Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin

An American Academy of Sleep Medicine Report

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These practice parameters pertain to the treatment of hypersomnias of central origin. They serve as both an update of previous practice parameters for the therapy of narcolepsy and as the first practice parameters to address treatment of other hypersomnias of central origin. They are based on evidence analyzed in the accompanying review paper. The specific disorders addressed by these parameters are narcolepsy (with cataplexy, without cataplexy, due to medical condition and unspecified), idiopathic hypersomnia (with long sleep time and without long sleep time), recurrent hypersomnia and hypersomnia due to medical condition. Successful treatment of hypersomnia of central origin requires an accurate diagnosis, individual tailoring of therapy to produce the fullest possible return of normal function, and regular follow-up to monitor response to treatment. Modafinil, sodium oxybate, amphetamine, methamphetamine, dextroamphetamine, methylphenidate, and selegiline are effective treatments for excessive sleepiness associated with narcolepsy, while tricyclic antidepressants and fluoxetine are effective treatments for cataplexy, sleep paralysis, and hypnagogic hallucinations; but the quality of published clinical evidence supporting them varies. Scheduled naps can be beneficial to combat sleepiness in narcolepsy patients. Based on available evidence, modafinil is an effective therapy for sleepiness due to idiopathic hypersomnia, Parkinson's disease, myotonic dystrophy, and multiple sclerosis. Based on evidence and/or long history of use in the therapy of narcolepsy committee consensus was that modafinil, amphetamine, methamphetamine, dextroamphetamine, and methylphenidate are reasonable options for the therapy of hypersomnias of central origin.

Keywords: Narcolepsy, idiopathic hypersomnia, recurrent hypersomnia, Parkinson's disease, myotonic dystrophy, multiple sclerosis, modafinil, sodium oxybate, amphetamine, methamphetamine, dextroamphetamine, methylphenidate, selegiline, tricyclic antidepressants, fluoxetine

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INTRODUCTION

EXCESSIVE DAYTIME SLEEPINESS HAS A SIGNIFICANT DETRIMENTAL IMPACT ON PSYCHOLOGICAL, SOCIAL AND VOCATIONAL FUNCTION AND PERSONAL SAFETY, thus adversely affecting quality of life. Sleepiness is an important public health issue among individuals who work in fields where the lack of attention can result in injury to self or others such as transportation and healthcare. Hypersomnia of central origin is a category of disorders in which daytime sleepiness is the primary complaint, but the cause of this symptom is not due to "disturbed nocturnal sleep or misaligned circadian rhythms."[1]

Narcolepsy, a disorder characterized by excessive daytime sleepiness and intermittent manifestations of REM sleep during wakefulness, is the best characterized and studied central hypersomnia. The use of stimulants for treatment of narcolepsy was the subject of an American Academy of Sleep Medicine (AASM) review paper in 1994, and formed the basis for practice parameters published by the Standards of Practice Committee (SPC) of the AASM on therapy of narcolepsy with stimulants.[2,3] In 2000, the SPC published a combined review and updated practice parameters on treatment of narcolepsy that included therapies other than stimulants.[4]

Since the publication of the 2000 paper, there have been significant advances concerning the treatment of hypersomnia to justify a practice parameters update. In addition, since the publication of the previous practice parameters, the AASM published a revised coding manual, the International Classification of Sleep Disorders, Second Edition (ICSD-2).[1] The ISCD-2 includes 12 disorders under the category of hypersomnia of central origin. This updated parameter paper and the accompanying review expanded the scope of the review and practice parameters to a subset of disorders in which the primary pathophysiology of hypersomnia is not related to sleep restriction, medication use or psychiatric disorder. For these disorders, the use of alerting medications often represent the primary mode of therapy. The specific disorders included in these practice parameters are narcolepsy (with cataplexy, without cataplexy, due to medical condition and unspecified) idiopathic hypersomnia (with long sleep time and without long sleep time), recurrent hypersomnia, and hypersomnia due to a medical condition. For the remainder of this manuscript, use of

