CONSENSUS DOCUMENT

Emergency management of epileptic seizures: a consensus statement

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This consensus statement was developed to optimize the emergency management of epileptic seizures in prehospital and hospital settings. A list of clinical questions was drafted and the literature on the emergency treatment of epileptic seizures was reviewed by a multidisciplinary team of emergency physicians, neurologists, and pediatric neurologists from 3 associations: the Spanish Epilepsy Society (SEEP), the Spanish Society of Emergency Medicine (SEMES), and the Spanish Neurology Society (SEN). The team members first answered the questions individually and then discussed them during a meeting of experts from the 3 associations, to reach consensus on the content of the present statement. The recommendations and protocols proposed attempt to standardize the emergency management epileptic seizures. Earlier concepts and definitions are reviewed, a new definition of an epileptic seizure emergency is proposed, treatment options are described for different clinical scenarios, and a crisis code for seizures is also set out.

Keywords: Epilepsy, seizure. Acute treatment. Urgent care, pre-hospital and hospital. Medical literature review.

Documento de consenso para el tratamiento del paciente con crisis epiléptica urgente

El presente documento de consenso se ha desarrollado con el objetivo de optimizar el tratamiento de pacientes con crisis epilépticas (CE) en los ámbitos de urgencias prehospitalario y hospitalario. Un equipo multidisciplinar formado por *urgenciólogos,* neurólogos y neuropediatras de tres sociedades científicas, la Sociedad Española de Epilepsia (SEEP), la Sociedad Española de Urgencias y Emergencias (SEMES) y la Sociedad Española de Neurología (SEN), elaboró un listado de preguntas clínicas y revisó la literatura científica sobre el tratamiento urgente del paciente con CE. Después de un periodo de trabajo individual dando respuesta a las preguntas planteadas, se discutieron y consensuaron en una reunión con expertos de las tres sociedades los contenidos del presente documento. Las recomendaciones y los protocolos que se proponen tratan de unificar el tratamiento urgente de los pacientes con CE. Se han revisado conceptos y definiciones previas y se ha propuesto una nueva definición de CE urgente, planteando diferentes recomendaciones terapéuticas según los escenarios clínicos, incluyendo una propuesta de código crisis.

Palabras clave: Crisis epiléptica urgente. Tratamiento agudo. Atención urgente prehospitalaria y hospitalaria. Revisión bibliográfica.

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Introduction

Epilepsy is a disease that affects about 350,000 people in Spain and 50 million worldwide[1]. The World Health Organization (WHO) estimates that one in ten people suffers an epileptic seizure (ES) during their lifetime should they live to be 80 years old. In addition to the high prevalence, it is a disease that carries a high morbidity, deterioration in quality of life and, even these days, social stigma. It is estimated that ESs account for up to 1% of care in emergency departments (EDs)[2]. In spite of this, the data on emergency care in the EDs are scarce. Most studies are unicenter studies, and recommendations are based on clinical guidelines and expert opinions[2,3]. A recent study by Spanish emergency physicians highlights once again the high prevalence of ESs, in addition to healthcare aspects of interest[4].

Most recent studies agree on the need for early and efficient ES care, since the duration of the ES has been clearly related to prognosis[5,6] both in animal models and in routine clinical practice. The axiom "time is brain" is valid not only for stroke, but also for seizures, and

this is reflected in the emerging times that define status epilepticus (SE)[6]. This reinforces the importance of early treatment of the ES and the interventions of the out-of-hospital emergency services (OHES) as well as in the hospital emergency departments (EDs)[7].

In spite of the importance of action times, the review of the literature shows that there is no consensus on how to act in these first moments in terms of basic support measures, treatment (drug and dose) and transfer to a health center[8,9]. The lack of scientific evidence and the need for a consensus to act early and homogeneously have motivated this work in which, from the perspective of emergency care and specialized care by neurologists, we address the issue in an interdisciplinary manner. The objective is to reach a consensus on recommendations that facilitate and speed up the treatment of patients with urgent ES.

Method

A multidisciplinary team made up of professionals linked to clinical care, teaching and research on ES care in the ED was responsible for the preparation of this document. Initially, two emergency physicians and four neurologists prepared a series of clinical questions and conducted a literature search aimed at clinical practice guidelines for the urgent management of epileptic seizures prioritizing the Official Guide of the Spanish Society of Neurology[2,3], documents of the International League Against Epilepsy (ILAE)[6], the American College of Emergency Physicians (ACEP)[10] and EMERGENCIAS[11]. A bibliographic search was carried out on PubMed aimed at review articles published in PUBMED in the last 10 years (May 2009-May 2019). The terms introduced in PubMed were "urgent seizure," "urgent treatment seizures," "seizure emergencies," "status epilepticus and emergency" selecting those that referred to the concept of urgent ES and the urgent treatment of patients with ES. After some individual work, the contents of this document were discussed and agreed upon in a meeting in the presence of a panel of experts.

The concept of urgent ES has been defined and the different lines of treatment have been updated. A series of therapeutic recommendations have been established according to different usual clinical scenarios, concluding with a proposal for a crisis code. This document has been endorsed by the three scientific societies involved in its preparation: the Spanish Epilepsy Society (SEEP), the Epilepsy Group of the Spanish Society of Neurology (SEN) and the NeuroIctus Group of the Spanish Society of Emergency Medicine (SEMES).

