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Management of Status Epilepticus in the Prehospital setting

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Abstract:

Status epilepticus (SE) is a time sensitive neurological emergency that requires rapid recognition and intervention to prevent long-term complications. This review explores current evidence and best practices for the prehospital and emergency department management of SE, focusing on early recognition, diagnostic tools, and pharmacologic strategies. Literature was sourced from PubMed using predefined keywords and inclusion criteria, emphasizing studies published within the last decade. The review highlights the challenges in prehospital care, particularly delays in treatment due to difficulties with intravenous access and underutilization of alternative drug delivery routes. Benzodiazepines (BZDs) remain the first-line therapy, with intramuscular midazolam emerging as a practical option when Intravenous (IV) access is not available. Non-IV routes such as Intranasal (IN) and buccal administration offer similar efficacy and are increasingly supported for prehospital use. Point-of-care EEG (PocEEG) shows promise in improving diagnosis, especially for non-convulsive status epilepticus (NCSE), though its adoption remains limited. Key gaps include lack of rapid diagnostic tools in the field, restricted availability of second-line agents, and underdosing due to fear of respiratory depression. Future directions should focus on protocol optimization, expanding access to non-invasive rescue

therapies, and integrating diagnostic innovations into emergency systems. Effective prehospital SE management depends on timely seizure control using the most accessible route, coupled with system-wide efforts to reduce treatment delays and improve patient outcomes.

Keywords: Status Epilepticus, Emergency Department Management, Acute management.

Abbreviations:

Status epilepticus - SE

Generalized convulsive status epilepticus - GCSE

Peripheral venous catheter - PVC

Intravenous - IV

Intranasal - IN

Intramuscular - IM

Benzodiazepines - BZDs

Electroencephalogram EEG

Point-of-care electroencephalography - PocEEG

Methodology:

Study Design

This literature review was conducted to integrate current evidence, standard practices and recommendations in regards to the prehospital and emergency department management of status epilepticus. The review focuses on pharmacological treatment, routes of administration, diagnostic considerations, and novel therapeutic strategies.

Search Strategy and Data Base

The articles for this review were gathered from the PubMed database. We searched using the keywords “Status Epilepticus", “Emergency Department Management”, “Acute management” and other associated keywords. For our review, we excluded books and documents from the search and only included articles in English published in the last 10 years.

Screening and Selection

We screened all the abstracts based on full-text availability, relevance and the content of the articles. These selected articles were then read through completely and included on the basis of relevance of information. Conflicts were resolved by consensus or by a third reviewer.

Introduction:

Status Epilepticus (SE) is a time-sensitive neurological emergency defined as a solitary seizure lasting more than 5 minutes, or multiple seizures with unconscious phases between them. It is also associated with irreversible neuronal injury and high rates of complications especially if it lasts more than 30 minutes. It has a bimodal distribution; occurring more often in children aged less than a year and adults over 65 years [2].

Management is time-sensitive making early intervention crucial to prevent complications. The International League Against Epilepsy recognises two key time points in management: t1 - around 5 minutes (that is when the treatment should begin), and t2 - around 30 minutes (when the risk of long-term brain damage rapidly increases) [6]. This definition is complex, so a more simplified definition is used in prehospital conditions simply as a seizure lasting more than 5 minutes [2].

Recognition of non-convulsive SE is especially challenging. It involves identifying a persistent change in mental status with subtle or absent motor signs, potentially accompanied by epileptiform EEG activity. Though effective strategies exist, hurdles such as underdosing, delayed administrations, etc limit their effect and implementation significantly [2,4]. This review aims to collect and present all literature on pre-hospital or emergency diagnosis of SE, treatment modalities and guidelines to prevent long-term complications.

Prehospital recognition and initial response:

SE arises from either a failure of seizure-terminating mechanisms or the initiation of mechanisms that lead to abnormally prolonged seizures [4,6]. SE can be convulsive, with limb stiffness and jerking, or non-convulsive, with altered consciousness and minimal limb movement [4]. Common causes of SE in adults include low levels of antiepileptic drugs, cerebrovascular diseases, metabolic abnormalities, alcohol-related causes, and hypoxia [4,6]. Additionally, SE can occur in people with or without a history of epilepsy, with an incidence reported as 10-60 per 100,000 population per year [4]. Incidence is highest among young and older adults [6].