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Table 1—AASM Classification of Evidence

Evidence Levels	Study Design
I	Randomized, well-designed trials with low alpha and beta error,* or meta-analyses of randomized controlled trials with homogeneity of results
II	Randomized trials with high alpha and beta error, methodologic problems, or high quality cohort studies*
III	Nonrandomized concurrently controlled studies (case-control studies)
IV	Case-control or cohort studies with methodological problems, or case series
V	Expert opinion, or studies based on physiology or bench research

Oxford levels adapted from Sackett [6,7] *Alpha (type I error) refers to the probability that the null hypothesis is rejected when in fact it is true (generally acceptable at 5% or less, or $P<0.05$). Beta (Type II error) refers to the probability that the null hypothesis is mistakenly accepted when in fact it is false (generally, trials accept a beta error of 0.20). The estimation of Type II error is generally the result of a power analysis. The power analysis takes into account the variability and the effect size to determine if sample size is adequate to find a difference in means when it is present (power generally acceptable at 80%-90%).

Table 2—AASM Levels of Recommendations

Term	Definition
Standard	This is a generally accepted patient-care strategy that reflects a high degree of clinical certainty. The term standard generally implies the use of level 1 evidence, which directly addresses the clinical issue, or overwhelming level 2 evidence.
Guideline	This is a patient-care strategy that reflects a moderate degree of clinical certainty. The term guideline implies the use of level 2 evidence or a consensus of level 3 evidence.
Option	This is a patient-care strategy that reflects uncertain clinical use. The term option implies either inconclusive or conflicting evidence or conflicting expert opinion.

Adapted from Eddy[8]

the term "hypersomnia of central origin" will refer to this subset of disorders.

Idiopathic hypersomnia presents as constant and severe excessive sleepiness with naps that are unrefreshing. Post awakening confusion (sleep drunkenness) is often reported. Idiopathic hypersomnia with long sleep time includes a prolonged sleep episode of at least 10 hours duration and is felt to be a unique disease entity.[1]

Recurrent hypersomnia is a rare disorder characterized by recurrent episodes of hypersomnia.[1] The Klein-Levin syndrome is the best characterized type and presents with associated behavioral abnormalities including binge eating and hypersexuality. Hypersomnia due to a medical condition refers to hypersomnia due to a co-existing medical condition in the absence of cataplexy.[1] Important subtypes of this diagnostic category include hypersomnia secondary to Parkinson's disease, posttraumatic hypersomnia, genetic disorders (e.g., Prader-Willi syndrome and myotonic dystrophy) and hypersomnia due to central nervous system lesions.

The purpose of this practice parameter paper is to present recommendations on therapy of hypersomnia of central origin. It updates the prior parameters for the treatment of narcolepsy and provides the first practice parameters on the therapy of other hypersomnias of central origin. Recommendations are based on the accompanying review paper produced by a Task Force established by the SPC.[5] The review paper provides a systematic and comprehensive review of the medical literature regarding treatment of hypersomnias of central origin and grades the evidence contained within the literature using the Oxford evidence grading system.[6]

METHODS

The Standards of Practice Committee of the AASM developed the clinical questions and scope of practice to be addressed in the present practice parameters. The AASM appointed a Task Force of content experts in 2005 to perform a comprehensive review of the medical literature regarding treatment of hypersomnias of central origin, and to grade the strength of evidence for each citation. The literature search was performed using Medline, and details regarding search terms, exclusions, and methods for screening by Task Force members, and questions addressed are provided in the accompanying review paper. The grading of evidence was performed by the Task Force in accordance with the scheme shown in Table 1. Three members of the Standards of Practice Committee (VK, TB, and TS) served as liaisons to facilitate communication between the Standards of Practice Committee and the Task Force. The Standards of Practice Committee used the evidence review of the Task Force, the prior practice parameters on narcolepsy, and the reviews upon which they were informed to develop these updated practice parameters, and rated the levels (strength) of recommendations using the AASM codification shown in Table 2. This practice parameter paper is referenced, where appropriate, using square-bracketed numbers to the relevant sections and tables in the accompanying review paper, or with additional references at the end of this paper. When scientific data were absent, insufficient or inconclusive, committee consensus was used to develop recommendations at an "Option" level (Table 2).

