

Expert Opinion Paper

Medical Advisory Board of the National Multiple Sclerosis Society

Treatment Recommendations for Physicians

Management of MS-Related Fatigue

BACKGROUND

Fatigue is the most common MS symptom—experienced by 75 to 95% of people with the disease. Approximately 50 to 60% of people with MS describe fatigue as one of their most troubling symptoms, regardless of their disease course or level of disability. The Social Security Administration recognizes fatigue as a significant cause of unemployment among people with MS.

Fatigue was recently defined by the Fatigue Management Panel of the Multiple Sclerosis Council on Clinical Practice Guidelines as:

A subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual and desired activities.

RECOMMENDATIONS

Based on clinical experience and careful review of the medical literature and research findings pertaining to MS-related fatigue, the Medical Advisory Board of the National MS Society makes the following recommendations:

- ◆ Because of the complexity of MS-related fatigue, the first step in effective treatment is to identify the cause(s) of the fatigue (e.g., any combination of factors, including co-existing medical illnesses, side effects of medications, depression, disrupted sleep, and fatigue caused by the MS itself).
- ◆ Once the source(s) of the fatigue have been identified, the treatment of MS-related fatigue is approached in a step-wise fashion in order to address all contributing factors. The treatment of fatigue should include **TWO** major steps:

1. Management and elimination of any secondary causes of fatigue:

- a. Treatment of any co-existing medical conditions (including depression) that are causing fatigue.
- b. Adjustment of any medications that may be producing excessive fatigue and/or sleepiness. Many common medications, including anticonvulsants, antihistamines, antihypertensives, sedatives, and certain antidepressants, have fatigue and/or sleepiness as a side effect.
- c. Management of any conditions or symptoms that interfere with sleep (e.g., sleep apnea, leg spasms, depression, MS symptoms such as bladder dysfunction, spasticity, or pain). Research indicates that 25 to 35% of people with MS experience disturbed sleep, which may contribute significantly to daytime fatigue.
- d. Management of any MS symptoms that may be producing additional fatigue. Symptoms such as weakness, spasticity, and ataxia may significantly increase the amount of exertion needed to carry out daily activities.
- e. Education about energy effectiveness strategies—defined as “the identification and development of activity modifications to reduce fatigue through a systematic analysis of daily work, home, and leisure activities. . . .” These strategies are frequently taught by a nurse or rehabilitation specialist (e.g., occupational and/or physical therapist)
 - i. Appropriate rest to activity ratio
 - ii. Use of assistive devices to conserve energy (*motorized scooters are particularly useful for ambulatory people who experience fatigue when walking*)
 - iii. Environmental modifications to make activities more energy-efficient
 - iv. Cooling strategies to avoid the fatigue caused by elevations in core body temperature due to heat, exercise-related exertion, and fever
 - v. Regular aerobic exercise, geared to the person’s ability, to promote cardiovascular health, strength, improved mood, and reduce fatigue
 - vi. Stress management techniques

2. Treatment of primary MS fatigue:

- a. Pharmacologic management of chronic fatigue that remains after other factors have been addressed. Although no drugs have been approved by the U.S. Food and Drug Administration specifically for MS, recommended medications include:
 - i. **Amantadine (Symmetrel®):** An antiviral agent that has been used to treat MS-related fatigue since the early 1980s. Approximately 20 to 40% of mild to moderately disabled people with MS experience significant reductions in fatigue while using amantadine. Side effects are generally mild. The recommended dose of amantadine is 100 mg morning and early afternoon.

- ii. **Modafinil (Provigil®):** A wakefulness-promoting agent currently approved by the FDA for the treatment of narcolepsy, which has been shown to reduce self-reported fatigue in people with MS. The recommended dose of modafinil is 200 mg per day.
- iii. **Methylphenidate (Ritalin®):** A central nervous system stimulant that has been used to treat MS-related fatigue. The usual effective dose is 10–20 mg early in the morning and again at noon. Those individuals who experience little or no fatigue in the morning can take a single dose in the early afternoon.

Note: Prokarin, a drug containing histamine, caffeine, and other undisclosed ingredients, has been marketed to pharmacists for compounding (creating a preparation using the ingredients) for individual patients. It was reported in a recent controlled trial to reduce fatigue in a small sample of patients with either relapsing-remitting or progressive MS. **It is the opinion of this board that while Prokarin does not appear to be harmful, its level of benefit does not justify its very high cost.**

- b. Maintenance of energy effectiveness strategies as previously described

SUMMARY

Fatigue is a complex, potentially debilitating symptom experienced by the majority of people with MS. Anyone experiencing ongoing fatigue, or the sudden onset of severe, disabling fatigue should consult his or her physician so that the factor(s) contributing to the fatigue can be identified and effectively managed. Successful treatment of fatigue may require a variety of interventions, including behavioral adaptations, environmental modifications, and medication.