Generalized convulsive status epilepticus (GCSE) is a neurological emergency, and is encountered in prehospital, emergency, and intensive care units. This type of SE is the most easily recognized because relatively little training is required to recognize the condition. Here, early recognition is crucial as an array of complications can develop including respiratory compromise, cardiovascular problems such as

cardiac arrhythmias and myocardial injury, metabolic disturbances (hyperthermia, acidosis, rhabdomyolysis), infectious, musculoskeletal and neuronal damage [6]. They are dynamic and rapidly evolving making identification and treatment challenging. Ongoing seizures quickly modify neuronal activity and synaptic function, which results in changes to behavioral seizures, EEG patterns, drug sensitivity, and the progression of neuronal injury and death.

Initial responses to SE include history taking, securing the airway, breathing, and circulation (ABCs), reversing underlying causes, and preventing further trauma [2]. The training of public, friends and family of known predisposed patients should be encouraged, as bystanders' response is crucial to management. Most importantly, they eliminate potential harm to the patient and expedite response. The information they provide dispatchers such as onset and description of the symptoms are of high significance in appropriate identification and classification influencing treatment modalities [2].

Emergency physicians immediately assess a patient's ABCs upon arrival. The patient should be placed in the left lateral decubitus position (if possible) to decrease the risk of aspiration. Use of bite blocks and oropharyngeal airways is prohibited due to the risk of trauma to both patient and rescuer and increased risk of airway obstruction. Oxygen saturation should be maintained >92%. If an airway device is needed, a nasopharyngeal airway is the recommended option. Intubation can become necessary in case of respiratory depression, recurrent seizure activity, or depressed mental status [2].

The diagnosis of SE is based mostly on the clinical picture and electroencephalogram (EEG) results. EEG is particularly important in diagnosing NCSE and is also useful in differentiating between the different types of SE and to monitor response to treatment. Additional tests such as brain imaging and blood tests, are used to identify the underlying causes of SE. Finally, a lumbar puncture and toxicology screening tests are performed when infection or drug/alcohol use is suspected, respectively.

Point-of-care electroencephalography (PocEEG) is a rapid-access device emerging as an alternative for conventional EEG in the diagnosis of NCSE. These devices are portable and can also be used for long-term monitoring. They are mostly used in time and resource-limited settings like a prehospital environment. Among the types of PocEEG, patient monitors equipped with EEG, may simplify implementation and be more cost-effective by upgrading existing equipment. PocEEG systems are designed for rapid setup and with reduced electrode arrays and integrated artificial intelligence assisted tools can make this tool accessible and understandable by non-experts. Overall, the use of PocEEG significantly reduces the number of hospital admissions and hospital stays, leading to significant cost savings [3,5].

Pharmacologic management in the prehospital setting:

Seizure emergencies predominantly originating outside of the hospital setting and the motion-intensive nature of epileptic episodes often create difficulties in establishing timely IV access critically slowing drug administration [8,9]. The current guidelines for managing SE recommend a stepwise

pharmacologic approach. The rapid administration of intravenous (IV) benzodiazepines (BZDs) is the primary treatment for seizure emergencies [1,7,8]. This recommendation is supported by strong evidence demonstrating the effectiveness, rapid onset, and generally favourable safety profile of BZDs which have remained the leading drug of use for SE. Commonly used BZDs are lorazepam, midazolam, diazepam and clonazepam, and they enhance the activity of gamma-aminobutyric acid (GABA) at the GABA-A receptor, causing anticonvulsant effects. Seizure control is mediated through this allosteric modulation, which increases inhibitory neurotransmission in the central nervous system [8].

The choice of agent and route of administration is often determined by the prehospital setting and the availability of intravenous access. Intramuscular (IM) midazolam is recommended as a first-line therapy for patients in a prehospital environment, especially when IV access is not readily available. A single IM dose has shown the fastest time of seizure termination in pediatric patients in the prehospital setting, specifically on ambulances. This route is considered equally efficient to IV lorazepam, which is the preferred and highly effective first-line agent [7,8,9,10].

