Short Term Modafinil Use During Sleep Disorder Evaluations: Focus on High Risk Professions and Behaviors

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Citation

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Abstract

Patients can present with undiagnosed sleep disorders. Modest fatigue can impair their neurological, functional and psychological capacities. Four patients demonstrated improved functioning on modafinil, during the months required for a complete sleep evaluation, specialist consults and successful treatment.

Sleep disorders increase morbidity or mortality until definitive diagnosis and full treatment. In four patients, modafinil was immediately useful as a bridging medication over 3-7 months until final successful diagnosis and treatment.

Even one month of significant fatigue is unacceptable. For example, driving a motor vehicle is dangerous with some sleep disorders. Falling asleep driving or involuntary "minisleep" at the wheel is a common cause of motor vehicle accidents. In the United States, sleep causes at least 56, 000 motor vehicle crashes each year, resulting in 1, 550 deaths. Over a year, 10% of men and 4% of women admitted to falling asleep while driving. Insight into drowsiness can be flawed, lagging behind electroencephalographic and other evidence that the process of falling asleep has actually started. In clinical care, the patient may be sleepy or fatigued, but not a clear risk to drive or work.

Further, many occupations do not allow for fatigue, sleepiness and errors, e.g., truck drivers, heavy construction operators, nurses dispensing medications, pilots, boat captains, military and police personnel using dangerous equipment, and childcare workers with children.

Modafinil was used because it may be more selective than traditional stimulants, has a low abuse potential, is already used in many specific sleep disorders, and has a reasonable safety record.

Modafinil's mechanism as a waking agent appears to be a more selective than amphetamine or methylphenidate in cats,

⁵ possibly causing less emotional side effects in humans, e.g., agitation and rebound depression. Perhaps due to this proposed selectivity, modafinil receives low ratings for abuse desirability, ⁶ and with a low solubility in water and instability at high temperatures, I.V. injections and smoking were less likely. ⁷ These are some reasons that modafinil might be considered in light of the non-specificity and addiction potential of traditional stimulants.

Modafinil has cognitive benefits in aviation alertness and functioning. 8, 9 It decreases fatigue in narcolepsy, obstructive sleep apnea, Parkinson's disease, multiple sclerosis, stroke and fibromyalgia. 10,111,12,13,14,15 Also, medically fragile patients seemed to tolerate modafinil. Our patients were much healthier than those treated with Parkinson's disease, stroke and multiple sclerosis.

These private patients were all waiting for a sleep specialist appointment. They read handouts on the common use of modafinil, e.g., narcolepsy. However, they understood they were trying it for the off-label purpose of daytime sleepiness. Rare questions were answered to their satisfaction.

INDIVIDUAL CASES

It was ascertained that all four patients had acceptable sleep hygiene. None used stimulants such as caffeine. None wanted "addictive" or "stimulating" traditional non-specific agents, e.g., mazindol, after reviewing the side effect profile. All were attempting to sleep eight hours a day. None appeared to be a clear driving risk based on their driving record and history.

CASE 1

A 46 year old male truck driver reported profound irritability, sadness and suicidal ideation. Citalopram 20 mg ended his Major Depression, but fatigue and irritability remained. 100 mg of modafinil twice a day caused an immediate decrease in fatigue and another 25% reduction in irritability. He needed 6 weeks to get both a sleep consult and polysomnography. He was diagnosed with Obstructive Sleep Apnea and Periodic Limb Movement Disorder (PLMD). He refused regular CPAP for the apnea, since he felt "he was choking." He had an uvulopalatoplasty. Finally, clonazepam 0.5 mg at bed treated his PLMD, with no return of his apnea. He successfully stopped modafinil with no significant return of his irritability. His baseline Epworth Sleepiness Scale 16 went from a 16 to a 7.

CASE 2

A 43 year old female nurse reported being "perimenopausal." Specifically, she had hot flashes, menstrual irregularities, increased pituitary gonadotropins, widely erratic estradiol levels on serial laboratory testing, plus fatigue and depression. She was treated with two isoflavones (soy and red clover) and given bio-identical compounded progesterone during her luteal-phase. Despite relief, she remained tired, admitting she was not "as alert as usual" dispensing medications. She took up to 200 mg before her shift. The modafinil allowed her to work "alertly," and her shift colleagues said she "seemed better." Her sleep study revealed significant PLMD. It took a total of 13 weeks for her to be treated with clonazepam 0.75 mg and to be removed from modafinil with no change in alertness. Her baseline Epworth Sleepiness Scale went from an 11 to 6.

CASE 3

A 52 year old female psychologist reported having "loud snoring and occasionally gasps for breath." She was concerned that many of her personality-disordered clients had commented she seemed sleepy in sessions. They "did not trust" her anymore. Some clients were suicidal. She feared "drifting off and having one of them feel rejected and committing suicide." Her sleep study showed mild apnea and occasional hypoxia. A throat and palate evaluation revealed a profoundly inflamed and swollen tongue base and edema of the posterior portion of the larynx, causing the sleep disorder. She was treated with omeprazole at dinner to decrease stomach acid and possible reflux disease while sleeping. She was later fitted with a mouthpiece, which pulled her lower jaw forward. Her full work up took 6

months. Then the modafinil was stopped. She no longer felt sleepy during sessions. Her baseline Epworth Sleepiness Scale went from a 12 to a 3.

