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Case report

Can intravenous lorazepam prevent postictal generalized EEG suppression? A case report

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ABSTRACT

Background: Postictal generalized electrographic suppression (PGES) may be considered an electrophysiological marker associated with an increased risk of sudden unexplained death in epilepsy (SUDEP).
Case Presentation: A case study is presented whereby a young man with focal to bilateral tonic-clonic seizures exhibited PGES after two spontaneously-aborted seizures; yet, after a third benzodiazepine-aborted seizure, PGES was absent.
Conclusion: This suggests that acutely administered benzodiazepines may offer direct anti-suppressive effects to prevent PGES, potentially reducing SUDEP risk.

1. Background

Sudden unexplained death in epilepsy (SUDEP) is one of the most feared consequences of epilepsy and is a leading cause of death in refractory epilepsy. Postictal generalized EEG suppression (PGES) is an electrophysiological marker associated with a potentially increased risk of SUDEP (Rajakulendran and Nashef, 2015). It stands to reason then that strategies to aid in the prevention of PGES can potentially lead to reduction in the risk of SUDEP.

Herein, we report a case of a young man with three focal to bilateral tonic-clonic electrographically and clinically stereotyped seizures captured during an Epilepsy Monitoring Unit (EMU) stay. PGES was present with the self-aborted seizures and PGES was absent with the seizure aborted with intravenous lorazepam. This suggests that there is a potential role of acutely administered benzodiazepine (BNZ) medications not only in shortening seizure duration but also in preventing PGES, a potential risk factor for SUDEP.

2. Case presentation

A 24-year-old man with focal epilepsy was admitted to the EMU for seizure localization as part of a phase I presurgical evaluation. During his hospitalization, his home levetiracetam was held starting the evening of his first day of admission. Interictal right anterior temporal sharp waves and right temporal intermittent rhythmic delta activity (TIRDA) were noted. On the second day of the hospitalization, the patient experienced three habitual clinically and electrographically stereotyped focal to bilateral tonic-clonic seizures. He exhibited an aura of enhanced senses (non-motor onset) then oral automatisms (motor onset) with loss of awareness and left hand dystonic posturing then figure-4 sign with left head turn, left arm extension, and right arm flexion then bilateral tonic-clonic activities. Electrographically, seizures originated in the right anterior temporal lobe with spread throughout the right hemisphere and then bi-hemispherically.

For seizure 1, the total seizure duration was 145 s and PGES lasted 34 s. For seizure 2, the total seizure duration was 160 s and PGES lasted 33 s (Fig. 1, Fig. 2). For seizures 1 and 2, after PGES, diffuse slowing was present that was maximal at the right temporal head region. The time to normalization of the EEG after electrographic offset was 27 min for seizure 1 and 17 min for seizure 2.

For seizure 3, the total seizure duration was 386 s, with intravenous lorazepam administered 362 s after the seizure clinical onset (Fig. 1), during the tonic-clonic phase. After electrographic offset, bifrontal slowing was noted. Over the left hemsiphere, posteriorly dominant 12–13 Hz activities were noted immediately after electrographic offset (Fig. 3). Bilateral posteriorly dominant alpha range activities emerged shortly thereafter, though focal right hemispheric slowing persisted until the EEG was self-discontinued by the patient about 20 min after electrographic offset.

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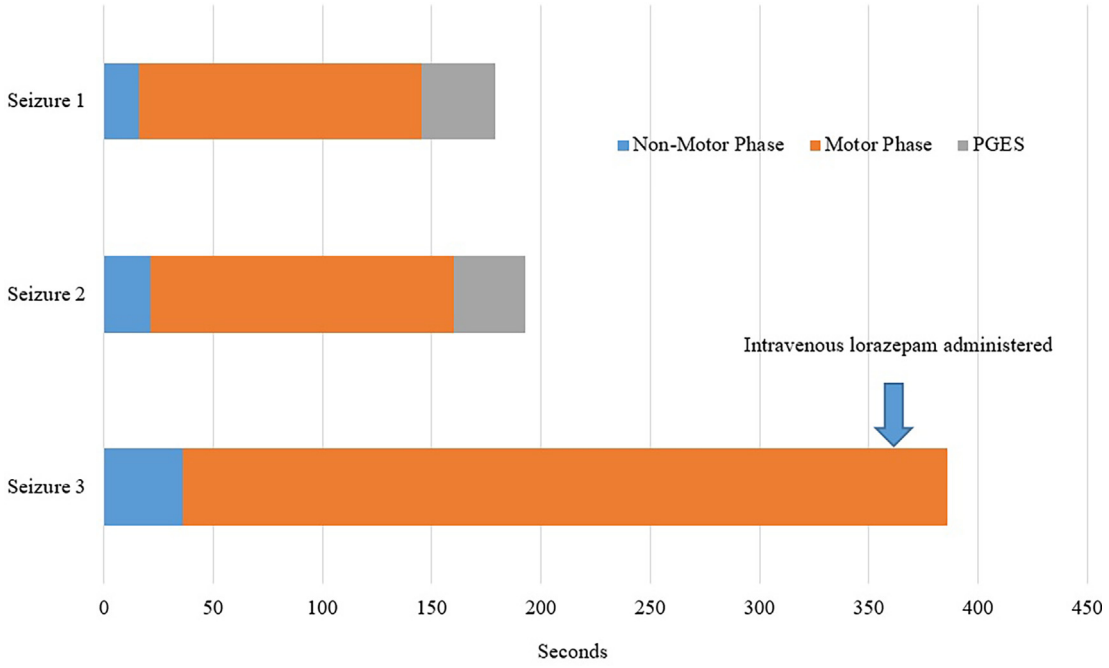

