Modafinil for the Treatment of Multiple Sclerosis–Related Fatigue

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Request

What is the efficacy and safety of modafinil for the treatment of multiple sclerosis (MS)–related fatigue?

OBJECTIVE: To review the efficacy and safety of off-label use of modafinil in the treatment of multiple sclerosis (MS)–related fatigue.

DATA SOURCES: Literature was accessed via MEDLINE (1966–January 2010) and *International Pharmaceutical Abstracts* (1960–2010), using the medical subject heading terms modafinil, multiple sclerosis, and fatigue.

STUDY SELECTION AND DATA EXTRACTION: All English-language, peer reviewed publications were analyzed for relevance. Studies appropriate to the objective were evaluated, including 3 open-label trials, 1 single-blind trial, and 2 randomized placebo-controlled trials.

DATA SYNTHESIS: Fatigue symptoms, assessed by a variety of self-reported symptom scales, improved in each of the uncontrolled studies reviewed when participants with MS received modafinil 200 mg or less daily for up to 12 weeks. These benefits were not maintained, however, in one uncontrolled study when modafinil was increased to 400 mg daily. Of the 2 randomized, controlled trials, 1 study found that modafinil 200 mg once daily resulted in a reduction in fatigue symptoms measured by the Fatigue Severity Scale at 8 weeks. The other study found no difference in the reduction of fatigue symptoms, measured by the Modified Fatigue Impact Scale at 5 weeks, between the placebo group and patients who received modafinil 100–200 mg twice daily. The most common adverse reactions associated with modafinil use in all studies included gastrointestinal and central nervous system effects.

CONCLUSIONS: Based on the available data, use of modafinil for the treatment of MS-related fatigue has demonstrated benefit in all uncontrolled studies but has conflicting results from 2 controlled studies. Modafinil is a reasonable therapeutic option in this patient population, although larger, long-term, randomized controlled studies are necessary to further elucidate the appropriate dose of modafinil, its effects on MS-related fatigue, and adverse effects associated with its use.

KEY WORDS: fatigue, modafinil, multiple sclerosis, stimulants, treatment.

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Response

BACKGROUND

Multiple sclerosis is an autoimmune demyelinating disease of the central nervous system (CNS) characterized by numerous disabling symptoms, including abnormal function of the motor, sensory, and visual systems.[1,2] The initial disease course often demonstrates multiple exacerbations and remissions, with the variety of symptoms chiefly determined by the location of the plaques in the brain and spinal cord. Fatigue, the most common symptom, is reported to affect 70–90% of all patients with MS.[3,4] In fact, 50–60% of patients describe fatigue as the most disabling symptom, a core cause of social isolation and inability to work despite otherwise minor physical deficits. [3,5-7] For one third of patients with MS, fatigue is the presenting symptom and is closely linked to the patient's perception of mental health and quality of life.[6]

Fatigue associated with MS is defined as a deficiency of physical and/or mental energy that interferes with usual and desired activities and is usually out of proportion to the degree of effort or level of physical disability.[5] Thus, the characterization of MS-related fatigue can be easily differentiated from fatigue experienced by physically healthy individuals after exertional physical activity.[6] MS-related fatigue is often unrelated to disease duration, occurs easily, presents for variable lengths of time, may be either tran-

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sient or persistent, and does not adequately decline after rest.[3,8] Physical symptoms include uncontrollable apathy, exhaustion, fatigability, and lack of energy, which may be related to physical stress but generally occurs even without stress. Symptoms of fatigue should be documented for greater than 6 weeks to justify a diagnosis of fatigue syndrome.[3]

The pathogenesis behind fatigue in MS remains uncertain. It has been hypothesized that the premotor, limbic, basal ganglia, or brainstem areas may be involved with decreased motivation or motor readiness; however, there do not appear to be any consistent anatomical indicators of fatigue in patients with MS.[9,10] Nonpathogenic factors may include sleep deficiencies, reduced physical activity, depression, psychological functioning, pain, and medication use.[8]

Therefore, an individualized and comprehensive approach to the treatment of MS-related fatigue should be specific to the patient's relative disabilities, needs, and support system.[6] This includes the use of a combination of pharmacologic and nonpharmacologic therapies, although there are currently no medications with indications approved by the Food and Drug Administration (FDA) for the treatment of MS-related fatigue. Nonpharmacologic therapies include education, cognitive therapy, temperature regulation, and exercise programs. Pharmacologic treatment options include amantadine, methylphenidate, selective serotonin-reuptake inhibitors (SSRIs), and modafinil.[5,11] Amantadine has demonstrated a reduction in fatigue of 20–40% in short-term studies.[12-15] Although both methylphenidate and SSRIs are used for MS-related fatigue, they have not been studied in controlled clinical trials.[5,11] Because of the variable success with the agents described above, the use of modafinil has been explored for the treatment of MS-related fatigue.