The Board of Directors of the AASM approved these recommendations. All members of the AASM Standards of Practice Committee and Board of Directors completed detailed conflict of interest statements and were found to have no conflicts of interest with regard to this subject. These practice parameters define principles of practice that should meet the needs of most patients in most situations. These guidelines should not, however, be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding propriety of any specific care must be made by the physician, in light of the individual circumstances presented by the patient, available diagnostic tools, accessible treatment options, and resources. The AASM expects these guidelines to have an impact on professional behavior, patient outcomes, and, possibly, health care costs. These practice parameters reflect the state of knowledge at the time of publication and will be reviewed, updated, and revised as new information becomes available.

RECOMMENDATIONS

Recommendations concerning narcolepsy which are similar to, or are an expansion of previous ones, and new recommendations are noted as such in the text. The recommendations concerning other hypersomnias of central origin represent the first recommendations on treatment of these disorders. Recommendations regarding use of medications apply only to adults except when specified.

1. An accurate diagnosis of a specific hypersomnia disorder of central origin should be established. The evaluation should include a thorough evaluation of other possible contributing causes of excessive daytime sleepiness. (Standard).

Prior to committing to long-term therapy of hypersomnia, an accurate diagnosis is important in order to choose an appropriate therapy. The ICSD-2 specifies necessary diagnostic tests and criteria for each disorder of hypersomnia of central origin.[1] Many other conditions produce such sleepiness and can mimic or coexist with a hypersomnia of central origin. These include sleep disordered breathing syndromes, periodic limb movements, insufficient sleep, psychiatric disorders, medications, and circadian rhythm disorders. All need to be considered in the differential diagnosis as possibly causing or contributing to the excessive sleepiness in a patient with a hypersomnia of central origin. Management of these primary or concomitant disorders will require specific therapeutic interventions apart from the use of CNS alerting agents or CNS neuromodulator agents. We acknowledge that this recommendation is based on committee consensus and is only slightly revised from a previous recommendation which was restricted to narcolepsy.[4] Typically consensus only merits an "Option" level of recommendation. Although there are no articles addressing the need for an accurate diagnosis, all subsequent evidence evaluating efficacy of treatments assumes an accurate diagnosis has been established. Therefore, the SPC left this recommendation at a "Standard" level.

2. Treatment objectives should include control of sleepiness and other sleep related symptoms when present. (Standard)

It has been previously recommended that a major objective of treatment of narcolepsy should be to alleviate daytime sleepiness. The goal should be to produce the fullest possible return of normal function for patients at work, at school, at home, and socially. This recommendation was revised by committee consensus to apply to the disorders of hypersomnia of central origin. A recommendation to control nocturnal symptoms of disrupted sleep is added to the previous recommendation to control cataplexy, hypnagogic hallucinations, and sleep paralysis, when present and troublesome in patients with narcolepsy. As previously recommended for narcolepsy, a healthcare provider should consider the benefit to risk ratio of medication for an individual patient, the cost of medication, convenience of administration, and the cost of ongoing care including possible laboratory tests when selecting a medication for treatment of any hypersomnia of central origin.

3. The following are treatment options for narcolepsy.

Most of the agents used to treat excessive sleepiness have little effect on cataplexy or other REM sleep associated symptoms. Conversely, most antidepressants and anticataplectics have little effect on alertness. However, some compounds act on both symptoms. We have indicated which symptoms are addressed by the various agents below. Compounds should be selected depending on the diagnosis and the targeted symptoms. Co-administration of two or more classes of compounds may be needed in some patients to adequately address their symptoms.

a. Modafinil is effective for treatment of daytime sleepiness due to narcolepsy [4.1.1.2] (Standard).

