Title: Effects of smoking on lymphocyte subpopulations in patients with MS on dimethyl fumarate

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Abstract:

Currently, patients on disease-modifying therapies such as Tecfidera®/dimethyl fumarate (DMF) are monitored for absolute lymphocyte count (ALC). DMF has previously shown to decrease ALC, but also specifically decrease CD4+ and CD8+ T cells. While many studies have linked smoking to multiple sclerosis (MS) susceptibility, few studies have investigated the impact of smoking on patients with MS during treatment. Multiple studies have shown that smoking increases lymphocyte proliferation, but only one study has examined the effects of smoking on ALC during treatment and found that non-smoking was associated with an increased risk of DMF-induced lymphopenia. Our objective was to determine if smoking affected different immune cell populations in patients with MS taking DMF. Understanding differences in immune cell changes between smokers and non-smokers will promote increased monitoring and awareness of factors which may increase the risk of lymphopenia in patients taking DMF.

We performed a retrospective longitudinal analysis of our cohort at the Fraser Health Multiple Sclerosis Clinic and stratified 264 patients with MS on DMF into two categories: smokers (including those who smoke occasionally, n=51) and non-smokers (including those who had quit prior to starting DMF, n=213). Linear regression models were created to predict changes in lymphocyte subpopulations over time. Smokers were found to have a significantly greater decrease in white blood cell count (-0.08±0.02), ALC (-0.04±0.005), and CD4+ T cells count (-0.02±0.003) compared to non-smokers (-0.04±0.005, -0.02±0.002 and -0.01±0.001 respectively) during DMF treatment. There were no significant differences in rate of change for CD8+ T cells, CD19+ B cells, NK cells or CD4:CD8 T cell ratio. Additionally, smoking did not appear to impact lymphocyte subpopulation recovery after treatment discontinuation. We conclude that smoking may have a synergistic effect with DMF which exacerbates decreases in certain lymphocyte populations.