Modafinil, a chemically and pharmacologically distinct non-amphetamine CNS stimulant, is indicated to improve wakefulness in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea, and shift-work sleep disorder.[16] Its mechanism is believed to be related to an increase in normal cortical activity in the frontal lobe, facilitating the regulation of normal wakefulness, and it has a lower abuse potential compared with other amphetamine-like medications used to treat fatigue.[2,17] Headache, nausea, nervousness, rhinitis, diarrhea, back pain, and anxiety are the most common adverse effects (≥5% of patients) associated with modafinil use in the treatment of FDA approved indications.[16] This article reviews the current literature to evaluate the efficacy and safety of modafinil for the treatment of MS-related fatigue.

Data Sources

A comprehensive search of MEDLINE (1966–January 2010) and *International Pharmaceutical Abstracts* (1960–2010), using the terms modafinil, multiple sclerosis, and fatigue, was utilized to identify relevant trials. Results were limited to peer-reviewed studies conducted on humans and published in English. Additional articles were obtained by manually searching recent reviews for relevant articles. References were evaluated if they prospectively assessed the effectiveness of modafinil in patients with MS-related fatigue. The literature search identified published reports of 3 open-label trials, 1 single-blind trial, and 2 randomized placebo-controlled studies (Table 1).[18-23]

Literature Review

An open-label trial was conducted to assess the efficacy, tolerability, and appropriate dosage of modafinil for MS-related fatigue over 3 months in patients with a diagnosis of MS who met the investigators' definition of chronic fatigue, including perceived symptoms, for more than 6 weeks. Fifty patients received 100 mg of modafinil, which could be titrated up to 400 mg daily, administered as a single dose. After 3 months, the mean daily dose of modafinil was 148 ± 61 mg. Fatigue Severity Scale (FSS) scores improved from a baseline of 30.3 ± 8.5 to 25.4 ± 3.7 after 3 months of treatment ($p < 0.001$). Daytime sleepiness evaluated by the Epworth Sleepiness Scale (ESS) improved from 9.7 ± 3.9 at baseline to 4.9 ± 2.9 ($p < 0.001$). Over 90% (n = 42) of the patients described tolerability as excellent. Three patients dropped out of the study due to nervousness and increased vertigo.[18]

Another small, open-label study evaluated the predictive value of visual and audio testing (P300) on treatment response in 33 patients with MS-related fatigue. After a 4-week baseline period, in which amantadine or 4-amino pyridine was discontinued, patients received modafinil 100 mg/day for 4 weeks, with the option to continue this dose or increase modafinil to 200 mg/day for an additional 8-week extension phase. Inclusion criteria consisted of an MS diagnosis, clinical complaint of fatigue, and an expanded disability status scale (EDSS) score of ≤6.5. Symptomology was evaluated using the visual analogue scale for fatigue (VAS-F). Compared with baseline VAS scores of 6.9 ± 0.6, treatment with modafinil resulted in significant benefits at weeks 4 and 12 (4.4 ± 0.4; $p = 0.003$ and 4.3 ± 0.4; $p = 0.003$, respectively). Nearly 50% (n = 16) of patients experienced an improvement of at least 20% in the VAS score. At week 12, the mean daily dose of modafinil was 188 mg. Auditory P300 latency correlated with treatment response, whereas visual latency did not predict response. Adverse effects were not reported.[19]

A third open-label study was conducted to analyze 40 patients with MS (n = 17), brainstem or diencephalic stroke (n = 14), or cortical stroke (n = 9). Patients were initiated on modafinil 50 mg/day, increasing up to 200 mg/day for a total of 3 months. Patients were then given a 1-month washout period. At the conclusion of both the ac-

tive and washout periods, fatigue was measured by the Fatigue Assessment Inventory (FAI), with sleepiness measured by the ESS. Compared with baseline in the MS group (n = 12), significant improvement was demonstrated at 3 months in the modafinil group when compared with baseline for the FAI assessment (4.53 ± 1.06 vs 5.60 ± 0.86; p = 0.006) but not the ESS measurement (9.08 ± 2.97 vs 9.25 ± 3.89; p ≥ 0.05). Statistical analysis for the 1-month washout period was not reported. The most common adverse effects reported were headache, excitability, and hypertension for all patients enrolled in the study. Five patients with MS dropped out due to intolerable adverse effects.[20]

