Wearing-Off Effect as a Predictor of Disability Progression in Multiple Sclerosis: A Five-Year Follow-Up Study

Idini E[1], Coghe G[1], Lorefice L[1], Frau J[1], Cocco E[1]

Affiliations: [1]Multiple Sclerosis Center, Binaghi Hospital, ASL Cagliari, Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy.

Background: Wearing-off effect (WOE) is a transient worsening of symptoms experienced by some patients in the days leading up to their next natalizumab infusion.

Aims:

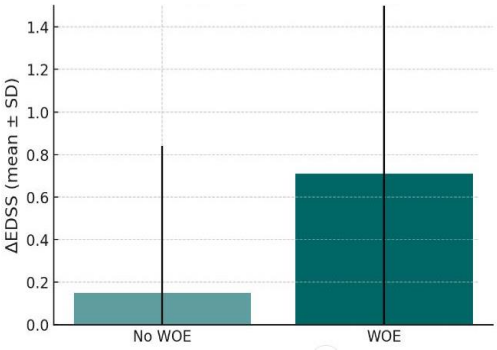
- Evaluate whether the presence of WOE in natalizumab-treated MS patients is associated with increased disability progression over 5 years.
- Assess whether WOE is an independent predictor of clinical worsening.

Methods: 52 RRMS on natalizumab (2020 baseline). ΔEDSS at 5 years. Groups: WOE vs no-WOE. Welch's t-test for group comparison; multiple linear regression (ΔEDSS) and multivariable logistic regression (ΔEDSS≥1) for independent predictors

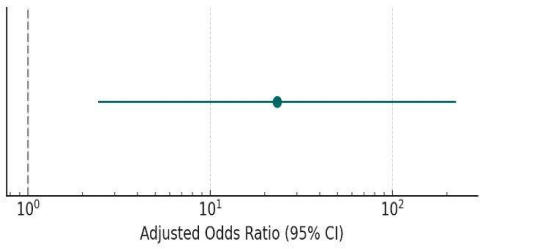
	No WOE (n=26)	WOE (n=26)	P-value
Age (yrs)	37±7	41±10	0.096
Female	21 (81%)	23 (88%)	0.452
Disease duration (yrs)	12 ± 6	14 ± 7	0.174
EDSS baseline	1.6 ± 1.2	2.8 ± 1.7	**0.029**

Group differences were tested with Welch's t-test, given unequal variances (Levene's test p<0.05)

Results:



Disability progression: WOE patients had greater 5-year worsening (**ΔEDSS 0.72±0.86 vs 0.15±0.69**; Welch's t=−2.58, p=0.013; **Cohen's d=0.71**).



Logistic regression (clinically significant progression, ΔEDSS ≥1): adjusted for age, sex, disease duration and baseline EDSS, WOE remained an independent predictor (**OR 23.3**; 95% CI 2.43–223.9; p=0.006)

Discussion and Conclusions

WOE was independently associated with greater disability progression over five years in natalizumab-treated MS patients. These findings suggest that WOE may represent an early clinical indicator of silent progression and a prognostic marker.