Original Article

Retrospective Review of Modafinil Use for Cerebral Palsy

Daniel L. Hurst, MD; Walter A. Lajara-Nanson, MD; Pradeep Dinakar, MD, MS; Randolph B. Schiffer, MD

ABSTRACT

A retrospective review was undertaken at Texas Tech University Health Sciences Center regarding the use of modafinil for the treatment of spasticity associated with cerebral palsy. Neurology clinic records were reviewed from January 1, 2000, until October 1, 2001. Thirty pediatric patients with cerebral palsy were identified who were treated empirically with modafinil during this time period. Twenty-three (76%) patients reported diminished spasticity with treatment, which was confirmed by physical examination; these patients had improved joint mobility. Seventeen (56%) patients continued treatment with modafinil by the end of the formal review period (September 30, 2001). Twenty-three percent (seven) of the patients stopped taking modafinil during the study owing to one of the following: decreased sleep time (four), decreased appetite (one), hyperactivity, and irritability (two). Thus, this retrospective review shows a reduction in spasticity from cerebral palsy, with only minor and reversible side effects noted from modafinil. A blinded, crossover study using modafinil for spastic cerebral palsy is planned. (*J Child Neurol* 2004;19:948–951).

After successful treatment with modafinil of a small group of pediatric patients with cerebral palsy, we undertook a pilot study using modafinil in pediatric patients with cerebral palsy and then published those results.[1] Because of apparent successful treatment of spasticity with modafinil, we have continued to use modafinil in selected patients with cerebral palsy. To confirm our treatment results, a retrospective review of modafinil use for cerebral palsy in the Texas Tech University Health Sciences Center child neurology clinics was performed covering the period from January 1, 2000, until October 1, 2001, in an attempt to determine the general overall usefulness and tolerability of modafinil. Thirty patients were identified; excluding those patients already involved in the earlier prospective pilot study, there were 10 patients. Our initial pilot study documented a short-term benefit from modafinil in spastic cerebral palsy. This new study of modafinil use looked at long-term results in spasticity reduction from cerebral palsy and for any side effects identified.

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From the Department of Neuropsychiatry (Drs Hurst, Lajara-Nanson, Dinakar, and Schiffer), Texas Tech University Health Sciences Center, Lubbock, TX.

Address correspondence to Dr Daniel L. Hurst, 3601 4th Street, Lubbock, TX 79430. Tel: 806-743-4999 ext 244; fax: 806-743-5687; e-mail: daniel.hurst@ttuhsc.edu.

METHODS

Following the prospective study, an open chart review was done on 30 patients with cerebral palsy to study the effect of empiric treatment with modafinil. The child neurology clinical records were reviewed for patients with spastic cerebral palsy on modafinil. One hundred thirty-one patients were identified with cerebral palsy, and 96 of them were 18 years of age or younger prior to September 30, 2001. Of the 96 patients with cerebral palsy, 30 were empirically treated with modafinil during this time period, excluding those who had participated in the modafinil pilot study.

RESULTS

Table 1 shows the deidentified list of the subjects involved in the empiric study with modafinil. The subjects have been deidentified for confidentiality purposes. The table compares the effect of modafinil in 30 different subjects on the benefits on spasticity, side effects, and compliance with therapy. It was observed that 23 (76%) reported diminished spasticity from treatment, and this was confirmed through clinical examination. These patients had reported improved joint mobility, and some of them had attained full extension and flexion at the elbows and knees. Seventeen (57%) patients were continuing treatment at the end of the review period and seven (23%) patients stopped taking modafinil owing to decreased sleep time (four), decreased appetite (one), or

Table 1. Deidentified List of 30 Subjects Showing Improvement, Side Effects, and Compliance With Empiric Treatment With Modafinil in Spastic Cerebral Palsy