A single-blind trial studied the effects of modafinil administered to 72 patients as 200 mg once daily for 2 weeks followed by 400 mg once daily for 2 weeks. Patients were included in the study if they were previously diagnosed with MS, and demonstrated a mean FSS score of >4 and an EDSS score ≤6.0. Improvement in fatigue, measured by the FSS, was the primary outcome. Before the initiation of modafinil, patients received placebo for 2 weeks and FSS scores from this time (5.5) were used as the placebo comparator group. After 2 weeks of treatment with modafinil 200 mg daily, mean FSS scores decreased significantly to 4.7 (p < 0.001). Following titration to 400 mg daily, modafinil did not sustain a significant reduction in FSS; mean scores increased to 5.3. Fatigue was also assessed using the modified fatigue impact scale (MFIS) and the VAS-F. Improvement was noted for both measures after patients received modafinil 200 mg daily for 2 weeks (37.7 vs 44.7; p < 0.001 and 5.4 vs 4.5; p = 0.003, respectively) but not with the 400-mg daily dose. Compared with baseline daytime sleepiness scores of 9.5 as measured by the ESS, modafinil-treated patients experienced less daytime sleepiness with both the 200-mg and 400-mg dosages (7.2 and 7.0, respectively; p < 0.001). The most common adverse events were headache, nausea, and asthenia; however, no serious adverse events occurred.[21]

A prospective, randomized, double-blind, placebo-controlled trial was conducted in 115 patients with MS who had chronic fatigue for at least 6 months, with an MFIS score ≥45 and an EDSS score ≤6.5. Patients were randomized to receive modafinil 200 mg/day, 100 mg in the morning and 100 mg at noon, with possible titration to a maximum dose of 400 mg/day in divided doses, or placebo for 5 weeks. The placebo and modafinil groups had similar MFIS scores at baseline (62.9 ± 9.4 and 61 ± 11.4, respectively). Each group improved significantly at 5 weeks compared with baseline (49.2 ± 16.6 placebo vs 52.3 ± 18.5 modafinil); however, there was no significant difference between groups (p = 0.27). Doses for more than 90% of patients in each group were titrated to at least 300 mg/day of the study drug. Adverse event rates were similar between

Table 1. Summary of Prospective Studies of Modafinil for the Treatment of Multiple Sclerosis–Related Fatigue

Reference	Design	Pts., n	Comparison Group	Outcomes	Results, %	p Value[a]	Adverse Events, %[b]
Zifko (2002)[18]	OL, 12 wk	50	Baseline	FSS ESS	↓16.2 ↓48.4	<0.0001 <0.0001	Nervousness (4), vertigo (2)
Nagels (2007)[19]	OL, 12 wk	33	Baseline	VAS-F: 4 wk VAS-F: 12 wk	↓36.2 ↓37.7	0.0026 0.00269	Not reported
Brioschi (2009)[20]	OL, 12 wk	17	Baseline	FAI ESS	↓19.1 ↓1.8	0.006 NS	Headache (30), excitability (16), hypertension (12), dizziness (8), thoracic pain (8), aggressiveness (4), dermatitis (4)
Rammohan (2002)[21]	SB, 9 wk	72	Placebo run-in	FSS: 200 mg FSS: 400 mg MFIS: 200 mg MFIS: 400 mg VAS-F: 200 mg[d] VAS-F: 400 mg[d] ESS: 200 mg ESS: 400 mg	↓14.5 ↓3.6 ↓15.7 ↓5.8 ↑20 ↑4.4 ↓24.2 ↓26.3	<0.001 NS <0.001 NS 0.003 NS <0.001 <0.001	Headache[c] (17), nausea (11), anxiety (9), dry mouth (7), nervousness (7), insomnia (6), diarrhea (4), asthenia (3)
Stankoff (2005)[22]	PC, DB, 5 wk	115	Placebo	MFIS: modafinil MFIS: placebo	↓17.1 ↓22.3	NS	Nausea (16), insomnia (14), epigastralgia (11), vomiting (4), diarrhea (4)
Lange (2009)[23]	PC, DB, 8 wk	21	Placebo	FSS: modafinil FSS: placebo	↓22.8 ↑1.0	0.01	Not reported

DB = double-blind; ESS = Epworth Sleepiness Scale; FAI = Fatigue Assessment Instrument; FSS = Fatigue Severity Scale; MFIS = Modified Fatigue Impact Scale; NS = nonsignificant; OL = open-label; PC= placebo-controlled; SB = single-blind; VAS = Visual Analog Scale; VAS-F = Fatigue Visual Analogue Scale.