This recommendation is unchanged from the previous recommendation. Fourteen additional studies including four level 1 studies and two level 2 studies support this recommendation.[9-14,15] The approved recommended dose of modafinil is 200 mg given once daily, but higher doses and split dose regimens have been investigated. Three level 1 studies indicated that the use of a split dose strategy provides better control of daytime sleepiness than a single daily dose.[12,14] One of the studies demonstrated that adding a dose of modafinil 200 mg at 12:00 after a 400 mg dose at 07:00 improved late day maintenance of wakefulness test (MWT) scores relative to a single 400 mg morning dose alone.[14] A second study demonstrated that a split dosing strategy either with 200 mg of modafinil at 07:00 and 12:00 or 400 mg in the morning and 200 mg at noon was significantly superior to a single morning 200 mg dose at 07:00.[12] Statistical comparisons to a group that received a 400 mg dose in the morning alone were not provided, but split dosing strategies trended towards improved control of sleepiness in the evening. A third study assessed subjects with reported persistent late afternoon or evening sleepiness despite a positive response to modafinil therapy. Subjects who received 400 mg per day in a divided dosage experienced improvement in subjective and objective measures of sleepiness in the afternoon or evening compared with those on a single 200 mg or 400 mg dosage.[13] A level 1 study by Black et al. compared combinations of active and placebo preparations of modafinil and sodium oxybate.[9] Subjects who received active modafinil showed improvement in objective and subjective sleepiness compared to placebo modafinil. Those subjects receiving both active modafinil and active sodium oxybate showed the most improvement suggesting an additive effect of the combination. One level 4 open label study showed modafinil was effective in improving sleepiness and was generally well tolerated in 13 children (mean age 11 years) with narcolepsy or idiopathic hypersomnia.[10]

One additional level 1 study of 196 subjects involved assessment of armodafinil (the longer half-life enantiomer of modafinil) for treatment of excessive sleepiness in patients with narcolepsy. Subjects receiving armodafinil experienced significant improvement in sleepiness as measured by the MWT mean sleep latency, and in the Clinical Global Impression of Change.[16]

b. Sodium oxybate is effective for treatment of cataplexy, daytime sleepiness, and disrupted sleep due to narcolepsy [4.2.1, 4.1.1.3, 4.3.1](Standard). Sodium oxybate may be effective for treatment of hypnagogic hallucinations and sleep paralysis [4.4.1] (Option).

This is a new recommendation, and is based on three level 1 and two level 4 studies. Three level 1 studies support the efficacy of sodium oxybate in treating cataplexy.[17-19] One of these studies also supported its efficacy in treating daytime sleepiness and dis-

rupted sleep but found no significant improvement in hypnagogic hallucinations or sleep paralysis.[17] Two additional level 1 studies supported its efficacy in treating daytime sleepiness.[9,20] There was one level 4 study that supported its efficacy in improving daytime sleepiness, nocturnal awakenings, sleep paralysis, and hypnagogic hallucinations.[21] Studies that supported efficacy in improving daytime sleepiness showed greater treatment effects and statistically significant effects most consistently at the highest dose (9 g/night). In addition, there was one level 4 study that supported its efficacy for cataplexy and daytime sleepiness.[22]

c. Amphetamine, methamphetamine, dextroamphetamine, and methylphenidate are effective for treatment of daytime sleepiness due to narcolepsy [4.1.1.1] (Guideline).