Fig. 1. Timeline of the clinical case. Timeline of non-motor and motor phases as well of duration of PGES for each seizure in seconds. Abbreviations: PGES – post-ictal generalized EEG suppression (PGES).

3. Discussion

PGES has been defined as the immediate postictal absence of EEG activity greater than 10 μV occurring within 30 s of seizure cessation (Lhatoo et al., 2010). The exact mechanism of how PGES may contribute to SUDEP is not well understood. PGES may result in a temporary cessation of breathing or cardiac activity, leading to a sudden and fatal event. Prolonged PGES is associated with increasing hypoxemia, another potential biomarker for SUDEP risk (Buchanan, 2019). PGES may suggest that post convulsive arousal mechanisms are failing, contributing to SUDEP risk (Buchanan, 2019). Alternatively, as PGES is dependent on seizure type and present most commonly after bilateral tonic-clonic seizures, PGES may act instead as a marker of severe seizures to indirectly increase SUDEP risk (Rajakulendran and Nashef, 2015).

Data is not available on the relationship between the acute administration of BNZs and inhibition of PGES. In a prospective SUDEP study of intractable epilepsy patients, patients on chronic BNZ treatment had shorter PGES durations (Lacuey et al., 2019). This was potentially explained by chronic BNZ use shortening the generalized convulsive phase of a seizure, reducing also the seizure severity. Of note, use of other medications with GABAergic properties was not investigated.

In Dravet Syndrome (DS), PGES occurs frequently. In the heterozygous Scn1a knockout (Scn1a−/+) mouse model, there is lower excitability in GABAergic interneurons suggesting that the origin of epilepsy and premature death in DS is linked to the compromised inhibitory efficacy of GABAergic system. This notion gains support from observations where the exclusive removal of NaV1.1 in GABAergic interneurons in the forebrain is enough to reproduce the intense, spontaneous convulsive seizures, and premature death witnessed in DS (Cheah et al., 2012). Increased incidence of PGES in Dravet syndrome may therefore potentially be linked to a dysfunctional GABAergic system, suggesting targeting GABA receptors, may be uniquely efficacious in preventing suppression, specifically, PGES.

In our case, we recorded three stereotyped habitual focal to bilateral tonic-clonic seizures. The first and second (Fig. 2) seizures spontaneously aborted and PGES was present. The third seizure (Fig. 3) was aborted with IV lorazepam and generalized anteriorly dominant delta frequency slowing was present after electrographic offset with posteriorly dominant 12–13 Hz frequency activities noted over the left hemisphere. Interestingly, the third seizure was the longest, including having the longest motor phase, and the BNZ was administered after the seizure had already generalized, during the bilateral tonic-clonic phase. Therefore, these findings would argue against an indirect mechanism of BNZ terminating suppression by shortening seizure duration, reducing seizure severity, or limiting seizure propogation. One theory would be that BNZ offer a direct anti-suppressive effect. It is possible that, in patients with intractable epilepsy and PGES, there is a dysfunction GABAergic system such that endogenous efforts to abort seizures lead to overinhibition and consequent PGES. Administering BNZ may therefore offer improved efficacy in targeting the GABA receptors, aborting the seizure without leading to the overinhibition and consequent PGES.

