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Safety and efficiency of medication withdrawal at home prior to long-term EEG video-monitoring

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ABSTRACT

Purpose: Long-term video-EEG monitoring (LTM) is frequently used for diagnostic purposes and in the workup of epilepsy surgery to determine the seizure onset zone. Different strategies are applied to provoke seizures during LTM, of which withdrawal of anti-epileptic drugs (AED) is most effective. Remarkably, there is no standardized manner of AED withdrawal. For instance, the majority of clinics taper medication during clinical admission, whereas we prefer to taper medication at home prior to admission. Our aim was to study the advantages (efficiency and diagnostic yield) and disadvantages (safety and complication rates) of predominantly tapering of medication at home.
Method: We report a retrospective observational cohort of 273 patients who had a LTM at our tertiary epilepsy center from 2005 until 2011. Provocation methods to induce seizures were determined on individual basis. Success rate (duration of admittance, time to first seizure, efficiency and diagnostic yield) and complications and serious adverse events were assessed.
Results: AED were tapered in 180 (66%) patients, in 93 (24%) of these patients with additional (partial) sleep deprivation. In all of these patients tapering started at home one to four weeks prior to admission. In the other patients, only (partial) sleep deprivation or none provocation method at all was applied. Seizure recordings were successful in 79,9% of patients. Complications occurred in 19 patients (10.9%) of which 3 had (1.7%) serious adverse events (status epilepticus (SE)) with AED withdrawal. These complications only occurred during admittance, not at home.
Conclusions: AED withdrawal at home prior to LTM is an efficient and convenient method to increase the diagnostic yield of LTM and appears relatively safe.

1. Introduction

Long-term EEG-video monitoring (LTM) is applied for diagnostic purposes (e.g. differentiation epilepsy and non-epileptic seizures) and in the workup for epilepsy surgery to determine the seizure onset zone, in which recording of mostly three to nine seizures is required [1]. LTM is demanding for the patient and is labor intensive, time consuming and expensive. Moreover, availability of the epilepsy monitoring unit (EMU) is limited. Thus, a cost effective and efficient way of LTM is needed. Preferably, both time to first seizure and duration of admission should be as short as possible. LTM is considered successful when an ictal event is recorded. These parameters were investigated in a few previous studies, however, data remains limited and results vary [2–12].

The success rate of LTM differs substantially, varying between 44% and 90.5% [5–12]. This variation might be explained by the differences in inclusion criteria.

Several provocation methods are used to increase the diagnostic yield of LTM. In some patients seizures are provoked by clear and specific triggers, such as photo stimulation, music or warm meals. If possible, these triggers are applied during LTM. In addition, (partial) sleep deprivation and AED withdrawal are the frequently applied provocation methods, when seizure frequency is too low to ensure sufficient seizure recording during LTM [13]. However, tapering should be considered carefully, as withdrawal can trigger tonic clonic seizures (which carries the risk of SUDEP), clusters of seizures or even life threatening status epilepticus [2,3,14]. A recent survey of 27 EMU's of the European Union-funded E-pilepsy network including 22 European countries demonstrated

Abbreviations: AED, anti-epileptic drug; EEG, electroencephalogram; EMU, Epilepsy monitoring unit; LTM, long term EEG-video monitoring; PNES, psychogenic non-epileptic seizures.

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13 EMU's not applying AED withdrawal and 14 EMU's applying AED withdrawal before admission of which three EMU's applying AED withdrawal at home, six in hospital setting and five individually based decisions were made [15]. In most studies AED withdrawal is performed during admission, which prolongs admission and is more expensive and more inconvenient for the patient. In our tertiary epilepsy center, we have experience with AED withdrawal at home. The aim of our study is to evaluate both efficiency and safety of our current routine clinical practice of AED withdrawal at home.

2. Methods

2.1. Patients

For this retrospective study we included all patients referred to our EMU in the period of 2005 till 2011 for LMT. The reason for referral was presurgical or diagnostic evaluation. Both adult patients and children were included.