This recommendation is unchanged from the previous recommendation. These medications have a long history of effective use in clinical practice but have limited information available on benefit-to-risk ratio.[4] This lack of information may reflect the limited sources of research funding for medications available in generic form rather than clinical utility of these medications.

d. Selegiline may be an effective treatment for cataplexy and daytime sleepiness. [4.1.1.4] (Option)

This recommendation was downgraded from the previous recommendation based on committee consensus. The current literature review did not identify additional studies that met inclusion criteria. The use of selegiline is limited by potential drug interactions and diet-induced interactions. Because of limited clinical experience with the use of this medication for narcolepsy and potential drug and diet interactions, the committee had significant reservations about this agent being used as the preferred initial choice for treatment of sleepiness in narcolepsy.

e. Ritanserin may be effective treatment of daytime sleepiness due to narcolepsy [4.1.1.6] (Option).

This is a new recommendation based on two level 2 studies of ritanserin, a 5-HT2 antagonist. One study demonstrated improvement in subjective sleepiness, but not in mean sleep latency on MSLT in narcolepsy patients (N=28) when ritanserin 5 mg/day was added to the medication regimen.[23] The other study, which compared 5 mg, 10 mg, or placebo in 134 subjects with narcolepsy, did not demonstrate significant improvement in sleepiness, but showed improvement in subjective sleep quality.[24] Ritanserin is not available for use in the United States.

f. Scheduled naps can be beneficial to combat sleepiness but seldom suffice as primary therapy for narcolepsy [4.1.2] (Guideline).

This recommendation is unchanged from the previous recommendation. The current search identified an additional level 2 study which supports the use of scheduled naps in narcolepsy patients who remain sleepy despite the use of medications.[25] The combination of regular bedtimes and two 15-minute regularly scheduled naps reduced unscheduled daytime sleep episodes and sleepiness when compared to stimulant therapy alone.

g. Pemoline has rare but potentially lethal liver toxicity, is no longer available in the United States, and is no longer recommended for treatment of narcolepsy [4.1.1.7] (Option).

This is a new recommendation based on committee consensus.

h. Tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), venlafaxine, and reboxetine may be effective treatment for cataplexy [4.2.2] (Guideline).

This recommendation is changed from the previous recommendation addressing treatment of cataplexy, hypnagogic hallucinations, and sleep paralysis. The medications recommended for treatment of cataplexy have been expanded to include SSRIs, venlafaxine, and reboxitine. A separate recommendation regarding treatment of hypnagogic hallucinations and sleep paralysis is addressed below as a separate parameter. There was limited evidence regarding treatment of cataplexy in the prior practice parameters. In the updated review, only one level 4 study[26] involving treatment of cataplexy with a medication other than sodium oxybate was identified. Reboxetine, a selective norepinephrine reuptake inhibitor, decreased cataplexy in 12 subjects with narcolepsy with cataplexy. Reboxetine is not available for use in the United States. The previous recommendation for the SSRI fluoxetine was based on one level 2 and one level 5 study supporting its efficacy for treatment of cataplexy. Additional studies of other SSRIs in the treatment of cataplexy and related symptoms did not meet our inclusion criteria as most were case reports and small open label studies. However, the clinical experience of sleep specialists and committee consensus, as well as the more limited open label studies with small numbers of subjects, reflect that additional SSRIs are useful for treating cataplexy in patients with narcolepsy. The antidepressant venlafaxine, which increases serotonin and norepinephrine uptake, may also reduce cataplexy, based on clinical experience, committee consensus, and a case study of 4 patients that did not meet inclusion criteria for our review.[27]

i. Tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), and venlafaxine may be effective treatment for treatment of sleep paralysis and hypnagogic hallucinations [4.4.2] (Option).

By consensus, this recommendation is revised from the prior recommendation. The recommendation level is reduced from guideline to option. Additional antidepressant medications are also recommended. No new pertinent studies have been identified in the current review. Recommendation level was downgraded to reflect that this recommendation is based on anectodal experience of committee members. These treatments may be considered for this indication when the treating physician and patient believe that the benefits of treatment outweigh the risks. In addition, based on clinical experience and committee consensus, the recommendations are extended to include additional antidepressant agents (SSRIs and venlafaxine).

