ABSTRACT

Introduction

Multiple sclerosis (MS) is a chronic inflammatory demyelinating and neurodegenerative disease affecting the central nervous system. Although research on the diagnosis and treatment of this serious illness has made significant advances, the MS etiology remains unknown. Although there is still much to be found in the MS pathogenetic mechanisms, understanding the mechanisms of immune-mediated damage to the central nervous system (CNS) components of MS allows not only the introduction of new drugs that positively modulate inflammatory inflammation but also the understanding of immune-mediated diseases affecting the CNS in a broader sense.

Methods

The Ph.D. thesis is a general introduction followed by an annotated set of author's publications on proteomics, lymphocytic population in MS and disability. Study 1: Proteomic analysis of cerebrospinal fluid for relapsing-remitting multiple sclerosis and clinically isolated syndrome was conducted to find changes in the low molecular cerebrospinal fluid (CSF) segment and to determine what native peptides and how much they are in cerebrospinal fluid among patients with clinically isolated syndrome (CIS) and relapsing-MS (RR MS) compared to a healthy population. Study 2: Lymphocytes in the treatment with interferon beta-1b targeted individual lymphocyte populations in MS patients with CIS or RR MS in order to detect the signs that are affected in patients treated with interferon beta. Study 3: Lymphocyte populations and their change during a five-year glatiramer acetate treatment were targeted at individual lymphocyte populations in patients with MS (CIS and RR MS) in order to detect the signs that are affected in patients treated with glatiramer acetate (GA). Study 4: Comparing the efficacy of subcutaneously administered interferon beta-1a and 44 μg, dimethyl fumarate and fingolimod in real clinical practice, a multicenter observational study compared the efficacy of subcutaneously administered interferon beta-1a 44 μg, dimethyl fumarate (DMF) and fingolimod in RR MS patients who started this treatment within 90 days of the onset of relapse in real clinical practice in the Czech Republic.

Results

In study 1, we identified a total of 26 proteins that were changed against healthy controls. In study 2, we demonstrated a significant decrease in the level of significance of 1% in absolute and relative values of CD69 protein, absolute and relative values of CD8 lymphocytes, total leukocyte count, and natural killers. A significant decrease in 5% significance was found in absolute lymphocytes, relative CD4 lymphocyte values, relative CD3+/CD69+ cell counts and CD8+/CD38+ cell absolute values. In study 3, we demonstrated a decrease in both absolute and relative CD3+/CD69+ cell values, absolute and relative CD69 protein values, relative CD8+/ CD38+ cell counts, and relative CD38 cell counts. A significant increase was observed in both absolute and relative CD5+/CD45RA+ and CD5+/CD45RO+ cell values. In Study 4, we demonstrated that the escalation of treatment with interferon beta-1a and 44 μg, DMF and fingolimod favorably affected the parameters of the EDSS (Expanded Disability Status Scale) and the time to the next relapse.

Conclusions

The proteomic analysis identified proteins in the cerebrospinal fluid of patients with MS. These proteins play a significant role in the initial activation of complement or irreversible progression of MS. The results of the studies showed individual lymphocyte populations that have long been affected by interferon beta and GA in patients with RS. The study focused on the comparison of the efficacy of subcutaneous interferon beta-1a, 44 μg, DMF, and fingolimod in real clinical practice has shown that the escalation of treatment with interferon beta-1a and 44 μg, DMF and fingolimod favorably affects EDSS change parameters and time to the next relapse.