CASE 4

A 22 year old year old obese, male had a three-year history of profound irritability and fights. He had been arrested once for assault, but the charges were dropped. Mood stabilizers, anti-depressants and anti-psychotics only increased his fatigue on low doses with no measurable improvement. He did not meet DSM IV-TR criteria for Major Depression or Mania.

He had a 47 cm (18 1/2 inch) neck and a narrowed posterior pharynx, so he was referred for a sleep evaluation. He was diagnosed with severe obstructive sleep apnea. He was placed on 100 mg modafinil at breakfast and lunch. His irritability and aggression decreased to only intermittent fantasies. He was operated on twice, eventually removing his uvula and surrounding soft palate tissue, and later his adenoids. His aggression and irritability decreased by over 90% after his second surgery. After seven months, his modafinil was stopped successfully. His Epworth Sleepiness Scale went from a baseline of 14 to a 7.

CONCLUSION

Short-term modafinil may be useful in patients with suspected sleep disorders. It may prevent problems during the period before successful treatment. Modafinil will not certainly not always be the final treatment for some sleep disorders, but it might be one useful initial option. Future research will need to explore the utility and ethics of prescribing for individuals with mild fatigue while driving. Of course, it should not be used as an alternative to decent sleep hygiene. None of these patients abused it this way.

What if no exact, treatable sleep disorder is found at the sleep consultation? A larger study comparing modafinil to other treatment options is required for such unfortunate patients. Such a study is outside the scope of this case series.

References

- 1. Lyznicki JM, Doege TC, Davis RM, Williams MA, for the Council on Scientific Affairs, American Medical Association. Sleepiness, driving, and motor vehicle crashes. JAMA. 1998;279:1908-1913.
- 2. Mahowald MW. Eyes wide shut. The dangers of sleepy driving. Minn Med. 2000;83:25-30.
- 3. Sagberg F. Road accidents caused by drivers falling asleep. Accid Anal Prev. 1999;31:639-649.
- 4. Hobson DE, Lang AE, Martin WR, Razmy A, Rivest J, Fleming J. Excessive daytime sleepiness and sudden-onset

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- sleep in Parkinson disease. JAMA. 2002:287.
- 5. Lin SH, Hou Y, Jouvet M. Potential brain neuronal targets for amphetamine-, methylphenidate-, and modafinil-induced wakefulness, evidenced by c-fos immunocytochemistry in the cat. Proc Natl Acad Sci. 1996;93:14128-14133.
- 6. Jasinski DR. An evaluation of the abuse potential of modafinil using methylphenidate as a reference. J Psychopharmacol. 2000;14:53-60.
- 7. Jasinski DR, Kovacevic-Ristanovic R. Evaluation of the abuse liability of modafinil and other drugs for excessive daytime sleepiness associated with narcolepsy. Clin Neuropharmacol. 2000;23:149-156.
- 8. Caldwell JA, Caldwell JL, Smythe NK 3rd, Hall KK. A double-blind, placebo controlled investigation of the efficacy of modafinil for sustaining the alertness and performance of aviators: a helicopter simulator study. Psychopharmacology (Berl). 2000;150:272-82.
- 9. Batejat DM, Lagarde DP. Naps and modafinil as countermeasures for the effects of sleep-deprivation on cognitive performance. Aviat Space Environ Med. 1999;70:493-498.

- 10. Billiard M, Carlander B. Wake disorders. I. Primary wake disorders. Rev Neurol (Paris). 1998;154:111-129.
- 11. Mitler MM, Harsh J, Hirshkowitz M, Guilleminault C. Long-term efficacy and safety of modafinil (ProvigilR) for treatment of excessive daytime sleepiness associated with narcolepsy. Sleep Medicine. 2000;1: 231-243.

 12. Arnulf I, Homeyer P, Garma L, Whitelaw WA, Derenne
- 12. Arnulf I, Homeyer P, Garma L, Whitelaw WA, Derenne JP, Modafinil in obstructive sleep apnea-hypopnea syndrome: a pilot study in 6 patients. Respiration. 1997;64:159-161.
- 13. Happe S, Pirker W, Sauter C, Klosch G, Zeitlhofer J. Successful treatment of excessive daytime sleepiness in Parkinson's disease with modafinil. J Neurol. 2001:248:632-634.
- 14. Silber MH. Sleep disorders. Neurol Clin. 2001;19:173-186.
- 15. Schaller JL, Behar D. Modafinil in fibromyalgia treatment. J Neuropsychiatry Clin Neurosci. 2001;13:530-531.
- 16. Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. Sleep. 1992;15:376-381.

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