), and neurofilament light chain (NfL) factors, all samples were thawed, processed, and assayed with immunoassay kits. Inclusion criteria were patients who were treated with fingolimod and natalizumab. The exclusion criteria were patients who had a chronic disease such as diabetes and patients who were treated with other MS drugs.

Data Analysis

The GraphPad Prism 6 software was used for data analysis. The *t* test was used for statically significant analysis ($P < 0.0001$) of the data.

Results

The results of NfL levels indicated that NfL levels in MS patients were higher than those in the control group and the drugs group. Moreover, the result showed that natalizumab can decrease the NfL level more compared to fingolimod (Figure 1A). Furthermore, the ESR level in MS patients was high than that in other groups. In addition, the results of the present study indicated no significant difference between the natalizumab and fingolimod groups, but the ESR level in both groups was lower than that in the MS group (Figure 1B). The findings regarding CRP levels also revealed the same results as NfL and ESR levels (Figure 1C).

Discussion

As discussed earlier biochemical factors affect brain lipids which are related to a person's nutrition.[29-37] Previous studies have focused on understanding the value of NfL measurements in MS by combining conventional MRI measurements and clinical data with NfL in the blood and/or cerebrospinal fluid.[38-46]

Another factor that can be effective is nitric oxide. There is a lot of evidence suggesting that nitric oxide can play a role in MS. This substance is also effective in various aspects of MS such as synaptic transmission, inflammation, axonal degeneration, and neuron loss. However, the exact mechanism for this disease has not yet been discovered, and there are many uncertainties in this regard. Further, there is still a long way to prevent damage to neurons through this substance.[47-51]

The other biochemical factor for MS is uric acid. It is a natural peroxynitrite scavenger, which can be relevant to MS. This chemical is believed to damage myelin and axon of neurons in inflammatory MS lesions. It is believed that the low level of serum uric acid in MS patients is due to the activity of the inflammatory disease and is not related to primary deficiency. Additionally, serum uric acid level can be a good indicator to monitor disease activity.

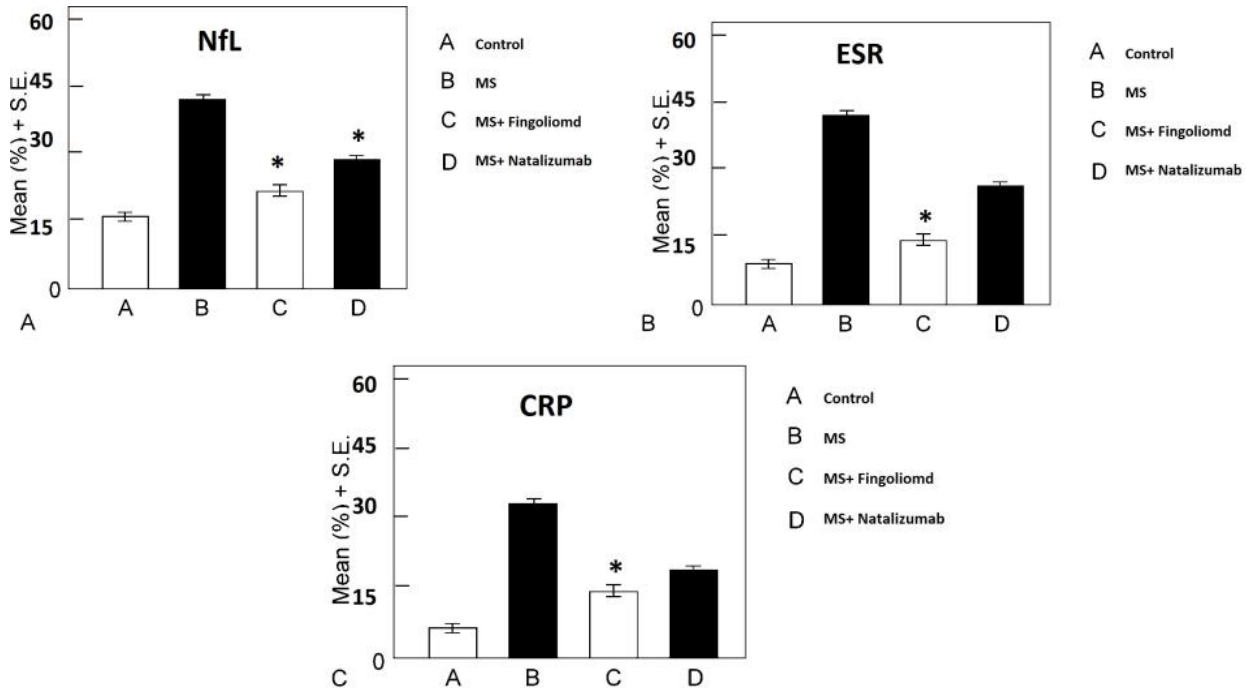

Figure 1. The Biochemical Marker Levels in MS Patients: (A) The NfL level decreased in the natalizumab and fingolimod groups compared with the MS group ($P < 0.0001$); (B) The ESR level decreased in the fingolimod group more the than in natalizumab group ($P < 0.0001$); (C) The CRP level decreased in fingolimod and natalizumab groups compared with MS group ($P < 0.0001$)

Note. MS: Multiple sclerosis; NfL: Neurofilament light chain; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

Therefore, increasing the serum level of uric acid can be a suitable measure for MS patients.[52]

It can be concluded that the level of ESR and NfL is high in MS patients, but natalizumab and fingolimod decrease these biochemical factors in MS patients.

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Authors' Contribution

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Ethical Approval

The study was approved by the the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1401.459).

Competing Interests

None.

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