If seizures persist beyond an expected time window, after the initial or a second dose of BZDs, the patient is considered to have established SE and a second-line antiseizure drug should be administered. This period varies with the route of administration: IV (1-3 minutes), intranasal (5-15 minutes), IM (5-45 minutes) and rectal (over 45 minutes) [8]. Fosphenytoin, a prodrug of phenytoin, is the most common nonsedating second-line agent followed by Levetiracetam which has an attractive safety profile. Sodium valproate can be useful in SE, however, it must be avoided in patients with liver disease. This paired with the limited knowledge often available in prehospital settings, renders it rarely administrable [1,10]. Restricted availability leads to rare utilization of second-line agents in prehospital settings despite their efficacy. As a result, patients may receive multiple doses of first-line agents, which increases the risk of hemodynamic instability or airway collapse. Lack of accessible options, hence, is considered to be a major challenge in prehospital management of SE [1,10].

Additionally, BZDs are known to lose effectiveness with ongoing seizure duration and delays in administration. Consequently, there has been extensive research into developing ideal non-intravenous rescue modalities that are effective and readily available for prehospital use. For pediatric patients approved therapies consist mostly of rectal diazepam, buccal midazolam and an advanced intranasal (IN) midazolam formulation which results in highest caregiver satisfaction [7,8,9,10]. A proprietary vitamin E solution-based diazepam nasal spray was approved for aborting seizure clusters in patients aged 6 years and older [9]. Another alternative is Ketamine, a noncompetitive NMDA receptor agonist and a short acting anesthetic. It is easily available in ambulances and has several modes of administrations, yet is only used when primary medications fail as its effectiveness and practical adaptability is not backed by evidence [1].

Route of Drug Delivery: Evidence & Practicality

BZDs differ from each other primarily by the onset of action and route of administration, which includes IV, IM, IN, buccal, rectal, and oral routes[8].

IV administration

The IV route is considered the gold standard for BZD administration. Lorazepam and Diazepam are commonly administered IV, and both show similar efficacy and onset of action of 1-3 minutes. The main limitation with it is the difficulty in achieving IV access especially in prehospital settings which leads to a delay in drug administration [4,8]. Considering that the responsiveness to benzodiazepines diminishes the longer the seizure continues, it is better to use non-IV, faster routes of administration than to lose time establishing IV access [8].

IM administration

IM midazolam is a common alternative, showing similar efficiency to IV Lorazepam, with a seizure cessation time of 5-45 minutes [4,8]. This was supported by a randomized controlled trial which showed seizure cessation in 94.2% of patients in home settings and 85.3% in the ER [7]. Additionally, autoinjectors have also been developed, making it one of the most practical routes of administration, especially in a prehospital and unsupervised setting [8].

IN administration

IN Midazolam provides easier administration and faster seizure cessation time of 5-15 minutes. Even though IV Lorazepam gives slightly better results, if the peripheral venous catheter (PVC) is not already inserted, giving immediate IN Midazolam administration would give us an equivalent result. However, this method is not yet fully established due to lack of clinical studies [8].

Buccal, rectal and oral routes:

The buccal route is considered first-line treatment for children, young adults, and adults with prolonged or repeated seizures, because it is noninvasive, needle-free, and overall easy to administer, even by a nonprofessional [7,8]. However, there are quite a few challenges with it as well such as jaw clenching, hypersalivation, and uncontrolled swallowing, which can all cause difficulty with administration and variability in pharmacodynamics [8]. The time of seizure cessation could also be prolonged, taking over 30 minutes [8].

Rectal, Buccal, and Intranasal routes show the same efficacy in resolving seizures and show no statistical difference between their outcomes [7]. However, due to social standards and the shame it may impose on the patient, as well as the caregiver, the rectal route is less frequently used and typically reserved for cases where buccal or intranasal routes are not available [8]. The oral route is not generally used due to the seizure cessation time being usually over an hour [8]. The complications are similar to the buccal route and overall, this route is risky because swallowing cannot be confirmed during episodes.

Comparative Evidence & Practical Considerations

If the PVC is already inserted, IV is always the preferred route. When not, routes like IM, IN and buccal routes show a very similar efficacy in both prehospital and hospital settings [7]. Likewise, the adverse effects are also similar. Somnolence is frequent with BZDs administration, and severe side effects like respiratory depression and hypoxia are a rare possibility in all routes (6.4% to 10.6%) [4,8]. Overall, considering the time of seizure cessation and limitations, IN, followed by IM, and then buccal would be the most preferable route.

Current Gaps and Future Directions

Significant progress has been made in the management of SE. Nevertheless, current protocols are still limited because of several key challenges. Early treatment is commonly delayed because benzodiazepines are frequently underdosed due to concerns about its side effects, and respiratory depression even though the seizures themselves pose a greater risk [6]. Access to second-line agents like levetiracetam and valproate is rare in prehospital emergency settings, so EMS providers are dependent on benzodiazepines and often administer multiple repeated doses, which increases the risk of intubation [1].