4. Modafinil may be effective for treatment of daytime sleepiness due to idiopathic hypersomnia [4.8] (Option).

One level 4 study that included 24 patients with narcolepsy and 18 with idiopathic hypersomnolence examined the efficacy

of modafinil in adults with idiopathic hypersomnia.[28] There were improvements in the mean number of drowsy episodes and sleep attacks as recorded in sleep diaries for both patient groups on this medication. This is a new recommendation.

5. The following medications may be effective treatments for specific types of hypersomnia due to a medical condition [4.9].

a. Modafinil may be effective for treatment of daytime sleepiness due to Parkinson's disease (Option).

This conclusion is based on: one level 1 study which showed improvement in the Epworth Sleepiness Scale (ESS) but no change in MWT[29]; one level 2 study which showed no improvement in subjective or objective measures of excessive daytime sleepiness[30]; one level 4 study which showed improvement in ESS[31]; and Committee consensus. However the benefit to risk ratio is not well documented because the published clinical trials include only small numbers of patients. This is a new recommendation.

b. Modafinil may be effective for treatment of daytime sleepiness due to myotonic dystrophy (Option).

This conclusion is based on one level 1 study which showed improvement in MWT but no significant change in ESS, and on committee consensus. The benefit to risk ratio is not well documented because the published clinical trial included only small numbers (n=20) of patients.[32] This is a new recommendation.

c. Methylphenidate may be effective for treatment of daytime sleepiness due to myotonic dystrophy (Option)

This conclusion is based on one small (N=11) level 4 study of methylphenidate for treatment of sleepiness associated with myotonic dystrophy that demonstrated improvement in subjective sleepiness in 7 of 11 subjects at doses up to 40 mg/day, and committee consensus.

d. Modafinil may be effective for treatment of daytime sleepiness due to multiple sclerosis (Guideline).

This conclusion is based on one level 2 study (N=72) and one level 4 study (N=50) which showed improvement on the ESS.[33,34] This is a new recommendation.

6. Lithium carbonate may be effective for treatment of recurrent hypersomnia and behavioral symptoms due to Kleine-Levin syndrome. [4.6] (Option)

This recommendation is based on one small case series (N=5) that indicated that the duration of hypersomnia episodes was shorter and there were no behavioral symptoms during episodes that were treated with lithium carbonate,[35] and committee consensus.

7. The following medications may be effective for treatment of daytime sleepiness in idiopathic hypersomnia (with and without long sleep time), recurrent hypersomnia, and hypersomnia due to a medical condition: amphetamine, methamphetamine, dextroamphetamine, methylphenidate, and modafinil [4.7, 4.8, 4.9] (Option)

The literature supporting the efficacy of these medications for other specific disorders such as narcolepsy have been reviewed. Where published evidence meeting search criteria is available for the use of any of these medications in the conditions listed, this has been provided in sections 4 and 5. This recommendation applies to those medications and conditions combinations for which published literature meeting search criteria is not available. Although there is no reason to suspect they will not improve alertness, individualized therapy and close follow-up to ensure efficacy and monitor for side effects is needed. The recommendations for these disorders are based on committee consensus.

8. The following are treatment recommendations previously applied to narcolepsy only. Their application is now extended to the hypersomnias of central origin covered by this practice parameter paper by committee consensus.

a. Combinations of long- and short-acting forms of stimulants may be indicated and effective for some patients (Option).

