Is SAD Lost to SAD?

By Siegfried Kasper, MD

Since 1984, 447 articles have been published using the acronym “SAD” for seasonal affective disorder in the heading of the publication, and since 1992, 59 articles have used “SAD” in the heading of the publication as an acronym for social anxiety disorder, according to MEDLINE. Using the acronym SAD for social anxiety disorder has been used with more frequency in recent scientific publications—interestingly, mostly in connection with newer antidepressants that have been found to be of therapeutic potential for this indication. To avoid possible confusions in research, the acronym “SOAD” was proposed for social anxiety disorder by Kasper and Winkler and “SAnD” by Nutt (D.J. Nutt, MD, PhD, unpublished data, 2004)—seemingly without success since these abbreviations are not seen in the literature. This month, CNS Spectrums focuses on the existing literature on the original acronym for SAD—seasonal affective disorder and its worldwide recognition.

In the early 1980s, Rosenthal and colleagues at the National Institute of Mental Health (NIMH) set out to describe a syndrome called SAD, not to be confused with the other, more recent SAD, social anxiety disorder. The original has been known to physicians since ancient times, dating back to Aretaeus the Cappadocian. However, the NIMH researchers for the first time systematically described the clinical symptomatology, compared it with healthy controls, and differentiated SAD from nonseasonal depression. Their work in tandem with emerging technology led to the discovery of the underlying pathophysiology of SAD and treatment approaches. The most important of these approaches were light therapy and pharmacotherapeutic options.

The articles in this issue summarize the existing literature on epidemiological, diagnostic, and symptomatological characteristics of SAD, and the underlying biology, which further elucidates the understanding of the mechanisms involved in affective disorders.

SAD research indicates that there is a dimension in the general population that spans from healthy individuals over subsyndromal SAD to SAD patients. As Andres Magnusson, MD, PhD, and Timo Partonen, MD, PhD, illustrate, epidemiological research reveals that SAD individuals are often drug-naïve and prefer light therapy, if any at all.

Next, Chang-Ho Sohn, MD, and Raymond W. Lam, MD, FRCP, update one of their previous studies, showing that biological research has elucidated that SAD patients are not fundamentally different in their pathophysiology compared with nonseasonal depression.

Light therapy is among the best-studied nonpharmacologic biological-oriented treatment approaches, and has emerged as the logical treatment for SAD. The analysis of existing data sets by Michael Terman, MD, PhD, and Juian Su Terman, PhD, substantiates that for the indication of SAD the effect size of light therapy is comparable with pharmacologic treatments and that ideally treatment should start in the morning hours. However, if this regimen cannot be followed, treatment during the day or in the late afternoon/evening is also acceptable.

Edda Pjrek, MD, and colleagues explain that biological studies accompanying light therapy indicate that neurotransmitter systems involved in psychotherapeutic biological-oriented treatment approaches are also involved in the pathophysiology of light therapy. The serotonin system has been the most extensively studied, and has revealed that after successful treatment with light therapy, values are comparable with healthy controls. Pharmacologic treatment indicates a positive effect for medication affecting the serotonergic as well as the noradrenergic system. However, the largest data set available is for only serotonergic medication, including sertraline and citalopram.

This issue is meant to summarize the set of available clinically relevant aspects of SAD and reinvigorate interest in this field. If these articles spur further research and, in turn, provide improved treatment for SAD patients, we have achieved our goal.
In managing insomnia

A good night's sleep... ...on course toward better days

Patients wake up refreshed the next day so they're ready to perform

- 2.5-hour half-life
  - Long enough to provide restful nights
  - Short enough to provide refreshed awakenings
- Minimal drug effect on next-day functioning
- Low abuse potential at recommended doses
- The #1 prescribed sleep agent in the US

*Next-day residual effects were evaluated in 7 studies involving normal volunteers. In 3 studies in adults (including 1 study in a phase-advance model of transient insomnia) and 1 study in elderly subjects, a small but statistically significant decrease in performance was observed in the Digit Symbol Substitution Test (DSST) when compared with placebo. Studies in nonelderly patients with insomnia did not detect evidence of next-day residual effects using the DSST, the Multiple Sleep Latency Test (MSLT), and patient ratings of alertness.1

AMBIEN is indicated for the short-term treatment of insomnia. In elderly or debilitated patients, or patients with hepatic dysfunction, treatment should be initiated with a 5-mg dose and patients closely monitored. Due to its rapid onset of action, patients should take AMBIEN right before going to bed and when ready for sleep. Patients should not take AMBIEN unless they are prepared to get a full night's sleep (7 to 8 hours) to avoid residual effects. Until they know how it will affect their physical or mental performance upon awakening, patients should not drive or operate hazardous machinery after taking AMBIEN or any other sleep medication. During short-term treatment with AMBIEN, the most commonly observed adverse effects in controlled clinical trials were drowsiness (2%), dizziness (1%), and diarrhea (1%). Because individuals with a history of addiction or substance abuse are at increased risk of habituation and dependence, they should be under careful surveillance when receiving AMBIEN or any other hypnotic. AMBIEN is classified as a Schedule IV controlled substance. Sedative hypnotics have produced withdrawal signs and symptoms following abrupt discontinuation. Hypnotics should generally be limited to 7 to 10 days of use, and reevaluation of the patient is recommended if they are taken for more than 2 to 3 weeks. Prescriptions for AMBIEN should not exceed a 1-month supply.

