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Is rapid withdrawal of anti-epileptic drug therapy during video EEG monitoring safe and efficacious?☆

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Summary
Purpose: Video electroencephalographic monitoring (VEM) is used to record ictal and interictal epileptiform activity and to ascertain the level of concordance between the two. Often, taper or discontinuation of anti-epileptic (AED) therapy is needed to facilitate seizure occurrence. The safety of this practice is unclear and long-term sequelae have yet to be elucidated.
Methods: This is a prospective study of 158 patients subjected to combined sleep-deprived VEM with rapid AED withdrawal, for evaluation of seizure-like episodes over 24 months under the care of an epileptologist with direct nursing observation and EEG technician support in our telemetry unit. In most cases, AEDs were discontinued within 24 h of admission. We assessed the diagnostic yield and safety of VEM as well as epilepsy surgery outcomes.
Results: VEM answered the study question in 90.5% of cases but failed to record ictal events in 9.5%. This diagnostic yield was achieved over a mean VEM duration of 4.53 ± 1.44 days, with no benefit of longer monitoring. These findings improved quality of life by optimizing medical and surgical therapeutic planning, leading to improved seizure control. Overall, 32.9% of the

Abbreviations: AED, anti-epileptic drug; CI, confidence interval; EEG, electroencephalography; EMU, epilepsy monitoring unit; IIAs, interictal abnormalities; MRI, magnetic resonance imaging; PNES, psychogenic non-epileptiform seizures; SlD, sleep-deprived; VEM, video electroencephalographic monitoring.

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cohort received epilepsy surgery. The complication rate was 5.06%, characterized largely by musculoskeletal pain secondary to clinical seizure activity, with no mortality observed. In the first month following VEM 2.5% of patients received emergency-room admission for seizure clustering. *Conclusions:* VEM with combined sleep deprivation and protocolized rapid AED withdrawal is a safe and effective investigative technique with no adverse long-term sequelae. It is a reliable strategy for therapeutic planning and can be used to determine candidacy for surgical treatment.

Introduction

Video-electroencephalographic monitoring (VEM) is the gold standard for distinguishing epileptic from psychogenic non-epileptic seizures (PNES), seizure type classification, and evaluation of patients with drug-resistant epilepsy for surgery (Benbadis et al., 2004). The disadvantages of VEM include the high cost of the electrophysiologic study, hospitalization to an epilepsy monitoring unit (EMU), and the need to maintain special resources and personnel (Moien-Afshari et al., 2009). The occurrence of seizure events can be unpredictable or infrequent. Moreover, spontaneous seizure frequency appears to decrease in refractory epilepsy patients on admission to an EMU (Chang et al., 2002). In an attempt to address these challenges, withdrawal of anti-epileptic drugs (AEDs) during VEM has been advocated as a means to contain costs, condense time needed for evaluation, and augment diagnostic yield.

Although AED withdrawal is commonly applied as part of a protocol-driven approach to seizure evaluation in the EMU, the safety of this practice is still the subject of debate. Previous studies have documented the occurrence of seizure clusters or secondary generalized seizures in up to 50% of patients, a finding that is more pronounced with acute AED withdrawal during VEM (Rose et al., 2003; Yen et al., 2001). There are concerns that rapid AED withdrawal may increase the risk of complications such as postictal psychosis, falls, electrode dislodgement, and status epilepticus as a result of prolonged, more severe and clustered seizures (Benbadis et al., 2004).

In light of the limited literature on this matter, further systematic investigation is needed to clarify the conditions under which AED cessation for purposes of seizure evaluation is likely to be both safe and effective. The present study represents a prospective evaluation of the safety and diagnostic yield of protocolized rapid AED withdrawal in conjunction with sleep deprivation (SlD) and its impact on long-term outcomes in 158 consecutive patients admitted to our EMU for seizure evaluation.

Material and methods

EMU set-up

Over 24 months, 158 patients who met the indications for VEM were admitted to our EMU under the direction of one epileptologist. Of these 158, 52 patients underwent epilepsy surgery.

The EMU is located on the neurosciences ward and consists of a central nursing station surrounded by 4 hospital beds. Each bed has in-room and centralized cardiac and electroencephalography (EEG) telemetry. Resuscitation equipment is readily accessible. Two registered nurses with specialized neurological training are present in the unit at all times. Vitals signs are monitored every 2 h. EEG technicians and the epileptologist are available in-hospital and on-call thereafter. VEM is continuous throughout admission and includes supervised overnight sleep deprivation and AED withdrawal. VEM was continued by decision of the attending epileptologist until sufficient numbers of seizures with good visual and EEG quality were recorded. With completion of VEM, patients were restarted on ongoing AEDs within a day. All patients had an available intravenous line and an order of sublingual Ativan of 2 mg in case of generalized tonic-clonic seizures or more than two complex partial seizures very close together.

In order to apply International League Against Epilepsy seizure classification to ictal phenomena, a minimum of 3 seizures had to be recorded. Additionally, seizures recorded during VEM were verified to be habitual ones by patient family members, friends and the charts. The diagnosis of PNES was made upon review of relevant video EEG recordings, including evidence of clinical events unaccompanied by ictal EEG changes, analysis of self-reported patient symptoms during these events, review of prior patient history and/or past EEG or video EEG telemetry recordings (if available).

AED withdrawal protocol

In patients with no prior history of status epilepticus all AEDs, with the exception of Phenobarbital, were titrated to half-dose on admission and discontinued at 24 h. In cases where there was a history of status epilepticus or in patients taking phenobarbital or high doses of benzodiazepines, AEDs were tapered by 25% of the initial dose and ultimately discontinued. Intravenous lorazepam was provisioned (2 mg every 3 min for cumulative dose of up to 8 mg) if any clinical seizure activity persisted past 5 min or if 2 more seizures occurred in this time without a return to baseline in between; these seizures were detected and treated based on the nurses clinical assessment. The patients were sleep deprived for the entire night for the first two nights. At the conclusion of VEM, patients with epilepsy were promptly restarted on baseline medications at their original pre-VEM dosages. If no serious adverse events were recorded during the VEM, patients were discharged home