[a]For comparisons of modafinil versus placebo or, if no comparator was used, for final results versus baseline.

[b]Reported incidence greater than placebo and greater than 1 patient.

[c]Modafinil 200-mg/day dose.

[d]Increase in score demonstrates improvement in fatigue symptoms.

the 2 groups. The most commonly observed events were related to the CNS and the gastrointestinal system.[22]

In a smaller double-blind, placebo-controlled trial of patients with MS, modafinil titrated to 200 mg once daily or placebo was given for 8 weeks. Patients were included if they demonstrated an FSS score ≥36 and an EDSS score <7.0. At baseline, the mean FSS scores for the modafinil and placebo groups were 57.0 and 52, respectively. Three hours after administration of the study drug, FSS scores were lower in the modafinil group, with a mean score of 45, compared with the placebo group, with a mean score of 55 ($p = 0.023$). At 8 weeks, the modafinil group sustained a significant improvement in fatigue, with a mean FSS score of 44, compared with the placebo group, with a mean FSS score of 52.5 ($p = 0.035$). FSS scores were not reported numerically and were estimated from a graph, with complete reports available for 19 patients. Adverse effects were not reported.[23]

Discussion

The high incidence of fatigue and its impact on the quality of life of patients with MS emphasizes the need for effective symptomatic treatment modalities. Before a pharmacologic intervention is considered, a comprehensive evaluation is necessary to identify additional contributing factors potentially involved in MS-related fatigue. Other causes of fatigue and daytime sleepiness, such as depression, thyroid disease, and anemia, should be ruled out. Nonpharmacologic treatments should be considered the initial management of fatigue, with particular emphasis on aerobic exercise and cognitive therapy. If patients have an inadequate response to these initial interventions, drug therapy should be initiated based on the patient's severity of symptoms.[3,5,9] In an effort to effectively treat symptomatic patients, modafinil has emerged as a reasonable treatment option with demonstrated short-term efficacy.

In the uncontrolled studies reviewed, modafinil demonstrated positive and significant improvements in MS-related fatigue from baseline (Table 1). Fatigue symptoms, assessed by a variety of self-reported symptom scales, improved in all participants receiving modafinil 200 mg or less daily for up to 12 weeks.[18-21] The benefit was not maintained, however, in 1 study when modafinil was increased to 400 mg once daily.[21] These trials are not without their limitations. A placebo group was absent from all 3 trials and 2 were open-label.

Of the 2 randomized controlled trials evaluating the use of modafinil for MS-related fatigue, 1 found that modafinil 200 mg once daily resulted in a 22.8% reduction in fatigue symptoms, measured by FSS at 8 weeks, whereas the second trial found no significant difference in the reduction of fatigue symptoms, measured by the MFIS at 5 weeks, between the placebo group and patients who received modafinil 100–200 mg twice daily.[22,23] The lack of improvement in fatigue in the later trial may be attributed to various factors, including the high placebo effect, differences in the fatigue scales used for symptom assessment and the modafinil dosing regimens.[24,25] The FSS, utilized in the study demonstrating modafinil benefit, is a widely used, one-dimensional scale designed to primarily assess fatigue, whereas the MFIS is a multidimensional scale with questions that may be affected by depression, cognitive impairment, or both.[9,24,26] Modafinil has not previously demonstrated efficacy against any of these potential confounding symptoms and if these symptoms were not ruled out prior to study initiation, they would have had the potential to bias clinical efficacy studies toward insignificance.[26] The authors, though, accounted for this influence and excluded patients with uncontrolled depressive disorder, anxiety, and dementia. Interestingly, results from the placebo crossover trial demonstrated improvement in self-reported fatigue, assessed by both the FSS and MFIS, in patients receiving modafinil 200 mg daily.[21] Although such methods of evaluation appear to be common in similar fatigue studies, without the administration of objective scores, such as a sleep study, the results may also be heavily influenced by the patient's own bias.