Diagnosis of SE is an area which considerably lacks efficiency. NCSE specifically, is often missed without EEG, yet conventional EEG is not feasible in most emergency settings. Notably, PocEEG systems have proven to be useful in both the adult and pediatric population. It allows seizure detection within minutes and leads to faster treatment [3,5]. However, their use is limited, as it has not been widely adapted yet. There are also training gaps and the lack of standardized protocols.

Moving forward, efforts should focus on updating treatment protocols, expanding the use of diagnostic tools like PocEEG, introducing medications like ketamine earlier in care, and making nonintravenous rescue therapies more accessible and easier to use. Overcoming these challenges is key to reducing complications and improving outcomes for patients with status epilepticus in prehospital and emergency settings.

Conclusion:

The prehospital management of SE is still considered a challenge for healthcare providers, as it requires immediate and efficient treatment to prevent life-threatening conditions [8]. Prehospital recognition and management is particularly crucial as all evidence supports significantly better patient outcomes, reduced complications and healthcare costs [4]. The effectiveness of prehospital SE management heavily depends on appropriate diagnosis, drug choice and route of administration and integration of these into response protocols. Together, these strategies ensure continuous support for responders, enhance rapid detection of seizures, improve management decisions, reduce treatment delays, minimize hospital stays and transfers, and ultimately, lead to better patient outcomes [1,2,3,5].

Although BZDs remain the first-line treatment for status epilepticus due to their rapid onset, high efficacy, and tolerability, lack of early administration, often due to difficulty establishing IV access or a lack of familiarity with alternative routes of administration, limit its efficiency considerably [1,2,3,4,8]. While the importance of selecting an appropriate drug is clear, the prompt administration of that drug is equally vital, especially in acute neurological emergencies, as delayed treatment reduces its effectiveness [6,8]. The additional necessity to tailor the drug regimes to the patient's age and setting, and choosing the appropriate route for administration, all during an acute episode makes it very challenging even for trained responders [8,9].

Over the years, only few technological advancements, such as the PocEEG allow for an improvement in recognition of otherwise unrecognisable episodes, though diagnostic variability still limits complete adaptability into routine protocols [3,5]. In summary, the goal of prehospital SE management must be rapid seizure control using the most effective and accessible route available, while adapting to individual patient needs and operational realities [2,3,5,7,8]. Ongoing research, education, protocol development, and systems-based planning are necessary to ensure that emerging evidence continues to translate into better care for patients in every setting.

References:

1. Ketamine Efficacy for Management of Status Epilepticus: Considerations for Prehospital Clinicians. https://pubmed.ncbi.nlm.nih.gov/38490790/
2. Adult Status Epilepticus: A Review of the Prehospital and Emergency Department Management. https://pubmed.ncbi.nlm.nih.gov/27563928/
3. Point-of-Care Electroencephalography in Acute Neurological Care: A Narrative Review. https://pubmed.ncbi.nlm.nih.gov/40278419/
4. Pre-hospital and emergency department treatment of convulsive status epilepticus in adults: an evidence synthesis. https://pubmed.ncbi.nlm.nih.gov/35333156/
5. Point-of-care EEG in the pediatric emergency department: a systematic review. https://pubmed.ncbi.nlm.nih.gov/40053132/
6. Strategies to innovate emergency care of status epilepticus.https://pubmed.ncbi.nlm.nih.gov/39701892/
7. Intranasal Versus Buccal Versus Intramuscular Midazolam for the Home and Emergency Treatment of Acute Seizures in Pediatric Patients: A Randomized Controlled Trial. https://pubmed.ncbi.nlm.nih.gov/39047345/
8. Benzodiazepines in the Management of Seizures and Status Epilepticus: A Review of Routes of Delivery, Pharmacokinetics, Efficacy, and Tolerability. https://pubmed.ncbi.nlm.nih.gov/35971024/
9. Rescue therapies for seizure emergencies: current and future landscape. https://pubmed.ncbi.nlm.nih.gov/34269935/
10. The Pharmacology and Clinical Efficacy of Antiseizure Medications: From Bromide Salts to Cenobamate and Beyond. https://pubmed.ncbi.nlm.nih.gov/34145528/