Subject	*Modafinil Used*	*Reviewed in Study*	*Improved*	*Side Effects*	*Continued Treatment*	*Comments*
1	Yes	Yes	Yes	No	Yes	
2	Yes	Yes	Yes	No	Yes	
3	Yes	Yes	Yes	No	Yes	
4	Yes	Yes	Yes	No	No	Discontinued for hyperbaric oxygen therapy
5	Yes	Yes	Yes	No	Yes	Telephone follow-up 3/21/02
6	Yes	Yes	Yes	No	Yes	
7	Yes	Yes	Yes	No	No	Discontinued—sleeping less
8	Yes	Yes	Yes	No	Yes	
9	Yes	Yes	Yes	No	Yes	
10	Yes	Yes	Unknown	Yes	No	Discontinued—sleeping less, increased activity
11	Yes	Yes	Yes	No	Yes	
12	Yes	Yes	Yes	No	Yes	
13	Yes	Yes	Unknown	Yes	No	Discontinued—did not sleep
14	Yes	Yes	Yes	No	No	Discontinued—complained of legs hurting
15	Yes	Yes	Yes	No	No	Discontinued by parents; switched medication
16	Yes	Yes	Yes	No	Yes	
17	Yes	Yes	Yes	No	Yes	
18	Yes	Yes	Yes	No	Yes	
19	Yes	Yes	Yes	No	Yes	
20	Yes	Yes	Yes	No	Unknown	Moved out of state (after study end)
21	Yes	Yes	No	Yes	No	Complained of nausea and vomiting; 2 trials
22	Yes	Yes	Yes	No	No	Discontinued owing to attention-deficit disorder
23	Yes	Yes	Yes	Yes	Yes	Complained of decreased appetite; held and restarted treatment owing to viral infection
24	Yes	No; lost to follow-up	Unknown	Unknown	Unknown	
25	Yes	Yes	Yes	No	Yes	
26	Yes	Yes	Yes	Yes	No	Discontinued—increased activity
27	Yes	Yes	Unknown	Yes	No	Discontinued—sleep problems
28	Yes	Yes	Yes	No	Yes	
29	Yes	No; lost to follow-up	Unknown	Unknown	Unknown	
30	Yes	No; lost to follow-up.	Unknown	Unknown	Unknown	

hyperactivity (two). All side effects reversed within 24 hours after stopping modafinil. Three (10%) patients were lost to follow-up and were presumed to have discontinued treatment.

Patients were considered as showing benefits based on written observation by a neurologist based on neurologic examinations, family report, and physical therapist evaluation.

Figure 1 represents the comparison between benefits, side effects, and compliance in patients on modafinil. In patients taking modafinil, the benefits are statistically significant compared with those in subjects not on the drug. (76% of 30 patients showed benefits, and only 23% had side effects). Figure 1 represents the data in Table 1 in the form of a bar chart. The x-axis shows the benefits, side effects, and compliance with treatment with modafinil and the y-axis shows the number of patients in the empiric study.

DISCUSSION

In our previous study, modafinil appeared to have a beneficial effect on spasticity in cerebral palsy. The current study retrospectively reviewed the empiric treatment experience at Texas Tech University Health Sciences Center in pediatric patients. Modafinil was assessed to have reduced spasticity in 76% of the patients reviewed (see Figure 1). Some of the study patients demonstrated major improvements in spasticity, allowing for full extension at the knees, resulting in an erect posture for the first time in their life. One patient with spastic diplegia could not take forward steps owing to severe scissoring of her legs. On modafinil, she can now take forward steps while holding on to her mother's arms. A teenage patient with congenital spastic hemiplegia reported that she walks better with modafinil treatment and that her spastic leg is less painful when she plays tennis. These observations and the continued use of modafinil by the study patients further suggest a benefit from modafinil for the treatment of spastic cerebral palsy.

Although several mechanisms of action are possible for the apparent muscle-relaxing effect of modafinil, a direct effect on subcortical structures has been postulated.[1] Modafinil is known to work at subcortical structures, producing its antinarcolepsy effect, and this has been well researched.[2–10] The beneficial effect of modafinil for multiple sclerosis–related fatigue has been documented.[11] Multiple sclerosis–related fatigue is felt to be a centrally mediated phenomenon, but the exact mechanism of this benefit to modafinil is poorly understood.[11–14] Furthermore, one study noted benefit at the lower dose of 200 mg/day compared with 400 mg/day, suggesting a different pathophysiologic mechanism than its benefit in narcolepsy.[11]