Please see brief summary of prescribing information on back.
Amien®

(zoopidem tartrate)

**BRIEF SUMMARY**

**INDICATIONS AND USAGE**

Amien tartrate is indicated for the short-term treatment of insomnia. It is intended for use only as needed, on an as-needed basis (up to a total of 8 consecutive days use), and re-treatment of patients at any one time.

**CONTRAINDICATIONS**

Amien, like other sedative/hypnotic drugs, has CNS-depressant effects. Due to the potential for abuse and dependence, Amien should not be used in patients with a history of drug abuse or alcoholism. In patients with a history of drug abuse or alcoholism, Amien should be administered with caution because of the risk of developing an abuse problem or of withdrawal symptoms from the drug during the postnatal period. In addition, neonatal abstinence syndrome has been observed in infants whose mothers used Amien during pregnancy. Infants exposed to Amien during the third trimester of pregnancy should be monitored for signs and symptoms of withdrawal. Infants born to mothers who used Amien during pregnancy should be observed for the occurrence of any new behavioral sign or symptom of concern and should be evaluated at frequent intervals.

Use in females, the only significant change was a 17% increase in the zoopidem half-life. In addition, clinical data indicate that Amien does not appear to pose a risk of respiratory depression, aspiration, opiate, cocaine, carnosamine, or emethionine in severe standard urine drug screens. Amien had been reported in association wit the use of sedative/hypnotic.

A variety of abnormal thinking and behavior changes have been reported to occur in patients with the use of Amien in clinical trials. The nature and frequency of these changes are unclear. In addition, various serious drug-related adverse events have occurred. The nature and severity of these adverse events are not always predictable and may be characterized by multiple affected organ systems. In general, evidence of a new behavioral alteration is not observed in drug-induced, spontaneous, or a result of an underlying disease or condition. Amien, other non benzodiazepine hypnotics, in addition to those reported in clinical trials, include the formation of new behavioral reactions, sleep continuity (e.g., restless sleep, nonrestful sleep, sleep disturbances), and depression.

**WARNINGS**

The development of tolerance and withdrawal syndromes with sedative/hypnotics has produced withdrawal signs and symptoms following abrupt withdrawal. The withdrawal syndrome may include the following clinical signs and symptoms: drowsiness, dizziness, anxiety, agitation, depression, disturbed sleep, confusion, muscle twitching, tremor, sweating, myoclonus, autonomic symptoms, nausea, vomiting, hyperpyrexia, hyperthermia, hypoglycemia, hypothermia, hyponatremia, hypotension, hypertension, tachycardia, bradycardia, hypoglycemia, hypoxia, hyperpnea, tachypnea, and apnea. The withdrawal syndrome may also result in the development of a withdrawal syndrome that may include abdominal and muscular discomfort, weakness, nervousness, irritability, and insomnia.

**OVERDOSAGE**

In the event of an overdose, the patient should be observed for at least 8 hours or until normal clinical parameters have been achieved. In addition, the use of a diazepam-phenobarbital combination may also be beneficial. The use of more than one dose of Amien (preferably in conjunction with a variety of other CNS-depressant agents) to manage the symptoms of severe sedative overdose is not recommended. Treatment of overdose should be symptomatic and supportive. The patient should be monitored at all times. In addition, the use of more than one CNS-depressant agent to manage the symptoms of severe sedative overdose is not recommended. Treatment of overdose should be symptomatic and supportive. The patient should be monitored at all times.

**Precautions**

Amien should not be administered to patients with a history of drug abuse or alcoholism. In patients with a history of drug abuse or alcoholism, Amien should be administered with caution because of the risk of developing an abuse problem or of withdrawal symptoms from the drug during the postnatal period. In addition, neonatal abstinence syndrome has been observed in infants whose mothers used Amien during pregnancy. Infants exposed to Amien during the third trimester of pregnancy should be monitored for signs and symptoms of withdrawal. Infants born to mothers who used Amien during pregnancy should be observed for the occurrence of any new behavioral sign or symptom of concern and should be evaluated at frequent intervals.

**Contraindications**

Amien is contraindicated for the short-term treatment of insomnia. It is intended for use only as needed, on an as-needed basis (up to a total of 8 consecutive days use), and re-treatment of patients at any one time.

**Warnings**

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**Adverse Events**

The adverse event profile for Amien was similar to that of placebo. The most commonly observed adverse events associated with Amien use were drowsiness, dizziness, dry mouth, somnolence, anxiety, and insomnia. The most commonly observed adverse events associated with Amien use were drowsiness, dizziness, dry mouth, somnolence, anxiety, and insomnia. The most commonly observed adverse events associated with Amien use were drowsiness, dizziness, dry mouth, somnolence, anxiety, and insomnia. The most commonly observed adverse events associated with Amien use were drowsiness, dizziness, dry mouth, somnolence, anxiety, and insomnia. The most commonly observed adverse events associated with Amien use were drowsiness, dizziness, dry mouth, somnolence, anxiety, and insomnia. The most commonly observed adverse events associated with Amien use were drowsiness, dizziness, dry mouth, somnolence, anxiety, and insomnia.