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**Patient and Physician Perspectives on the Wearing-off Effect in Multiple Sclerosis: Results From Structured Interviews**

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**Abstract:**

**Background:** The wearing-off effect (WOE) refers to symptoms such as fatigue, cognitive dysfunction, sensory symptoms, and pain that occur toward the end of treatment cycles. There is limited information available on patients' and clinicians' perspectives regarding the wearing-off phenomenon of disease-modifying therapies (DMTs) in multiple sclerosis (MS).

**Objectives:** To identify key symptoms reported by patients and observed by clinicians due to the WOE associated with MS DMTs, and to better understand patient and physician perspectives on the WOE.

**Methods:** Thirty adults with MS and 9 clinicians underwent structured interviews, focusing on disease experience, relapse and remission, and WOE symptoms. Patients were also asked about their experience with their neurologists, while clinicians were asked about their perspective on the WOE.

**Results:** All patients recognized  $\geq 1$  WOE-associated symptoms, irrespective of the type, route of administration, and frequency of DMT received, whereas 7/9 clinicians reported observing WOE in their practice. Most patients (n=22/30) were able to differentiate WOE from relapse-related symptoms. Fatigue was the most common WOE symptom reported by patients (n=29/30) and clinicians (n=7/7) and was also indicated as the most bothersome symptom. Other common symptoms reported by patients were cognitive difficulties (28/30) and sensory dysfunction or numbness (20/30). In comparison, clinicians most often identified weakness, cognitive difficulties, or pain (n=5/7 each) as related to WOE. All patients reported WOE symptoms negatively impacted their daily activities. 25/30 patients discussed WOE symptoms with their neurologists; 15/25 patients perceived that the attention received was appropriate. The primary coping mechanisms recommended to patients included stress management and prescription of medications. Clinician perspectives on WOE varied describing it as psychosomatic manifestations, lack of efficacy, or placebo effect.

**Conclusions:** Perception and comprehension of the WOE differs between MS patients and clinicians indicating the need for effective health communication, and further work to elucidate the mechanisms of the WOE.

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