In conclusion, this case report suggests a potential direct anti-suppressive effect of BNZ administration. The main limitiation to this case is that only a sampling of three seizures in single patient is presented. Therefore, it is possible that the lack of PGES in the benzodiazepine-aborted seizure is due to chance. The mechanism by which BNZ may directly affect suppression is also not clear and is only theorized. This case report therefore illustrates a need to perform future research assessing whether there is an

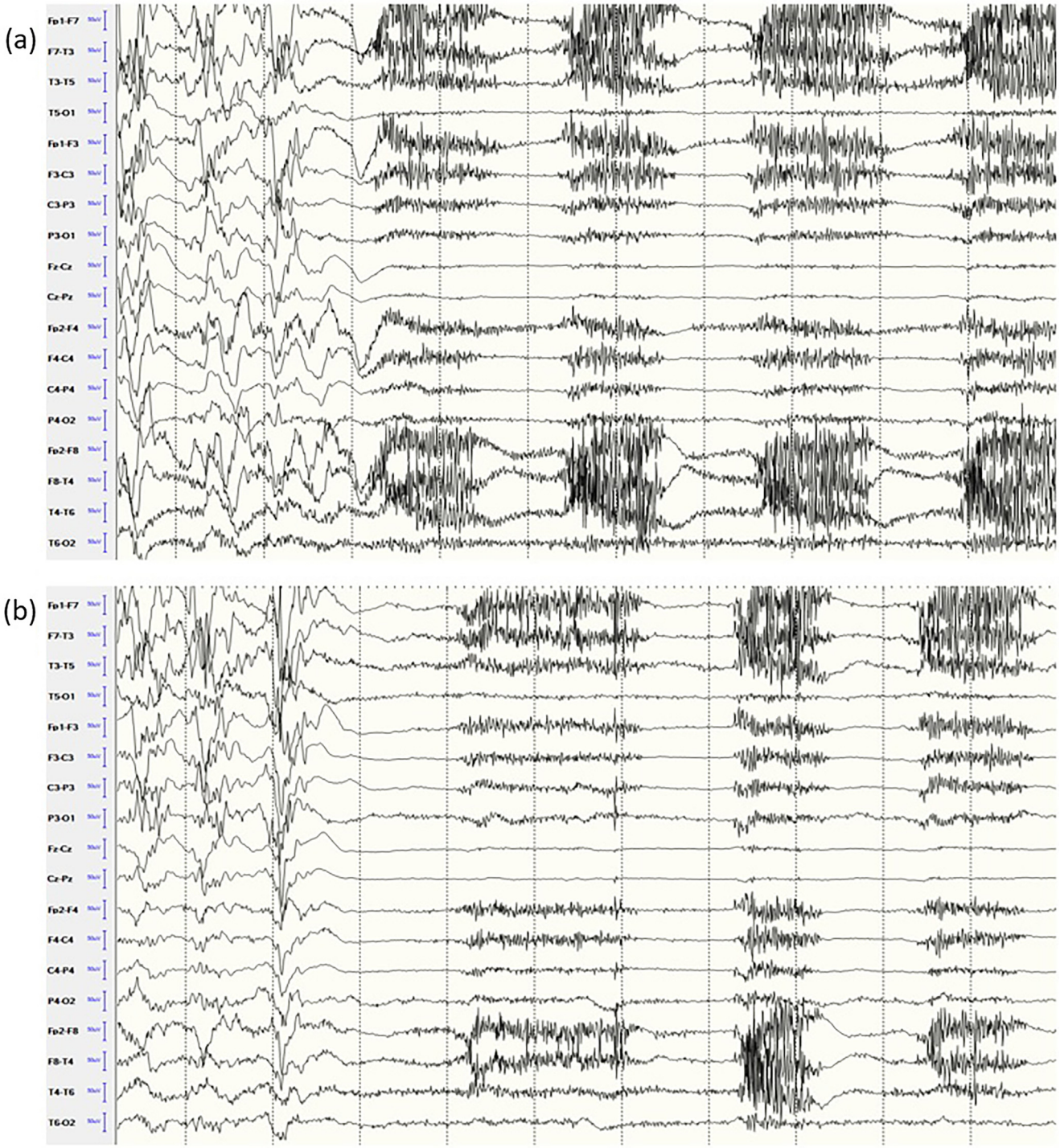

Fig. 2. Suppression patterns after first and second seizures. PGES was present after the first (b) and second (c) focal to bilateral tonic-clonic seizures. 8 s after electrographic offset is visualized for each seizure. Longitudinal bipolar montage with viewing settings of: sensitivity 7 mV, TC 0.1 s, HFF 30 Hz, notch 60 Hz. Dashed vertical lines represent 1 s intervals. Abbreviations: PGES – post-ictal generalized EEG suppression (PGES).

association between BNZ administration and PGES incidence, further exploring the compromised inhibitory efficacy of the GABAergic system in persons with epilepsy, and assessing if BNZ offer an anti-suppressive effects. Likewise, future studies assessing whether chronic use of GABAergic medications affect PGES incidence should be considered. This research is especially important as the presence of PGES may herald an increased risk of SUDEP; therefore, preventing PGES may lower SUDEP risk.