2.2. AED withdrawal

A few weeks prior to admission, LTM candidates were seen at the outpatient clinic by the neurologist/neurophysiologist and physician assistant to discuss AED withdrawal. For patients with irregular (i.e. long interval between seizures or seizure clusters) or infrequent seizures (i.e. less than 2–3 seizures per week), AED withdrawal was discussed prior to admittance. People with daily seizures did not need AED withdrawal. In patients with a cluster of seizures a few days every month, the LTM was planned in this period (if predictable), and often combined with AED withdrawal. A risk assessment of safety of AED withdrawal in the home situation was made by the neurologist and/or physician assistant. Several individual patient factors were taken into account, such as seizure frequency, status epilepticus in the history and home situation (living alone or supervised by family etc.). Also psychological factors were taken into account. If patients were known with mental illness and we were not convinced patients could handle AED withdrawal at home we admitted patients a week earlier at the clinic for AED withdrawal, if needed on base of seizure frequency. Admittance of patients prior to LTM could also be a possibility for patients with high risk of status epilepticus or living alone. AED withdrawal at home or during LTM depended on type of AED and seizure frequency. This was determined individually per patient although guided by a local protocol (Table 1). Less rigorous withdrawal was applied at home in case of high seizure frequency.

Occasionally admittance was needed a week(end) prior to LTM to taper the remaining amount of AED. In patients with polytherapy, only one AED was tapered at home, and if needed more AEDs were tapered during LTM. Often, we first tapered the AED with longest duration to stop or the one that was the most effective to reduce seizures (from a patient perspective). The risks of AED withdrawal were always discussed with the patient and/or caregiver.

When LTM was successful the AED was restarted in 1 or 2 days. A successful LTM was defined as recording of at least one seizure.

If clustering of seizures occurred, patients were prescribed extra clobazam for 3 days during AED restart.

2.3. EMU

Patients were monitored in a living room and during the night in their own bedroom with continuous EEG and video monitoring over 1–5 days. For EEG monitoring, a 40-channel Lanotta long-term monitoring amplifier was used with a Stellate Harmonie Epilepsy Monitoring System including EEG (standard electrodes of the 10–20 system 10–20 and FT11, FT12, P9, P10), electrocardiography (EKG), electro-oculography (EOG), electromyography (EMG) and respiration (piezo respiratory effort sensor). In case of complications (e.g. a possible status epilepticus) the nurses and staff used dedicated protocols and in case of a tonic clonic seizure or seizure clustering we administered Midazolam 10 mg (intranasal) in adults, in children appropriate dosages were used dependent on their weight.

2.4. Database

Patient information and EEG reports were retrospectively gathered from electronic patient files. EEG reports were described by well trained technicians and concluded by a dedicated neurologist/neurophysiologist. When reports did not provide all information like time to first seizure or total time of LTM, this was revised. Efficiency of LTM was defined as time to first seizure, duration of admission and success rate. Safety of LTM was evaluated based on seizure clustering (three or more seizures in four hours), tonic clonic seizures (both when this was not part of someone's regular seizure pattern) and status epilepticus. These parameters as well as demographic variables, reason for admittance and number of seizures were documented.

2.5. Statistics

The Kolmgorov-Smirnov tests were used to determine whether data was normally distributed in demographical data, time of admittance, number of seizures, time to first seizure and successful recordings. Correlation between the time to first seizure,the duration (number of nights) of admittance, the AED withdrawal and the application of sleep deprivation were compared with Spearman Rho tests (SR). The diagnostic group was compared with

Table 1
Local protocol medication withdrawal.

Medication	Withdrawal protocol	Restart medication
CBZ, OXCB	STOP the evening before admittance*	Direct restart normal doses
LTG, LEV, TPM, LCS	START withdrawal gradually one week before admittance Taper until half the doses on 2 days before admittance and STOP the evening before admittance*	Build up in 1 or 2 days
VPA	START withdrawal gradually in 4 weeks before admittance and STOP one week before admittance*	Build up in 1 or 2 days
Benzodiapines	only STOP during admittance*	Direct restart normal doses

Legend: Medication is listed in order of preference with CBZ and OXCB as first preferable AED to discontinue. CBZ = Carbamazepine, OXCB = Oxcarbazepine, LTG = Lamotrigine, LEV = Levetiracetam, TPM = Topiramate, LCS = Lacosamide, VPA = valproic acid.

* In case of severe increase of seizures, extra clobazam is used with a withdrawal protocol during 3 days; 3 times 10 mg daily, 2 times 10 mg daily, once 10 mg daily and then stop.