Studies examining the effectiveness of modafinil for MS-related fatigue all involved relatively small numbers of patients, with a maximum treatment period of 12 weeks. Therefore, the external validity of the reviewed studies may be limited and long-term efficacy of modafinil for MS-related fatigue is currently unknown. Larger randomized controlled studies are necessary to further elucidate the appropriate dose of modafinil, its long-term effects on MS-related fatigue, and associated adverse effects. This recommendation includes head-to-head studies demonstrating the efficacy of modafinil versus an appropriate comparator drug, such as amantadine. This would provide practitioners evidence-based guidance to determine the most safe and efficacious medication with which to treat patients with MS-related fatigue because, to our knowledge, no comparative trials of similar patient populations have been performed to guide the clinician. When the results of independent efficacy studies of both modafinil and amantadine are compared, both medications appear to be similarly efficacious.

Overall, 2 of the 6 studies reviewed did not report adverse effect data.[19,23] The most commonly reported adverse effects of modafinil in all presented studies were insomnia, headache, excitability, nausea, vomiting, and diarrhea. Modafinil 400 mg per day was associated with increased reports of asthenia compared with modafinil 200 mg per day.[21] Approximately 5.6–29% of patients receiving modafinil discontinued treatment due to an adverse effect.

If therapy with modafinil is clinically warranted, a structured titration regimen is recommended. The doses used in the described studies ranged from 50 mg to 400 mg daily for periods of 5 and 12 weeks. These doses are within the

range indicated for control of narcolepsy, obstructive sleep apnea, and shift-work sleep disorders. Based on the schedules of treatment titration used in the study protocols described above, it is reasonable to start modafinil at 100 mg each morning on days 1 through 7, increasing to 200 mg every morning as the maintenance dose.[3,9,18-23] Such stepwise titrations were well tolerated in the clinical studies and have the advantage of being simple, yet they can rapidly escalate to the recommended maintenance dose, which may also improve patient adherence. Subsequent dosage adjustments should be based on patient response assessed in no less than 1-week intervals. Due to lack of safety and efficacy data, doses exceeding 400 mg daily should be avoided. Generally, a single daily dose of 200 mg each morning is efficacious in minimizing MS-related fatigue, but modafinil may be divided between morning and noon in patients experiencing post-noon fatigue. Because of modafinil's long half-life, approximately 15 hours after multiple doses, dosing later than noon may increase the incidence of insomnia, causing a paroxysmal increase in daytime fatigue.[16] Such adverse effects negate the potential benefits of modafinil therapy for treating MS-related fatigue.

Summary

Fatigue is a common symptom of MS; it negatively affects the quality of life of a majority of patients. In patients with MS-related fatigue, an individualized and comprehensive approach to treatment should be specific to the patient, including the use of both pharmacologic and nonpharmacologic therapies. Modafinil has been evaluated for the treatment of MS-related fatigue in 4 uncontrolled studies, all of which demonstrated short-term efficacy (up to 12 weeks) and in 2 placebo-controlled trials that produced conflicting results. The efficacy of modafinil for MS-related fatigue beyond 12 weeks remains undetermined. The most commonly reported adverse effects of modafinil were insomnia, headache, excitability, nausea, vomiting, and diarrhea. Based on the available data, modafinil appears to be a reasonable treatment option for MS-related fatigue, although larger randomized controlled studies are necessary to further determine both the efficacy and safety of modafinil for short- and long-term treatment of MS-related fatigue.

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Modafinil para el Tratamiento de la Fatiga Relacionada a Esclerosis Múltiple

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EXTRACTO

OBJETIVO: Repasar la eficacia y la seguridad del uso de modafinil fuera de la indicación oficial aprobada, para el tratamiento de la fatiga relacionada a esclerosis múltiple (EM).

FUENTES DE INFORMACIÓN: Se obtuvo acceso a la literatura a través de MEDLINE (1966-enero de 2010) y del *Abstractos Farmacéuticos Internacionales* (1960-2010) usando los términos médicos de búsqueda en inglés modafinil, multiple sclerosis, y fatigue.

SELECCIÓN DE FUENTES Y MÉTODO DE EXTRACCIÓN DE INFORMACIÓN: Todas las publicaciones en el idioma inglés con revisión por expertos fueron analizadas para determinar su relevancia. Los estudios apropiados para el objetivo fueron evaluados incluyendo 3 estudios de rótulo abierto, un estudio ciego unitario y 2 estudios aleatorios con control de placebo.

