

RISK OF SEIZURES DURING WAKEFULNESS IN PATIENTS WITH PURE SLEEP EPILEPSY

Risk of Seizures while Awake in Pure Sleep Epilepsies: A Prospective Study

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OBJECTIVE: To estimate the risk of seizures while awake in pure sleep epilepsies in a prospective study.

METHODS: From October 1, 1992, to October 31, 1996, all patients with pure sleep epilepsy presenting at a participating center were enrolled. Children with benign rolandic epilepsy and patients with frontal lobe epilepsy were excluded. Patients were followed up for at least 2 up to 6 years. The primary end point was the occurrence of a seizure while awake.

RESULTS: The authors enrolled 161 patients (64% male). Age at the time of inclusion ranged from 11 to 83 years (mean, 43.2; median, 39). Eighty-five percent had generalized tonic-clonic seizures. Both sleep seizures and seizures while awake were absent for 2 years after inclusion in the study in 78% of patients. Eighteen patients had a seizure while awake. The estimated risk of a seizure while awake during 6 years of follow-up was 13% (95% CI, 7% to 18%). Multivariate analysis showed that episodes of sudden withdrawal of therapy and a higher frequency of seizures at inclusion were associated with an increased risk of seizures while awake. The estimated risk of a seizure while awake in patients with none of the above risk factors was 6.5% (95% CI, 1.5% to 11.3%) during 6 years of follow-up.

CONCLUSIONS: The clinical picture of pure sleep epilepsies is characterized by a preponderance of generalized tonic-clonic seizures, low seizure frequency, and a good prognosis. The risk of occurrence of a seizure while awake is low, particularly among patients with rare seizures and good compliance with the therapy.

COMMENTARY

The relation between sleep and epilepsy can best be understood by considering the timing of seizures during the 24-hour sleep-wake cycle, that is, whether seizures occur during the day (diurnal), during the night (nocturnal), or during the day and the night (diffuse). Seizures that occur exclusively during the night are called the *pure sleep epilepsies*. These seizure categories and their distribution over time were described initially by Janz (1) and later reproduced by Billiard (2). The two works became the first comprehensive expositions of the timing of generalized seizures during the 24-hour sleep-wake cycle. Subsequently, the concept of circadian rhythm was applied to the timing of seizures across the different states of vigilance and is used to express how these states significantly influence the expression or suppression of seizures.

Pure sleep epilepsies are considered to be rare and raise more problems in making an accurate diagnosis than do the seizures of wakefulness. It is commonly recognized that pure sleep epilepsies do not belong to any specific epileptic syndrome. Furthermore, the epileptic syndromes associated with the category of *sleep-related* seizures are not always consistent with the concept of *pure sleep epilepsies* (3).

As addressed in the present study, clinicians frequently question: "What is the risk of a seizure occurring during wakefulness in epilepsy patients whose seizures occur exclusively during the night?" and also "Which variables, if any, may put this group of patients more at risk to have a seizure during wakefulness?" Risk factors often considered include type of seizure (generalized versus partial); duration of epilepsy; frequency of the seizures; age of the patient; and gradual or sudden antiepileptic drug (AED) withdrawal. Yet because little is known about these risk factors, important treatment controversies are associated with pure sleep epilepsies, for example, issues pertaining to the need for AEDS and when, and if, to discontinue their use. Furthermore, lack of reliable data regarding the risk of daytime seizure affects social concerns, such as driving, employment, and other quality-of-life issues.

The study by D'Alessandro et al. was designed for the clinician approaching a patient with seizures that occur exclusively during sleep. It is a prospective study with a sample population

larger than those in the previous two retrospective studies (4,6) on pure sleep epilepsy and is an unbiased study, enrolling consecutive patients who were treated in 11 of 19 public neurologic clinics of the Emilia Romagna Region of northeast Italy. The inclusion criteria were at least two separate and unprovoked seizures during sleep and at least one within 2 years of study enrollment—a group of patients who, for the most part, have a *mild* form of epilepsy. An eyewitness account of at least one seizure was necessary. Patients were followed up every 6 months or until a seizure during wakefulness was witnessed. Standard EEG and EEG after sleep deprivation were performed. In a few patients, EEG was done during sleep.

Results showed 85% ($n = 137$) of patients had generalized tonic-clonic seizures, and 42 of these had focal discharge on EEG, raising the possibility of a focal origin for the seizure. Twenty-four patients had partial seizures; however, if a focal onset was missed, and the seizure was secondarily generalized, then it was counted as a generalized seizure. Overall, the risk of a seizure to occur during wakefulness was 13%. After 2 years, 78% of patients were seizure free. A poor prognosis was correlated with a higher frequency of seizures before inclusion in the study and with the sudden discontinuation of AEDS. In three previous studies, using similar methods and inclusion criteria (i.e., mild epilepsy), the risk of a seizure occurring during wakefulness was 19% (4), 11% (4), and 19% (5)—results somewhat similar to those found in the D'Alessandro et al. study. However, the previous studies were less reliable because of their retrospective nature and small sample sizes. In one of these studies (5), two additional poor prognostic variables were suggested: partial seizures with or without generalization and duration of epilepsy.

A clear limitation to the study by D'Alessandro et al. is the lack of video-EEG polysomnography (PSG), a technique that is not typically accessible to the general clinician and is primarily available only in epilepsy referral centers. To date, most studies using video-EEG PSG to record seizures in the 24-hour sleep-wake cycle do so with patients whose seizures occur dur-

ing wakefulness, sleep, or both wakefulness and sleep—but not exclusively during sleep. This is the first prospective study to evaluate the risk of seizures during wakefulness in pure sleep epilepsy and provides preliminary data actually applicable to general clinical practice. Future prospective studies are needed. More importantly, the technique of video-EEG PSG must be used and studied in the mild-to-refractory pure sleep epilepsies and nocturnal epileptic syndromes with both pediatric and adult populations. From the data presented by D'Alessandro et al., it may be possible to speculate that the refractory seizure population (i.e., those patients with higher seizure frequency during sleep) may have a higher risk for a seizure during wakefulness. Other issues pertaining to pure sleep epilepsy that should be examined include partial versus generalized epilepsy, temporal versus frontal lobe epilepsy, and coincidence of sleep disorders, particularly sleep apnea and restless legs syndrome. Finally, research in the area of pure sleep epilepsy must examine the question of *why* seizures are preferentially facilitated by sleep.

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References

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