Effects of smoking on lymphocyte subpopulations in patients with MS on dimethyl fumarate (ID: 11)

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Background

Previous studies have that patients with multiple sclerosis (pwMS) can develop lymphopenia during treatment with dimethyl fumarate (DMF)[1], therefore regular blood tests monitore absolute lymphocyte count (ALC).

While many studies have linked smoking to multiple sclerosis (MS) susceptibility[2,3], few studies have investigated the impact of smoking on MS disease course and/or treatment.

Multiple studies have shown that has different effects on various immune cell populations[4,5].

Only one study has examined the effects of smoking on ALC in pwMS during DMF treatment and found that non-smoking was associated with an increased risk of lymphopenia[6].

Objective and Hypothesis

Our objective was to characterize the immune landscape during and after DMF treatment in pwMS and determine how smoking affects changes in immune cell counts.

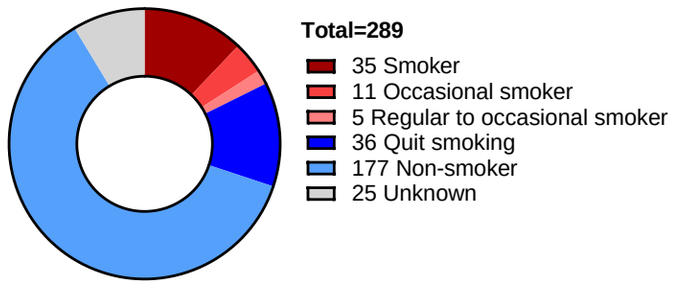
We hypothesized that pwMS on DMF who are smokers will have different changes in immune cells compared to non-smokers.

Methods

A retrospective analysis of longitudinal data from 289 pwMS who have been treated with DMF at the Fraser Health Multiple Sclerosis Clinic in British Columbia, Canada. The blood test results were acquired from January 1, 2013 to April 1, 2020. The average cell count at each month up until 31 months post treatment start date and 6 months post treatment end date are used. Patients who self-identified as smokers, occasional smokers and regular to occasional smoker were categorized as “Smokers”. Patients who identified as non-smokers or have previously quit were categorized as “Non-smokers”.

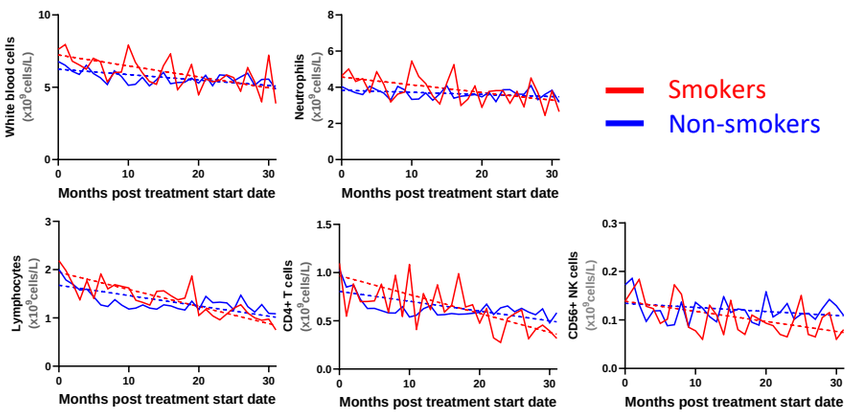
Results

Demographics



During treatment, smokers have a greater decrease in white blood cell, neutrophil, lymphocyte, and CD4+ T cell count compared to non-smokers.

Cell type	Treatment	Slope	Are lines different?
White blood cells	Smokers	-0.08±0.02	**
	Non-smokers	-0.02±0.005	
Neutrophils	Smokers	-0.04±0.01	**
	Non-smokers	-0.01±0.004	
Lymphocytes	Smokers	-0.04±0.005	**
	Non-smokers	-0.02±0.002	
CD4+ T cells	Smokers	-0.02±0.003	**
	Non-smokers	-0.01±0.001	
CD8+ T cells	Smokers	-0.01±0.002	ns
	Non-smokers	-0.008±0.0007	
CD19+ B cells	Smokers	-0.0008±0.001	ns
	Non-smokers	-0.0009±0.0002	
CD56+ NK cells	Smokers	-0.002±0.0006	ns
	Non-smokers	-0.0008±0.0004	
CD4:CD8 T cells	Smokers	0.08±0.02	ns
	Non-smokers	0.06±0.009	



Results

After treatment, no statistically significant differences between smokers and non-smokers in immune cell recovery.

Cell type	Treatment	Slope	Are lines different?
White blood cells	Smoker	0.04±0.2	ns
	Non-smokers	0.04±0.06	
Neutrophils	Smoker	-0.04±0.1	ns
	Non-smokers	0.01±0.05	
Lymphocytes	Smoker	0.0004±0.06	ns
	Non-smokers	-0.04±0.02	
CD4+ T cells	Smoker	0.06±0.05	ns
	Non-smokers	0.01±0.02	
CD8+ T cells	Smoker	0.06±0.03	ns
	Non-smokers	0.02±0.01	
CD19+ B cells	Smoker	0.02±0.02	ns
	Non-smokers	0.004±0.01	
CD56+ NK cells	Smoker	0.02±0.01	ns
	Non-smokers	0.003±0.006	
CD4:CD8 T cells	Smoker	-0.09±0.3	ns
	Non-smokers	-0.2±0.1	

Discussion

During treatment, smoking appears to increase the rate of decline in white blood cells, neutrophils and lymphocytes. Specifically, CD4+ T cells were affected.

Smoking does not appear to affect immune cell recovery after treatment discontinuation.

These preliminary results demonstrate a potential synergistic effect of smoking and DMF on lymphocytes.

Conclusion

We recommend that patients with MS who smoke and are prescribed DMF be carefully monitored for decreased levels of lymphocytes.

1. Mehta D et al. Neurology 2019; 92:e1724-e1738. 2. Wingerchuk DM. Ther Adv Neurol Disord. 2012; 5(1): 13–22. 3. Zhang P et al. PeerJ 2016; 4: e1797. 4. Higuchi T et al. Prev Med Rep 2016; 4: 417–422. 5. Qiu F et al. Oncotarget 2017; 8(1): 268–284. 6. Morales FS et al. J Neurol 2020; 1: 125-131.