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Short Communication

Tailored Treatment for Status Epilepticus in Intensive Care

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Abstract

Status Epilepticus (SE) is a medical emergency for which there are numerous guidelines but little aimed to tailor treatment to the individual patient. Either benzodiazepines, especially midazolam, or, if ineffective, barbiturate anesthesia, is used to abort the SE thereby providing a window of opportunity to establish long acting Antiepileptic Medications (AEMs) offered in boluses, determined by AEM blood level determination to ensure achieving a therapeutic window of dosage upon which can be determined the long-term regimen to be followed after hospital discharge.

Keywords: Status Epilepticus; Tailored treatment; Antiepileptic medications; Blood levels; Therapeutic levels

Introduction

Status Epilepticus (SE) is a medical emergency with an incidence of ~60 per 100,000 per year and a mortality rate of between 16% to 25% [1,2]. While there are numerous guidelines for the management of SE [3-5], in reality, the treatment provided, at different institutions, is often empirical and based on the idiosyncratic practices within that institution, rather than tailoring treatment, specifically, to each individual patient's needs. This presentation offers an alternative approach which does cater for the individual and monitors that treatment, within each individual patient's situation, and helps to predict the appropriate ongoing long-term care.

Methods

Benzodiazepines (BDZs) remain the benchmark for the initial approach to achieve cessation of the active seizure, lasting ≥ 5 minutes [1,6]. Of these, at least in Australia, midazolam is the agent of first choice because it is water soluble and can be administer by various routes, including: nasally; to buccal mucosa; to the gums; or Parenterally, either intramuscularly or intravenously (IVI) [7].This is given with the aim of aborting the current seizure activity (and should NOT be given if the seizure has self-arrested/limited). Midazolam can be administered by non-medical careers and trained personnel who are specifically taught how to give it, within the community, even prior to arrival of the ambulance or transfer the person to a medical facility [7]. If the midazolam is effective, with the first dosage, there may not be a need for the patient to be transferred to a medical facility, depending on the nature and history of the epilepsy, in that individual patient, and assuming there are no further prolonged recurrent seizures within a 24 hours period. Should there be need to administer a further dose of midazolam, within 24 hours, and then it is advisable to transfer the patient, to a medical facility, for further evaluation to identify and treat any possible cause for the SE, such as urinary tract infection.

The use of BDZs is to abort the seizure activity, while providing a window of opportunity in which to initiate long-term protection against seizure recurrence. Long acting Antiepileptic Medications (AEMs), such as Valproate (VPA) or Carbamazepine (CBZ), can offer long-term protection, once the SE has stopped. These AEMs are dispensed as an initial bolus, with blood sample taken, after an hour from administration, and AEM blood levels determined. Further boluses are provided, either parenterally (IV) for VPA or gastro-intestinally, either via a Naso-Gastric tube (NG) or rectally (PR), using the CBZ syrup, based on the results of the AEM levels determination, until therapeutic levels are achieved. Once such therapeutic levels are achieved, the on-going regimen is decided on the basis of the amount of AEM required to achieve therapeutic levels and the patient's response.

Where the BDZs failed to achieve seizure control, it may be necessary to rely on short term barbiturate anesthesia to abort the initial SE [8]. This should be limited to as short a time period as is possible, aiming for <48 hours, being acutely aware of the potential infusion syndrome [8]. Electroencephalography (EEG) is useful to confirm the presence of a burst/suppression pattern, as the goal of such anesthesia [9]. The need to resort to short term barbiturate anesthesia should not interfere with the objective of achieving a therapeutic window for the chosen long-term AEM.

The choice of which long-term AEM to administer should be based on previous knowledge of the patient, where available. If the patient is someone, known to have epilepsy, which had previously experienced good seizure control, with an identified long acting AEM, without Adverse Events (AEs), then that is the AEM which should be administered during the widow of protection. In such situations, it is reasonable to offer the regimen that had previously

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proven efficacious, supplemented by a larger loading dose, assuming that the SE was consequent to an episode of non-compliance. AEM blood level determination, where available, should still be used to ensure adequate dosing.

In a previously undiagnosed person with epilepsy, it makes good sense to administer an AEM for which AEM blood level determination is easily available, at the institution where administration is provided. The target regime, in someone for whom previously there has not been an identified successful AEM, is to aim for that which achieves a therapeutic blood level in the majority of people with epilepsy and to maintain it.

The regimen, upon which the patient is discharged from hospital, should be based on an appreciation of what was required to achieve, and maintain, a therapeutic range, while the person was in hospital, during the critical period of the SE and beyond.

Protocol

Once the immediate SE is terminated, assuming the patient has not had previously diagnosed and successfully treated epilepsy, either 1gm VPA (IVI) or 400 mg CBZ (either NG or PR) is administered, depending on whether the presumptive diagnosis is that of a generalized or focal epilepsy, at the start of the SE, or as is determined by history and EEG. Blood samples (from the contralateral arm for IVI VPA) are measured after 1hour from the initial dose of either CBZ or VPA. These AEM levels are determined, on an urgent basis, notifying the laboratory of the urgency required (not simply expecting the laboratory to anticipate same and also asking the laboratory to notify of the results, as soon as is practicably). Based on the results of this blood level determination, a further bolus of the same AEM, at similar dosage, is administered, if the results of AEM levels are sub therapeutic (below the expected/accepted therapeutic window). This process is repeated until therapeutic levels are achieved.

Once therapeutic levels have been achieved, the ongoing regime is determined, based on amount of AEM required to achieve these levels and those levels are closely monitored to protect against either over, or under, dosing. There is little risk of problem, if the patient is overdosed, as (s) he is in hospital with adequate support and any AEs also can be closely monitored and promptly managed.

Discussion

Rather than adopting a "one size fits all" approach to SE, the method, set out in this poster, offers an individualized regimen, specifically designed for the ongoing patient care of the person being treated. This offers an indication to devise the long-term strategies to treat the underlying epilepsy that provoked the SE. This regimen is based on the dosages required to achieve therapeutic AEM blood levels. This approach ensures that the patient receives adequate dosing of the long acting AEM, in the acute period, confirming therapeutic window for the AEM, either during the window, provided by the BDZ or during the anesthesia. Such approach is also useful in determining the long-term strategy/dosing regimen to treat that individual's ongoing epilepsy, once the SE has been successfully controlled.

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