Does smoking affect disability in AQP4 antibody positive NMOSD and MS patients, and what is the mechanism?

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Introduction: Smoking may be a risk factor for worse outcome in Multiple Sclerosis (MS) through unclear mechanisms. The effect of smoking on Neuromyelitis Optica Spectrum Disorder (NMOSD) is unknown. Our study aimed to compare the effect of smoking on relapse and disability in MS and aquaporin-4 antibody positive (AQP4-Ab+ve) NMOSD.

Methods: From the Oxford MS and NMOSD databases we collected the following data from relapsing remitting and secondary progressive (SP) MS and AQP4-Ab+ve NMOSD patients: smoking status (ever/never), onset age, sex, disease duration, time to first relapse, the number of relapses within the first 2 years from disease onset, the time to EDSS 6, time to conversion from clinically defined MS to SPMS, recovery from onset attack and from first relapse in NMOSD patients. Smokers and non-smoker were age and sex matched.

Results: We have included 101 NMOSD AQP4 positive cases (31 ever smokers, 70 never smokers) and 159 MS cases (53 ever smokers, 106 never smokers). Annualised relapse rate in the first two years did not differ between smoker and non smokers in either groups. Smoking increased the risk to reach EDSS 6 in NMOSD patients (univariate, HR=2.25, p=0.049, 95% CI 1.0-5.0). In MS, when controlling for age and sex, smoking affected the risk of converting to SPMS (multivariate, HR=2.32, p=0.013, 95% CI 1.2-4.5). In the NMOSD group we found a good recovery from onset relapse in 42.6% of never-smokers and 35.5% of ever-smokers. After the first relapse we found a good recovery in 54.3% of never-smokers and 44.4% among the ever-smokers. When considering the onset transverse myelitis, we found a good recovery in 45% of never-smokers and 38.5% among the ever-smokers.

Conclusions: Despite the relatively small sample sizes, our study supports previous observations in MS and suggests that there is a detrimental effect of smoking on AQP4+NMOSD. Smoking does not affect relapse rate but may affect disability by reducing recovery from relapses. One explanation is that smoking induced ischemia or hypoxia might increase tissue damage during inflammatory attacks.