Some stimulants have a short (3 to 4 hours) effective period (e.g., methylphenidate). Others have longer duration of activity and longer onset of action (e.g., modafinil, sustained-release amphetamine, sustained-release methylphenidate). By combining stimulants with different activity characteristics, it may be possible to achieve alertness quickly and for longer periods of time and succeed in avoiding insomnia as an unwanted side effect.[4]

b. Treatment of hypersomnias of central origin with methylphenidate or modafinil in children between the ages of 6 and 15 appears to be relatively safe. [4.1.1.2, 4.8, 5.1.1](Option)

There is considerable experience with the use of methylphenidate for treatment of attention deficit disorder.[4] There is one level 4 study of modafinil in children with narcolepsy or idiopathic hypersomnolence that indicated it was safe and well tolerated in children who did not have other preexisting neurologic or psychiatric conditions.[10]

c. Regular follow-up of patients with hypersomnia of central origin is necessary to monitor response to treatment, to respond to potential side effects of medications, and to enhance the patient's adaptation to the disorder [4.10] (Standard).

i. A patient previously stabilized on stimulant medication should be seen regularly by a health care provider at least once per year, and preferably once every 6 months, to assess the development of medication side effects, including sleep disturbances, mood changes, and cardiovascular or metabolic abnormalities.

ii. Follow-up is necessary to determine adherence and response to treatment; to monitor for the safety of medications in individual patients; and to assist the patient with occupational and social problems.

iii. Patients with severe sleepiness should be advised to avoid potentially dangerous activities at home and at work, and should not operate a motor vehicle until sleepiness is appropriately controlled by stimulant medications.

iv. Of the stimulants used to treat hypersomnia of central origin, amphetamines, especially at high doses, are the most likely to result in the development of tolerance

v. Patients who fail to respond to adequate doses of stimulant medication should be carefully assessed for other sleep disorders that may contribute to excessive sleepiness such as insufficient sleep, inadequate sleep hygiene, circadian rhythm disorders, obstructive sleep apnea syndrome, or periodic limb movement disorder.

vi. For side effects, dosage ranges, use in pregnancy and by nursing mothers, and contraindications , see Tables 6 and 7 in the accompanying review paper.[4]

vii. Health care providers should assist the patient with occupational and social accommodation for disabilities due to hypersomnia of central origin.

viii. Polysomnographic re-evaluation of patients should be considered if symptoms of sleepiness increase significantly or if specific symptoms develop that suggest new or increased sleep abnormalities that might occur in disorders such as sleep apnea or periodic limb movement disorder.

Areas for Future Research

The preparation of this practice parameter and the accompanying review highlighted the need for additional research regarding treatment of hypersomnia of central origin.

1. Comparisons of traditional stimulants to newer somnolytic agents for hypersomnia due to narcolepsy.

Several large randomized, placebo-controlled studies indicate that modafinil and sodium oxybate are effective for treatment of hypersomnia associated with narcolepsy. The traditional stimulants (amphetamine, methamphetamine, dextroamphetamine, and methylphenidate) which are available in generic form and are less expensive, have a long history of use in clinical practice, but have limited high-level evidence from published studies. There is a need for randomized trials that compare the newer agents to the traditional stimulants to establish relative efficacy and safety of these agents to guide the clinician in choosing between them for individual patients.

2. Additional assessment of antidepressants and comparison to sodium oxybate for treatment of cataplexy.

The recommendation for use of antidepressants for cataplexy is based largely on clinical experience and lower evidence level clinical trials. Randomized controlled trials of these agents, particularly with comparison to sodium oxybate, a more expensive medication that has high level evidence of efficacy, are needed to assist the clinician in medication selection.

3. New therapies for treatment of hypersomnia due to narcolepsy.

As indicated by the accompanying review, traditional stimulants, modafinil and sodium oxybate provide, at best, only moderate improvement in sleepiness in patients with narcolepsy. Future investigations should be directed toward development of more effective and better tolerated therapies, and primary prevention.

4. Need for studies on treatment of hypersomnias of central origin other than narcolepsy.

The review identifies very few studies that address the treatment of sleepiness in specific hypersomnia disorders other than narcolepsy. There is a need for studies, particularly testing the use of traditional stimulants in these disorders.

5. Need for peer-reviewed literature regarding special populations including children, elderly patients, and pregnant and nursing women.

The review identified very few studies that involve special populations with hypersomnia such as children, older adults, or pregnant or nursing women. There is a need for studies that address safety issues specific to these populations.

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