SÍNTESIS: Los síntomas de fatiga evaluados a través de una variedad de escalas de síntomas reportados por los propios pacientes mejoraron en cada uno de los estudios no controlados revisados cuando los participantes con EM recibieron 200 mg o menos de modafinil una vez al día por un período máximo de 12 semanas. Sin embargo, estos beneficios no se mantuvieron en un estudio no controlado cuando la dosis de modafinil se aumentó a 400 mg diarios. De los dos estudios aleatorios, controlados un estudio encontró que modafinil en dosis de 200 mg una vez al día resultó en una reducción de los síntomas de fatiga según medidos por la Escala de Severidad de Fatiga a las 8 semanas. El otro estudio no encontró diferencia en la reducción de los síntomas de fatiga medidos por la Escala Modificada del Impacto de Fatiga a las 5 semanas, entre el grupo de placebo y aquellos que recibieron modafinil 100–200 mg 2 veces al día. Las reacciones adversas más comunes asociadas con el uso de modafinil en todos los estudios incluyen efectos gastrointestinales y del sistema nervioso central.

CONCLUSIONES: En base a la información disponible, el uso de modafinil para el tratamiento de la fatiga asociada con EM ha demostrado beneficios en todos los estudios no controlados pero ha producido resultados conflictivos en 2 estudios controlados. Modafinil es una opción terapéutica razonable en esta población de pacientes aunque estudios más extensos, aleatorios, controlados, a largo plazo son necesarios para elucidar la dosis apropiada de modafinil, sus efectos sobre la fatiga asociada con EM y los efectos adversos asociados con su uso.

Traducido por Brenda R. Morand

Le Modafinil pour le Traitement de la Fatigue liée à la Sclérose en Plaques

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RÉSUMÉ

OBJECTIF: Revoir les données concernant l'efficacité et l'innocuité du modafinil, utilisé hors indication approuvée, pour le traitement de la fatigue liée à la sclérose en plaques.

REVUE DE LA LITTÉRATURE: Les articles pertinents ont été identifiés à l'aide d'une recherche dans les banques de données informatisées MEDLINE (1966–janvier 2010) et *International Pharmaceutique Résumé* (1960–2010) en utilisant les mots-clé modafinil, sclérose en plaques et fatigue.

SÉLECTION DES ÉTUDES ET DE L'INFORMATION: Tous les articles de langue anglaise et revisés par des pairs ont été évalués pour la pertinence. Les études correspondant aux objectifs de cet article de revue ont été évalués, incluant 3 études ouvertes, une étude en simple aveugle, et 2 études randomisées et contrôlées contre placebo.

SYNTHÈSE DES DONNÉES: Les symptômes de fatigue, mesurés selon diverses échelles où le sujet s'évalue lui-même, ont été améliorés dans chacune des études non contrôlées lorsque le modafinil était donné à raison de 200 mg ou moins à chaque jour, jusqu'à une durée totale de traitement de 12 semaines. Dans une seule étude non contrôlée, les bénéfices n'ont pas été maintenus si la dose était augmentée à 400 mg par jour. Des 2 études randomisées et contrôlées, une seule étude a montré une réduction des symptômes de la fatigue mesurés par l'échelle de sévérité de la fatigue à 8 semaines de traitement et le modafinil était donné à raison de 200 mg une fois par jour. L'autre étude n'a montré aucune différence entre le groupe placebo et ceux qui ont reçu 100-200 mg 2 fois par jour de modafinil dans la réduction des symptômes de la fatigue mesurés par l'échelle modifiée de l'impact de la fatigue à 5 semaines de traitement. Les effets indésirables les plus fréquents du modafinil dans ces études étaient les effets au niveau du tractus gastro-intestinal et du système nerveux central.

CONCLUSIONS: En se basant sur les données disponibles, l'emploi du modafinil pour le traitement de la fatigue liée à la sclérose en plaques a montré des bénéfices dans toutes les études non contrôlées mais des résultats divergents dans 2 études contrôlées. Le modafinil semble une option thérapeutique possible chez cette population, même si des études randomisées, contrôlées et à long terme sont nécessaires pour préciser l'efficacité sur la fatigue, les doses optimales et les effets indésirables de ce médicament.

Traduit par Denyse Demers