SLEEP DISORDERS

KLEINE-LEVIN SYNDROME RESPONSE TO CARBAMAZEPINE

A 16-year-old male adolescent began having recurrent episodes of severe hypersomnia which persisted 5 or 6 times a year up to age 27, when he was treated with carbamazepine at the American University of Beirut, Medical Center, Lebanon. Each episode lasted 4-7 days and recurred every 2-3 months. During the episode his mean daily sleep time was 20 hours; he woke to eat and void and then went back to sleep. He stated that he felt depressed with suicidal thoughts, and displayed abnormal sexual behavior. Hyperphagia or binge eating was not a symptom. At the end of the episode, he described partial amnesia for the event, and functioned normally without daytime drowsiness. Family history was negative for similar symptoms. Neurologic examination, EEG between episodes, and brain MRI were normal. Initially, he was misdiagnosed with complex partial seizures and was treated with valproate. Therapeutic levels of valproate were ineffective, and treatment with carbamazepine was initiated at 400 mg/day, later increased to 600 mg/day, with a level of 9.2 mg/L. Complete freedom from episodic hypersomnia for 2 years was followed by recurrence when carbamazepine was discontinued. After 3 episodes over 4 months, each lasting 4-5 days, carbamazepine was resumed, followed by complete resolution of attacks. The diagnosis of Kleine-Levin syndrome was confirmed by polysomnogram, recording normal sleep architecture between attacks. (Hajj TE, Nasreddine W, Korri H, Atweh S, Beydoun A. A case of Kleine-Levin syndrome with a complete and sustained response to carbamazepine. **Epilepsy & Behav** July 2009;15:391-392) (Respond: Dr Ahmad Beydoun, American University of Beirut, Medical Center, Beirut, Lebanon. E-mail: ab29@aub.edu.lb).

COMMENT. By John J Millichap MD. Discussant. Case report and Review of Kleine-Levin syndrome for Psychiatry Rounds, CMH, July 2009. Hypersomnia, the cardinal symptom of Kleine-Levin syndrome (KLS), was described by Willi Kleine (1925), and hyperphagia added as a frequently associated symptom by Max Levin (1936). The eponym KLS was coined by M Critchley and Hoffman (1942). Approximately 200 cases are reported, male>female, with onset in adolescence. American Academy of Sleep Medicine and International Classification of Sleep Disorders characterize KLS as a rare disorder affecting predominantly adolescent boys, with recurring episodes of hypersomnia (100%), frequently and variably associated with behavioral and cognitive disturbances (96%), compulsive eating behavior (80%), and hypersexuality (43%). The diagnosis is frequently delayed and often labeled incorrectly as an epilepsy. Differential diagnosis includes non-convulsive status epilepticus, narcolepsy, encephalitis, psychotic affective or dissociative disorders, hypothalamic lesion, and migraine. Median sleep duration during episodes is 18 h/day (range 12-24 h/day), median duration of episodes is 10 days, and interval between episodes is 3 months. Hypothetical etiologies include diencephalic-hypothalamic dysfunction, neurotransmitter imbalance, viral infection, autoimmune HLA, and genetic factors. Triggers include stress, sleep deprivation, and alcohol abuse. Cochrane Review of Treatments finds no evidence that pharmacological agents are consistently effective and safe, stimulants improve sleepiness but not other symptoms, antidepressants have no effect in preventing relapses (except one case using MAOI), anticonvulsant carbamazepine, in single case, improved abnormal behavior, and lithium significantly improves abnormal behavior and recovery, but

only in 3 of 12 patients treated. Median duration of KLS is 8 years (range 0.5 to 41 years). Course is longer for women, and shorter in cases with high number of episodes in first year.

ATTENTION DEFICIT DISORDERS

CARDIOVASCULAR EFFECTS OF LONGER-TERM, HIGH-DOSE OROS METHYLPHENIDATE IN ADOLESCENTS WITH ADHD

The short-term and longer-term cardiovascular safety of high daily doses of OROS methylphenidate (MPH) of up to 1.5 mg/kg in 114 adolescents with ADHD is reported from Massachusetts General Hospital, Boston, MA. Small but statistically significant increase in diastolic BP and heart rate were observed at 6 weeks, without further increases up to 6 months' follow-up. The mean total daily dose of OROS-MPH at 6 weeks was 63.1 +/- 25.0 mg; 50% of subjects were taking >72 mg daily; at month 6 these doses were 67.2 +/- 24.3 mg and >72 mg, respectively. A small but statistically significant increase in systolic BP was observed over time. No changes in ECG were observed and no serious cardiovascular adverse events occurred. (Hammerness P, Wilens T, Mick E, et al. Cardiovascular effects of longer-term, high-dose OROS methylphenidate in adolescents with attention deficit hyperactivity disorder. **J Pediatr** July 2009;155:84-89). (Reprints: Dr Paul Hammerness, Pediatric Psychopharmacology, 185 Alewife Brook Parkway, Suite 2000, Cambridge, MA 02138. E-mail: phammerness@partners.org).

COMMENT. Small but statistically significant increases in blood pressure and heart rate were observed in adolescents treated with relatively higher doses of OROS methylphenidate, without changes in the ECG. The CV effects noted in adolescents with higher doses were similar to the previously documented effects in children with lower doses of OROS-MPH. In an editorial, Dr Stephen R Daniels advises caution in patients with BP elevation or tachycardia (**J Pediatr** 2009;155:A3).

COMPARATIVE CARDIAC RISKS OF METHYLPHENIDATE AND AMPHETAMINES IN TREATMENT OF ADHD

The risk for adverse cardiac events in subjects between 3 and 20 years of age treated with methylphenidate or amphetamine salts for ADHD was determined in a retrospective study at University of Florida, Gainesville, FL. Cardiac events were defined as first ED visit for cardiac disease or symptoms. The percentage of patients observed for at least 6 months on stimulants was similar for MPH (54.5%) and amphetamines (52.6%). A total of 456 youth visited the ED for cardiac reasons during 52,783 years of follow-up. The risk for cardiac ED visits was similar among current users of MPH or amphetamines. Periods of former use had a similar risk in subjects exposed. Variables showing positive associations with ED visits with both models were use of bronchodilators, use of antidepressants, antipsychotics at age 15 and older, congenital anomalies, and history of circulatory disease or cardiac symptoms. (Winterstein AG, Gerhard T, Shuster J, Saidi A. Cardiac safety of methylphenidate versus amphetamine salts in the treatment of ADHD. **Pediatrics** July 2009;124:e75-e80). (Respond: