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Management of 468 Status Epilepticus Cases in the Intensive Care Unit of the University Teaching Hospital of Yaoundé

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Abstract

Purpose: Status epilepticus (SE) constitutes a therapeutic emergency for medical practitioners working in the Intensive Care Unit (ICU). Here, we highlight and propose a contextualized medical approach for the efficient management of SE in a 1st-class clinical setting, mostly attended by a low-income population. **Methods**: A total of 468 cases of patients presenting with seizures were received at the ICU of the University Teaching Hospital (UTH) of Yaoundé. From: 1) the recognition of the diagnosis, 2) the search for the etiology, 3) the cessation of convulsions, 4) the administration of appropriate treatment medication that stops the seizures before referring to the specialist, we accumulated critical information to understand and tailor our therapeutic approaches for SE. **Results:** A total of 319 (68.16%) of patients with seizures were associated with loss of consciousness, tonic and/or clonic movements of the extremities, signs of tongue biting, and incontinence. Only 83 (26.0%) patients with SE failed to respond to first- and second-line anticonvulsant treatment administered. The mortality rate for SE varied from 5% (16/319) in simple cases to over 30.2% (45/149) in severe or super-refractory cases. We have identified direct factors associated with the severity of SE and indirect factors to be considered when choosing a specific treatment. Diazepam, Lorazepam, or Midazolam were the best options to stop the seizures, while Levetiracetam, Depakine, Phenobarbital, or Tegretol were recommended for maintenance. **Conclusion:** For successful management of SE, the choice of one or two first-line medications to stop the seizure before it becomes refractory is critical.

Keywords

Status Epilepticus, Therapeutic Approach, UTH, ICU

1. Introduction

Status epilepticus (SE) is a neurological emergency whereby the patient experiences a seizure or convulsion that lasts for a prolonged period (more than 5 minutes) or is repeated sufficiently to prevent recovery of consciousness between seizure episodes (more than 30 minutes) [1] [2]. In fact, the thirty (30) minute limit is usually set as a sufficient duration that may cause irreversible brain damage in SE associated with tonic-clonic seizures/convulsions or generalized tonic-clonic seizures (GTCS). In contrast, the five-minute limit is set based on the observation that GTCS, previously called Grand Mal seizures, rarely last less than five (5) minutes and that spontaneous cessation of the seizure is less likely after this period [3] [4]. Therefore, in view of the high risk of brain damage, the vital, functional, or physical risks created by SE associated with generalized tonic-clonic seizures, we generally speak of SE as soon as three (3) successive seizures are noted without recovery of consciousness or when continuous convulsive activity continues beyond ten (10) minutes [5] [6]. Considering some irreversible neurophysiological risks associated with physical trauma, successive and prolonged seizures usually cause irreversible cerebral lesions that demand immediate attention by the medical practitioner who receives the patient at the Intensive Care Unit (ICU).

The University Teaching Hospital (UTH) of Yaoundé receives an average of three (3) cases per week of patients admitted to the ICU for loss of consciousness, repeated, and prolonged seizures associated with tonic-clonic movements. Usually, a rapid screening is performed by a medical practitioner upon the patient's arrival to assess the clinical picture and initiate appropriate action that will address the emergency. Practically, a systematic and rapid head-to-toe assessment, including neurological (Glasgow Coma Scale and pupil reaction), airway/breathing (sounds of the lungs and ventilator parameters), and circulation (heart rate, rhythm, and blood pressure), is documented with the aim of immediate stabilization of the patient's critical condition. In the meantime, oxygenation is provided, and capillary blood glucose is measured immediately to rule out hypoglycemia. For a suspected SE, our first line of treatment consists of administering intravenously (IV) Benzodiazepines (Lorazepam 0.1 mg/kg or diazepam 0.1 - 0.2 mg/kg) if the patient is actively seizing [7] [8]. In case the seizure continues, we then administer IV every 20 - 30 minutes an anti-epileptic drug, including Depakine (20 - 40 mg/kg) or Levetiracetam (60 mg/kg), or Phenytoin (20 mg/kg) as a second line of treatment when we suspect SE [9] [10]. At this stage, beyond 3 anti-epileptic drug administrations within 3 hours, the persistence of the seizure will suggest refractory SE to be considered and treated as such until further examination, and the patient is usually put under general anesthesia [11] [12].

So far, it should be noted that our definition of SE and its subdivisions is context-dependent due to many factors, including age, sex, ethnicity, and, most importantly, the clinical setting at the UTH, which is primarily attended by a population with low financial means.

2. Materials and Methods

This study was conducted in strict accordance with the ethical principles outlined in the Declaration of Helsinki. The clinical protocol or code of practice was reviewed and approved by the UTH's review board and the Ethics Committee of the UTH of Yaoundé. Patient confidentiality and data privacy were strictly maintained throughout the study. All data extracted from medical file records were entirely anonymized, and no personal identification such as names or addresses was collected. Because of the observational nature of the study and the use of anonymized data, the requirement for obtaining written informed consent was waived.

This observational cohort study was conducted over 2 years from October 1, 2023, to October 1, 2025. All patients aged from 10 to 85 years who were admitted to the ICU and presenting symptoms of status epilepticus (SE) were included in the study. In addition, potential cases were initially flagged using International Classification of Diseases, Tenth Revision (ICD-10) diagnostic codes related to SE. Exclusion criteria consisted of patients with a history of psychogenic nonepileptic seizures, pregnant patients, and patients with incomplete medical records. Clinical notes, EEG reports, and anticonvulsant medication were reviewed to confirm the diagnosis based on the standard clinical definition of a seizure and its subtypes [13] [14]. Through this systematic screening process, a total of 468 cases of SE met the eligibility criteria and were included in the final analysis.

3. Results

Out of 468 patients included in this study, the primary cohort of 68.16% (319/468) of SE cases exhibited a high prevalence of acute seizure activity, with 80.88% (258/319) of cases demonstrating favorable responses to first- or second-line treatments. Interestingly, patients with seizures demonstrated a significantly lower mortality rate of 5% (16/319) compared to patients without seizures who experienced a mortality rate of 30.2% (45/149). Calculated out of the total seizure cohort (N = 319), we found 55.2% (176/319) of GCSE cases, 34.8% (111/319) of NCSE cases, and 10.0% (32/319) cases of focal SE with impaired awareness. In refractory cases, out of the seizure cohort (N = 319), 62.1% (198/319) cases were responsive to first-line Benzodiazepines, 26.0% (83/319) cases failed first- and second-line anti-seizure medications, and 11.9% (38/319) cases were super-refractory SE, hence were under anesthetic medications.

Concerning maintenance of seizure (in or out ICU/hospital), calculated out of the total of surviving patients (N = 407), 68.3% (278/407) of cases were successfully controlled with a monotherapy (one anti-seizure medication), 23.1% (94/407) with a duo therapy (two anti-seizure medications), and 8.6% (34.407) with a polytherapy (three or more anti-seizure medications).

Calculated out of the total deaths (N = 61), 57.4% (35/61) of the death cases were attributed to primary neurological injury, 29.5% (18/61) to systemic compli-

cations, and 13.1% (8/61) to withdrawal of life -sustaining therapy.

4. Discussion

4.1. Classification of Status Epilepticus and Incidence of Cases

At the UTH of Yaoundé, the classification of SE is first made between a generalized convulsive status epilepticus (GCSE) and non-convulsive SE, and based on treatment resistance, a second subdivision is further made. In fact, it is well established that most SE cases fall into one of the following categories: generalized, simple, partial, or complex [6] [12]. However, as cases may be complex and differ in an ICU setting where actions must be rapidly and appropriately taken, we have been led to evaluate each case by considering both clinical and physiological signs to guide the urgent medical treatment approach to be implemented. We, therefore, categorize the SE case based on whether the patient exhibits prominent motor activity (tonic-clonic, tonic, myoclonic, or focal motor) or not (absence or complex partial seizure) to initiate and anticipate a treatment response as precisely described in **Figure 1**.



Figure 1. Refined classification of Status Epilepticus used at the UTH of Yaoundé.

Clinically, GCSE or GTCS is usually easily recognized and therefore requires immediate management due to its high morbidity and mortality [15] [16]. In a total of 468 patients seen (in two years), 319 (68.16%) of patients were presenting with loss of consciousness, tonic and/or clonic movements of the extremities, signs of tongue biting, and incontinence. These symptoms sometimes progressed to: 1) subtle SE, where the unconscious patient exhibited rhythmic twitching of the face, hands or eyes (nystagmus), to 2) focal motor SE, where the conscious patient exhibited continuous or rapid recurring rhythmic jerking in one part of the body (face, arm or leg) lasting usually for more than 5 minutes, to 3) Myoclonic SE, where the patient in a partial consciousness exhibited rapid, brief, involuntary muscle jerks of the shoulders, arms or entire body lasting over 30 minutes.

On the other hand, a non-convulsive SE signature involves an alteration of consciousness (behavioral and/or cognitive changes) without jerking movements lasting for at least 30 minutes [17]-[19]. Non-convulsive SE will therefore feature: 1) Absence SE characterized by a long-lasting (hours-long) state of impaired consciousness, confusion, "blank" look, eye fluttering or behavioral change, or 2) Complex Partial SE characterized by a prolonged or recurrent confusion, delirium with automatisms (lip-smacking, eye twilight, picking movements) that causes a persistent alteration in consciousness or behavior and lasts for at least 30 minutes. In fact, while non-convulsive SE can be suggested by slow cerebral activity, isolated spikes, polyspikes, or spike-like waves in an electroencephalogram (EEG) exam, in general, GCSE begins with a flattening of normal background rhythms followed by generalized low-voltage fast activity or polyspikes that augment in amplitude [20]-[25]. A routine EEG exam may therefore document behavioral changes in progress, whether in a focal region of the cortex or generalized [24] [25].

At the UTH of Yaoundé, out of the 468 SE patients included in the study, we have documented 34.8% (111/319) of NCSE cases, most of them in a comatose state. Indeed, for those cases, we confirmed our diagnosis with complementary exams, including a multimodal approach where we combined structural (MRI) and functional (PET, SPECT, and EEG) neuroimaging when available. It is worth noting that at the UTH of Yaoundé, we have made EEG an essential exam to detect convulsive or non-convulsive SE reliably, to guide the treatment in comatose or paralyzed patients, and for monitoring seizure recurrence. For instance, in a suspected SE case, an EEG exam (ideally within an hour of the suspected onset) was requested in order to determine the correct etiology and prognosis. This way, the EEG exam had a better chance to detect and detail any epileptogenic brain regions and /or any focalization, or focal epilepsy [26] [27].

On the other hand, close to 19.12% (61/319) of SE cases received at the UTH of Yaoundé failed to respond to a first-line (Benzodiazepines) and second-line anticonvulsant (Phenytoin, Depakine, Levetiracetam) treatment administered. Under

these circumstances, we further classify SE into super refractory SE, refractory SE, or new-onset refractory SE [28]-[30]. In fact, it has been shown that treatment resistance may occur because repeated seizure activity can dysregulate normal brain chemistry, such as internalizing GABA receptors (benzodiazepine effectiveness is reduced) and upregulating multidrug transporters (drug concentration in the brain is reduced) [31] [32]. The management approach we have therefore proposed at the UTH of Yaoundé includes continuous EEG monitoring for non-convulsive seizures, anesthetic infusion with high doses of midazolam or Propofol (or pentobarbital) to reduce brain electrical activity, or implementing alternative treatment with immunomodulators (if autoimmune-mediated), ketogenic diet, or lastly surgical intervention.

The prognosis for SE depends on its etiology, the type of SE, the duration of the condition before treatment, and the patient's age [33] [34]. Etiology is one of the most important prognostic factors. At the UTH of Yaoundé, the overall average mortality rate for our SE cases varied from 5% (16/319) in simple cases to over 30.2% (45/149) in severe or super-refractory cases (seizures do not cease despite medications). Interestingly, we noted that adult patients between 20 and 60 years of age and above had significantly higher mortality rates compared to children. In most of our SE cases, the causes of death were mostly facilitated by cerebral anoxia, hypoxia, stroke, tumors, metabolic disorders, or related to medication non-compliance. In fact, it has been shown that underlying illnesses/conditions, as well as seizure-complication-induced ischemic brain injury or neuronal necrosis, may increase the mortality rate for SE [35]-[37]. We noted that although partial SE can last several days, it still had a favorable outcome. The duration of convulsive SE, therefore, played a prognostic role. For instance, the 30-day mortality rate was about 3% if the attack lasted less than 30 minutes; it increased to about 20% for an attack lasting more than 30 minutes and to about 37% if the episode lasted for about an hour. In refractory SE, the mortality rate was around 53%.

In addition, it was interesting to note that factors such as age, sex, and place of residence influenced the incidence of our SE cases. In fact, we found that the incidence of SE increased by about 25% in patients over the age of 60, in male patients (11%) versus a 7% increase in female patients. However, while the incidence of our SE cases cannot be directly linked to a specific ethnic group, we further noted that about 51% of our patients resided in an onchocerciasis-endemic region where the presence of the *Onchocerca volvulus* parasite and the blackfly vector are still active [38]-[41]. Yaoundé, being a cosmopolitan town, it was intriguing to find such figures, which may imply refining our definition of SE to also take into consideration the anthropological/ethnic group aspect, which represented a non-negligible number of the cases included in this study.

4.2. Pathophysiology of Status Epilepticus

The pathophysiology of SE is complex and involves several body systems and

mechanisms, including membrane dysfunction of voltage-gated sodium and calcium channels, and synaptic imbalance between the inhibitory GABAergic and the excitatory glutamatergic systems [42]-[44]. As previously described, resistance to a SE treatment approach is also linked to an overreach of the endogenous protective system. For instance, Gamma-aminobutyric acid (GABA) is the primary inhibitory neurotransmitter in the central nervous system, and activation of GABA receptors usually aims to stop seizures [45]-[47]. Conversely, activation of NMDA (N-methyl-D-aspartate) receptors by glutamate is critical for the prolongation of seizures, as it increases intracellular calcium concentration, which is known to be responsible for neuronal damage [48]-[50]. Clinically, a prolonged SE is difficult to control because GABA receptors become altered and less sensitive to benzodiazepines [28] [51] [52]. The deleterious cerebral effects induced by repeated seizures correlate well with systemic side effects from catecholamine release, which leads to neuronal cell death and aberrant neural plasticity. Therefore, it is expected that prolonged SE may, for example, contribute to the most common cause of drug resistance, which targets focal brain areas hyper- or hypo-activated during seizures and/or interconnected organ systems.

The four (4) factors associated with the severity of our SE cases included arterial hypotension, hyperthermia, hypoxemia, and the duration of the episode. During a GCSE episode, a blood test showed a massive increase in plasma catecholamines, hyperthermia, and hypoxemia associated with hypercapnia due to airway obstruction by bronchial secretions. Indeed, it was expected that normal respiratory movements are most of the time not enough to ensure adequate ventilation, causing the inhalation of oropharyngeal or gastric contents into the lower respiratory tract [53] [54]. We noted that lactic acidosis may develop in SE due to intense muscle contractions in a local hypoxic condition. We noted that hypoxemia may lead to a loss of autoregulation of cerebral circulation, which can result in cerebral hypoperfusion, a condition that can perpetuate the episode of SE and somehow favor neuronal damage [55]-[57]. Knowing that catecholamines can increase heart rate and blood pressure, and, like acidosis, these hormones can cause cardiac arrhythmias, we have suspected that this may be one of the causes of death in some of our SE cases.

However, it is also important to note that hyperglycemia observed at the onset of the SE episode is usually secondary to the production of catecholamines, the activation of hepatic glycolysis, and the release of glucagon [42] [58]. Hyperkalemia related to muscle activation usually leads to arrhythmias, and rhabdomyolysis may result in myoglobinuria and contribute to renal failure through tubular damage [59] [60]. Therefore, in case SE episode is prolonged, hypoglycemia may, for instance, induce increased insulin secretion, marked lactic acidosis, and increased intracranial pressure, resulting in hyperthermia [61]. **Table 1** below details the widespread damages or dysfunctions recorded in our 468 SE cases concerning the respiratory, cardiovascular, nervous, metabolic, and renal systems, and the emergency response proposed by the UTH of Yaoundé.

Table 1. Dysfunctions noted in the 468 SE cases related to the respiratory, cardiovascular, nervous, metabolic, and renal systems, and the emergency response proposed by the UTH of Yaoundé.

System	Early sign	Late sign	Response
Respiratory	Apnea, Hypoxia, Hypercapnia, Tachypnea.	Apnea, Cheyne-Stokes, aspiration pneumonia, Neurogenic pulmonary edema.	1) Application of the ABC (Airway, Breathing, Circulation) framework. 2) Stop the seizure with benzodiazepines (first line e.g., lorazepam) or Antiepileptic drugs (second line e.g., Valproic acid) or Anesthesia (third line e.g., Propofol/midazolam). 3) Clear the secretions. Intravenous hydration (e.g., Isotonic saline).
Cardiovascular	Tachycardia, Hypertension.	Bradycardia, Hypotension, stroke, cardiogenic choc.	
Nervous	Mydriasis Salivary or tracheobronchial hypersecretion (foaming).	Hyperthermia.	
Metabolic/Gastrointestinal	Lactic acidosis, Hyperkalemia, Hyperglycemia, Emesis, Incontinence, Abdominal pain, Paralytic Ileus.	Lactic acidosis, hypoglycemia, liver failure, increased prolactin.	
Renal	Rhabdomyolysis.	Acute tubular necrosis, myoglobinuria, kidney failure.	

4.3. Treatment Approaches for Status Epilepticus

SE can be controlled or successfully treated with an appropriate treatment strategy [62]-[64]. At the ICU of the UTH of Yaoundé, our treatment approaches aimed to stop the seizures, control the temperature, blood pressure, and oxygenation of the patient before specialized procedures start. Clinically, this means maintaining adequate ventilation even though some patients may be cyanotic, and even if one may experience apnea during the tonic phase of the crisis.

All patients were generally adequately ventilated as long as the airway remained open. In case intubation was necessary, a non-depolarizing agent (rocuronium 1 mg/kg body weight), which does not increase intracranial pressure, was used for the induction of anesthesia [65]. If there was a risk of rhabdomyolysis, succinylcholine was contraindicated because the potential hyperkalemia would have led to cardiac arrhythmias [66]. We noted that acidosis was resolved once ventilation was established and the seizures had stopped. Furthermore, because hyperthermia in some of our SE cases exacerbated neuronal damage, temperature fluctuations were treated aggressively with external cooling. Blood glucose levels were regularly monitored, and if hypoglycemic episodes emerged, they were corrected with glucose administration (and thiamine beforehand). In case of rhabdomyolysis, the patient's blood volume was carefully controlled to prevent renal failure due to tubular necrosis.

SE is a medical emergency requiring rapid and aggressive treatment to prevent irreversible brain damage. The longer SE persists without treatment, the more resistant it becomes, with the risk of becoming refractory to common treatments that lead to chronic epilepsy. At the UTH of Yaoundé, we promote a medication that reaches the brain as quickly as possible, has a short half-life (does not accu-

mulate), has minimal or no interactions with other medications, and a medication that is effective for multiple seizure types, and has minimal side effects.

Benzodiazepines such as Diazepam, Lorazepam, and Midazolam were preferred as first-line treatment therapies when suspecting SE. In fact, it has been shown that Benzodiazepines bind to the GABA receptor and increase GABAergic transmission [67]. Our choice was based on studies that compared the different first-line treatments and demonstrated that early administration of Benzodiazepines is safe, effective, stops seizures, and does not cause major complications or side effects [8] [68] [69]. However, we have noticed that the duration of seizures in patients treated with Lorazepam was shorter than that of patients treated with Diazepam, although the risk of respiratory depression was greater with Diazepam. In this observational cohort study, we highlighted the efficacy of Diazepam, Lorazepam, Midazolam, Levetiracetam, Depakine, Propofol, Phenobarbital, and Phenytoin (antiepileptic drug whose primary action lies in the blockage of voltage-gated sodium channels). A treatment was considered effective if the seizure was controlled within minutes of administration and did not recur within at least 40 minutes after administration. Lorazepam was one of the fast-acting drugs and was effective in about 51% of patients, followed by Midazolam and Diazepam effective in 25% and 24% of patients, respectively. Interestingly, we noted that SE gradually became resistant to Diazepam treatment, a finding in agreement with other studies that have shown that there is a change over time in the sensitivity of the GABA receptor to Benzodiazepines [64] [70]-[72].

In our context, when Lorazepam, Midazolam, or Diazepam, which were our treatment of choice to terminate seizure activity, failed, we usually shifted to non-sedating anti-seizure medications, including Levetiracetam, Phenytoin, or Depakine, which were largely equally effective for resistant SE. Phenobarbital, Propofol, or Midazolam were subsequently recommended for long-term seizure therapy when seizures continued despite first- and second-line drugs (in case of refractory SE), in both adults and children. All these drugs have the advantage of being mostly affordable for most of our patients and were always available. However, it has to be mentioned that the use of Diazepam or Phenobarbital treatment to control prolonged seizures or to prevent the recurrence of seizures, especially for patients who were not regaining consciousness quickly (postictal state), required specific clinical distinctions. For all these reasons, at the UTH of Yaoundé, Propofol (effective to control the patient in a coma and stop the persistent seizure activity), Midazolam combined with Propofol, or Phenobarbital alone to suppress refractory seizure activity were recommended. **Table 2** below details the first-, second-, and third-line most used treatments for SE at UTH of Yaoundé.

In addition, various other medications mentioned or not in **Table 2** were also used to achieve specific goals. For instance, Barbiturates (e.g., Thiopental, Pentobarbital) were used to act on the postsynaptic GABA receptor and increase the opening of calcium channels in an intubated patient, where EEG monitoring was essential [73]. However, the main drawback of Barbiturates we noted was their large volume of distribution, which sometimes led to significant accumulation in

Table 2. First-, second-, and third-line most used treatments, the dosage and route of administration, the mechanism of action, and the side effects noted on the 468 SE cases at UTH of Yaoundé.

Medication	Dosage and Route of administration	Main mechanism of action	Side effects	Interactions	Comments
First-line treatment: Benzodiazepines					
Lorazepam	0.05 - 0.1 mg/kg/24h; Intravenous (IV)	GABA receptors.	↓AHT; ↓Respiratory rhythm; Coma; Drowsiness; Hallucination; Sedation.	Opioids (narcotics); Alcohol; Antihistamines; Antidepressants; Others sedatives and tranquilizers.	Depress the central nervous system and can cause additive.
Midazolam	0.15 - 0.4 mg/kg/24h; Intramuscular (IM) or Intranasal (IN) or Intravenous (IV) or buccal or rectal.	GABA receptors.	Drowsiness; Coma; ↓AHT; ↓Respiratory rhythm.	Opioids; Alcohol; Others sedative/anesthetic drugs.	Suppress the central nervous system or affect liver enzymes that break it down. Preferred out-of-hospital use.
Diazepam (Valium)	0.15 - 3 mg/kg/24h; Intravenous (IV) or Rectal.	GABA receptors.	↓Muscular tonus; ↓Respiratory rhythm; Drowsiness; Coma.	Opioids; Alcohol; Sleep medications; Gastrointestinal medications; Muscle relaxants; Grapefruit products.	Depress the central nervous system. To be associated with second-line treatment due to its reduced half-life.
Second-line treatment					
Levetiracetam (Keppra)	500 - 1500 mg/kg/24h; Intravenous (IV) or Oral.	Synaptic Vesicle Protein 2A.	Sleepiness; Dizziness; Difficulty concentrating.	Fewer drug-drug interactions.	Combination with opioids, anesthetics, alcohol/cannabis, sedating antihistamines, antidepressants, antipsychotics may increase overlapping side effects (e.g., fatigue)
Depakine (Valproate/Valproic acid)	20 - 30 mg/kg then 1 - 6 mg/kg/h; 0.15 - 3 mg/kg/24h Intravenous (IV) or Rectal.	Na^+ and Ca^{2+} channel.	Nausea Encephalopathy; Tremors; Hyperammonia; Hepatotoxicity; Hemostasis disorder.	Other anti-convulsant drugs; Anticoagulants; Alcohol; Central nervous system depressants; Antibiotics; Pain relievers; Antimalarial drugs.	Contra-indicated to patient with chronic renal failure.
Phenytoin	15 - 18 mg/kg in 30 minute then 5 mg/kg/24h; Intravenous (IV) or Oral.	Na^+ channel.	Drowsiness, Confusion/Diplopia; Dizziness; Ataxia; Dysarthria; Skin rash; cardiac arrythmia.	Antifungals; Antibiotics; Gastrointestinal drugs; Other anticonvulsants drugs.	Induces liver enzymes and is highly bound to blood protein.

Continued

Third-line treatment					
Propofol	1 - 2 mg/kg bolus then 1 - 10 mg/kg/h Intravenous (IV).	GABA receptors NMDA receptors.	↓Respiratory rhythm; ↓AHT; Metabolic acidosis.	Opioids; Anesthetics; Benzodiazepines; Neuromuscular blockers; Antidepressants; Antifungals/Antibiotics.	Additive to Central Nervous System and Cardiovascular depression.
Phenobarbital	5 - 20 mg/kg then 0.5 - 3 mg/kg/h Intravenous (IV) or Oral.	GABA receptors.	↓AHT; ↓Respiratory rhythm; Coma; Ataxia; Dysarthria.	Alcohol; Opioid pain medications; Benzodiazepines; Sleep medications; Antihistamines.	Neuroprotective propriety.

tissues and, consequently, a prolonged weaning time from mechanical ventilation. Also, we noted that Barbiturates induced significant hypotension, which required the addition of vasopressors. Propofol (activator of GABA receptors and inhibitor of NMDA receptors) was our good alternative for intubated patient with the advantage of being less hypotensive than Barbiturates, and, more importantly, weaning was rapid [74]. The rare complications we noted included perfusion syndrome, severe metabolic acidosis associated with rhabdomyolysis, and renal failure, probably due to the doses of the drug used. Some other complications occurred in severely compromised patients who were receiving corticosteroids and catecholamines. Studies have attributed these complications to a direct necrotic effect of Propofol on peripheral muscles, where it uncouples the respiratory chain at the mitochondrial level [75]-[77].

Tegretol (Carbamazepine) was also used for SE cases because of its known relatively good clinical tolerance and other effects (e.g., mildly sedating; causing little hypotension or respiratory depression) in children, adults, and the elderly, including those with chronic respiratory failure [78]. In most of our patients with SE, Tegretol treatment ensured maintenance and avoided the recurrence of seizures without major side effects or complications out of the hospital. However, it was sometimes necessary to couple it with specific multivitamin or mineral supplements to manage possible nerve damage due to prior seizure episodes. **Figure 2** below details the UTH of Yaoundé's proposed algorithm used to optimize the management of SE at their ICU.

4.4. Paraclinical Exam for Status Epilepticus

Various paraclinical or biological exams are critical for functional explorations of the nervous system in the case of SE. Brain imaging and, indeed, electroencephalography (EEG) are key means to confirm a suspected SE. In some cases, to understand the etiology of a prolonged seizure, we often order a lumbar puncture (spinal tap) to rule out a central nervous system infection or an autoimmune condition [79] [80]. Routine biological exams, including complete blood count (CBC), comprehensive metabolic panel (CMP), or toxicology screens, are usually helpful to identify the immediate and reversible triggers of the seizure [81].

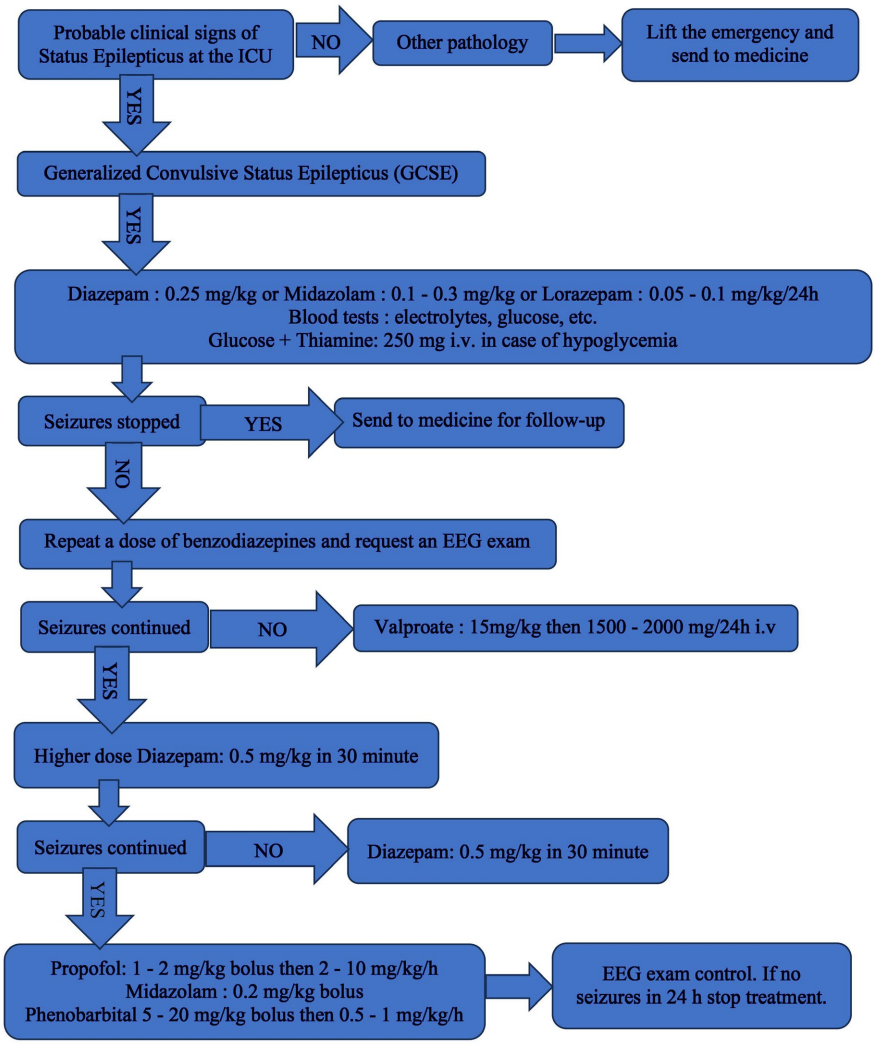


Figure 2. Algorithm of the management of status epilepticus at the UTH of Yaoundé.

At the UTH of Yaoundé, it has become evident that correcting hypoglycemia or electrolyte imbalance (e.g., low magnesium or sodium) or even addressing a systemic infection (e.g., cerebral malaria, meningitis, encephalitis) may directly resolve seizures. Concerning brain imaging such as MRI, this exam was ordered when we suspected acute seizure-induced brain abnormalities to pinpoint the underlying cause [82] [83]. In some of our SE cases, specific MRI sequences detailed neuronal stress, blood-brain barrier disruption, and/or temporary fluid shifts (cytotoxic or vasogenic edema) affecting brain structures such as the hippocampus, the thalamus, or within the cerebral cortex [83]-[85]. We were able to confirm that since a seizure does not usually affect the entire brain randomly, SE often lights up specific brain areas on MRI [84] [86].

On the other hand, among the paraclinical and/or biological techniques used to confirm SE, EEG was one of the exams of choice requested as soon as the patient was cooperating and/or stable to monitor cerebral activity, phases, and/or type of SE [64] [87]. In fact, in an emergency setting, an EEG exam alone can reliably

confirm a suspected SE diagnosis [88] [89]. Furthermore, EEG monitoring gives visual and clear electrophysiological evidence of each phase, each subtype of SE, and eventually documents whether the implemented treatment approach is beneficial or not to the patient in order to adjust or reevaluate the clinical care on time [90]. At the UTH of Yaoundé, we have noted that some patients may experience non-convulsive seizures (no obvious physical or clinical signs) at their admission to the ICU. An EEG exam was also requested for those cases to detect hidden seizure activity, guide the treatment approach, and identify possible underlying life-threatening medical or neurological causes. For instance, we have noted that EEG monitoring of patients with brain trauma, stroke, or cerebral tumor may have episodic non-suspected seizures, sometimes with behavioral or consciousness dysfunction. It was advantageous for the UTH of Yaoundé to run various EEG monitoring techniques, including routine EEG (a standard 30 - 40-minute random recording), continuous EEG (triggered at regular intervals or during specific clinical manifestations), sleep EEG (recording brain activity during sleep), and EEG monitoring records (triggered in case of suspicious activity) tailored for each patient and essential to adjust treatment and verify the resolution of seizures. At the UTH of Yaoundé, an EEG exam was, therefore, important to document seizure cessation or a burst-suppression pattern (paroxysmal bursts followed by global electrogenesis depression) with an interval of 2 - 30 seconds between bursts. Once this pattern was maintained for 12 to 24 hours, the medication withdrawal was attempted, even if the patient remained on EEG monitoring to prevent recurrence, and because we have noted cases where SE persisted despite the cessation of clinical manifestations or patients experienced intermittent seizures.

4.5. Control, Maintenance, and Preventive Medications for Status Epilepticus

The available treatment for SE follows a strict, phased progression to maintain/control or prevent the seizures. To prevent or control seizure episodes, the UTH of Yaoundé followed the American Epilepsy Society protocol, with minor refinements [91] [92]. In fact, the daily appropriate maintenance anti-seizure medication was chosen based on identifying underlying triggers such as missed doses, metabolic imbalance, or infections [93] [94]. In our context, several medications were available, affordable, and well-tolerated. However, because convulsive and non-convulsive SE are physiological dysfunctions happening within the nervous system and spreading their effects across many organs of the body, the choice of anti-seizure medications also considered the patient's age, sex, and any reported underlying conditions (e.g., pregnancy, allergy, or weight) that may affect the patient's health.

Tegretol (Carbamazepine) was the anti-seizure medication primarily used to prevent or manage focal/partial, generalized tonic-clonic, or mixed seizures [95] [96]. The drug is known to act by reducing neuronal hyperactivity, hence preventing the spread of the seizure activity. Typical doses for seizure control or prevention ranged from 800 mg to 1200 mg daily for adults, starting with the lower dose

and increasing gradually until the maximum benefit was achieved for each patient [78] [95]. Common side effects (dizziness, drowsiness, nausea, etc) noted were watched for and corrected as soon as the patient reported them. Depakine (valproate or Valproic acid/sodium), a broad-spectrum anti-seizure medication, was used alone or as an adjunctive treatment for SE and most subtype cases [97] [98]. The drug was used to suppress neuronal hyperactivity that triggers seizures by increasing GABA concentration in the brain [98]-[100]. Depakine had a wide side effects profile ranging from minor gastrointestinal dysfunction (e.g., nausea, diarrhea, indigestion) and neurological effects (e.g., drowsiness, dizziness, tremors), to rare but serious pancreatic or liver toxicity [101] [102]. The drug was usually contraindicated during pregnancy (exclusion criteria in our study). Levetiracetam (Keppra) was primarily used for chronic SE cases, because of its specific anti-seizure potential, which includes dampening excessive neuronal hyperactivity [103]-[105]. The drug was prescribed as an adjunctive or monotherapy for SE, with the benefit of having minimal interactions with other medications the patient could have been on [105]. Common reported side effects included drowsiness, dizziness, fatigue, and behavioral change (e.g., irritability) referred to as "Keppra rage" [13] [106] [107]. Phenobarbital was considered our first-line therapy for the control or maintenance of seizures in children [14] [108]. The remarkably long half-life (50 - 140 hours), approximately 2 to 6 days, made it ideal for long-term seizure control [109] [110]. However, major side effects such as respiratory and/or metabolic dysfunction were monitored when administering for acute emergencies [110]. Above all, at the UTH of Yaoundé, our immediate seizure control was achieved via fast-acting benzodiazepines, followed by non-sedating anti-seizure medication for maintenance and seizure termination, and it ended with selected consistent medications known to prevent identifiable seizure triggers.

5. Conclusion

The increased incidence of SE cases at the UTH of Yaoundé may emphasize the complex character of most brain disorders or dysfunctions, which need refined, reliable, and tailored therapeutic approaches to limit the complications. Here, we highlighted how SE, a neurological emergency, can be controlled to avoid or minimize irreversible cerebral brain lesions and resistance, using available and affordable conventional treatments in a population with limited financial resources. We have proposed specific benzodiazepines as first-line treatment for confirmed SE, followed by various anti-seizure medications such as Diazepam, Depakine, Levetiracetam, Valproate, or Midazolam in case of persistent clinical symptoms or resistance. Depakine, Levetiracetam, Valproate, Phenobarbital, and Tegretol were also used for maintenance, and a 3-month routine EEG was always recommended to monitor cerebral activity and the effectiveness of the treatment before any treatment discontinuation is attempted.

6. Limitations of the Study

We acknowledge that some of the outcomes of this study may only be restricted

or limited to the UTH of Yaoundé. Our results may not be generalized to other hospitals. It is possible that the tertiary nature of the UTH of Yaoundé has attracted more refractory cases. There are still possibilities that incomplete diagnosis was due to resource constraints for patients, and some of our data need to be standardized and comparable to evaluate the efficacy of each specific treatment approach.

Conflicts of Interest

None.

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