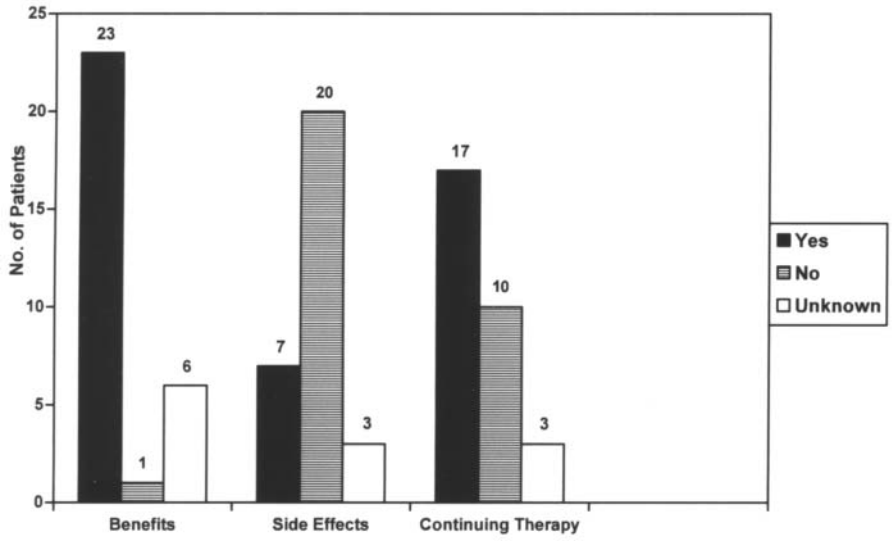

Figure 1 Comparison between benefits, side effects, and compliance in patients on modafinil.

The side effects noted in this study leading to the discontinuation of modafinil in seven patients during the study period were all minor and reversible. Some of these seven study patients have restarted modafinil treatment following the end of the study period, including one patient who stopped because of irritability. The patient was restarted on modafinil at a lower dose but now receives the same dose as during the study. Both the patient and his mother are pleased with his increased mobility on modafinil. The three patients lost to follow-up returned after the end of the study and review of the study results. Two of these patients requested new modafinil refills. Including this group, post-study follow-up revealed that 20 of 30 study patients (66%) were still on treatment by the end of the study period. Because not all patients who stopped taking modafinil during the study stayed off treatment, modafinil was more beneficial and better tolerated than originally determined. At least one patient and family were satisfied with a start low and go-slow approach.

The potential side effects to modafinil have been well studied.[15–17] A recent article on the use of modafinil for attention-deficit disorder in 15 children noted only "transient and readily managed" side effects.[18] The authors felt that the modafinil side effects compared well with other stimulants used for attention-deficit disorder[18–22]; this experience is similar to the current review of modafinil for cerebral palsy, revealing only minor and reversible side effects in our treatment group.

There are multiple therapeutic options in treating the spasticity seen in cerebral palsy. The available muscle relaxants used in cerebral palsy, benzodiazepines, baclofen, dantrolene, and tizanidine hydrochloride, are all limited owing to sedating side effects and the therapeutic tendency to make spastic muscles weak.[23] Constant intraspinal infusion via an implanted constant infusion pump requires surgery and the risks of surgical complications.[24] The use of botulinum toxin to temporarily paralyze selected spastic muscle groups risks antibody-related resistance and the variability of response owing to the requirement of repetitive injections.[25] Selective posterior rhizotomy and orthopedic procedures carry surgical risks as well. Despite these available treatments, limited benefit has been obtained in reducing the severity of cerebral palsy, resulting in an ongoing search for newer approaches and treatment combinations.[26,27]

Cerebral palsy occurs with an incidence of approximately 1 in 1000, and because of this high frequency, it is a major handicapping condition in children.[26] In adults treated for narcolepsy and in some children treated for attention-deficit disorder or cerebral palsy, modafinil has been well tolerated, with only minor side effects.[1,15–18] When compared with the currently available treatments for cerebral palsy and their potential side effects and complications, modafinil has a favorable side-effect profile.[23–27] Considering the high incidence of cerebral palsy, the lack of significant spontaneous improvement, and the lack of effective nonsedating muscle relaxants for spastic cerebral palsy, modafinil could be a valuable new treatment for cerebral palsy as an adjunct therapy or as monotherapy. Further controlled studies are planned.

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