Conflict of interest

The authors have no conflicts of interest or funding sources to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report.

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

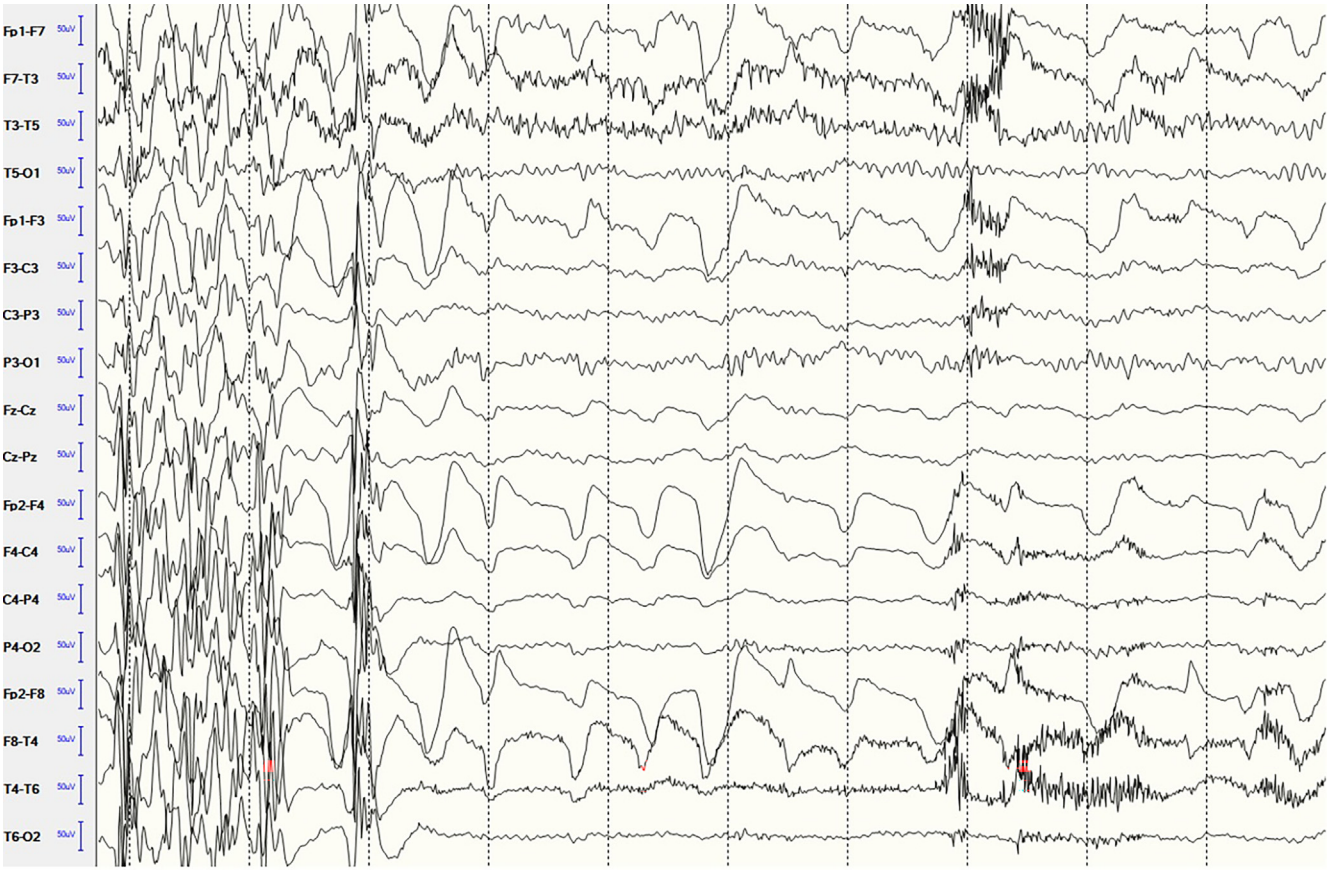

Fig. 3. Post-ictal pattern after third seizure. After the third focal to bilateral tonic clonic seizure, low amplitude posteriorly dominant 12–13 Hz activities were present over the left hemisphere after electrographic offset with otherwise anteriorly dominant generalized slowing present. 8 s after electrographic offset is visualized. Longitudinal bipolar montage with viewing settings of: sensitivity 7 mV, TC 0.1 s, HFF 30 Hz, notch 60 Hz. Dashed vertical lines represent 1 s intervals.

Ethics approval and consent to participate

Written informed consent was obtained from the patient.

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