Concept of urgent epileptic seizure

This is a new concept that was born with the intention of identifying those patients who require priority attention. It includes patients with SE, repeated crises in accumulation and high-risk crises (Figure 1).

Status epilepticus

Status epilecticus (SE) is a neurological emergency that accounts for approximately 10% of emergency crises[10] and is associated with 20% short-term mortality[12]. The concept of SE has evolved in recent years and the timing has been reduced. According to the latest proposal of ILAE[6], a first time (t1) describing the beginning of SE after the failure of the mechanisms responsible for the termination of the crises is defined. It is established that it is at 5 minutes in convulsive SE (CSE) generalized tonic-clonic (GTC), at 10 minutes in focal SE with alteration of the level of consciousness and at 10-15 min in focal SE without alteration of the level of consciousness or in the SE of absences. At the same time, a second time (t2) is defined, from which long term consequences appear, since there is a risk of altering the neuronal networks, the crisis is perpetuated or even neuronal death. This time would be 30 minutes in the case of GTC CSE and 60 minutes in the focal SE with alteration of consciousness, without being defined in the case of focal SE without alteration of consciousness nor in the SE of absences.

SE is considered refractory (RSE) when critical activity persists despite the administration of two parenteral drugs at appropriate doses, including at least one benzodiazepine (BZD)[18]. A specific time of RSE has not been defined, but it is close to t2[6]. SE is called super-refractory (SRES) if it lasts more than 24 hours despite appropriate treatment, or reappears after the decrease or suspension of anesthesia.

Cumulative epileptic seizures

Cumulative ESs (from "seizure clusters") or recurrent acute crises, represent almost 20% of the total

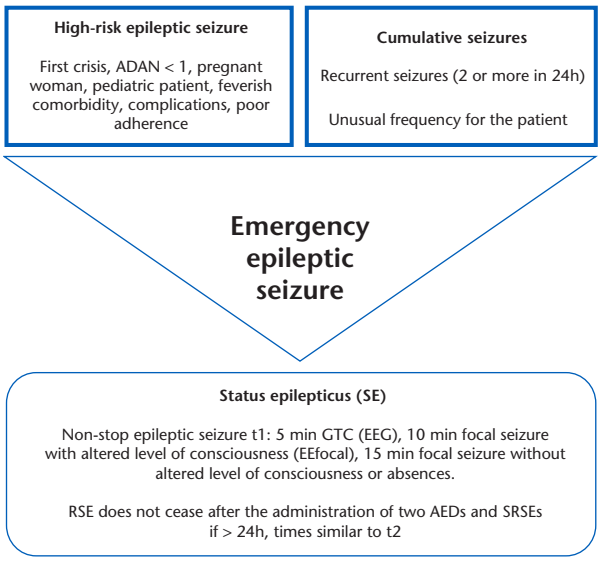

Figure 1. Concept of urgent epileptic seizure.
GTC: generalized tonic-clonic; CSE: convulsive state epilepticus; RSE: refractory state epilepticus; AEDs: antielphile drugs; SRSE: suprefractory state epilepticus.

ADAN scale

Abnormal language	No Yes	0 1
Ocular deviation	No Yes	0 1
Automation	No Yes	0 1
Number of seizures	0-1 2 >2	0 1 2
Total		(0-5)

Probable status epilepticus (SE) (ADAN > 1)

Modified STESS scale (mSTESS)

Level of consciousness	Alert or sleepy/confused Stuporous or in a coma	0 1
Type of seizure	Simple partial Partial complex, myoclonic, absence Convulsive Generalized or non-convulsive in coma	0 1 2
Age	< 70 years-old ≥ 70 years-old	0 2
History of previous seizures	Yes No or unknown	0 1
Modified Rankin Scale (mRS) basal	0 (no disability) 1-3 (mild-moderate disability) ≥ 4 (moderate-severe)	0 1 2
Total		(0-8)

Probable death on admission on SE (mSTESS > 4)

RACESUR scale

Non-Generalized Tonic-Clonic Seizure (GTC) as a reason for consultation	No Yes	0 1
Regular consumption of ≥ 3 drugs	No Yes	0 1
Visit to the Hospital Emergency Department in the previous semester	No Yes	0 1
Total		(0-3)

Probable adverse outcome within 30 days of ED discharge (crisis recurrence, ED revisit, hospitalization, or death) (RACESUR > 2)

Figure 2. Scales with prognostic value in epileptic seizures. ED: hospital emergency department.

crises in the emergency department[4,14]. In the absence of a unanimous definition, the most widely accepted are the recurrence of 3 or more crises in 24 hours, 2 or more crises in 6 hours and more frequently 2 or more crises in 24 hours with recovery between crises and without SE criteria[14]. These concepts must be adapted individually, since the frequency of seizures varies greatly according to the type and etiology of epilepsy and individual factors of the patient. Cumulative ESs can be the beginning of an SE ("a pre-SE") and are associated with both a greater amount of resources and frequent visits to the emergency department, generating a negative impact on the quality of life of patients and caregivers[14].

High-risk epileptic seizure

ES that, although isolated, have a series of characteristics identifiable by anamnesis that indicate a high risk of recurrence or development of ES are included. In this regard, a series of prognostic scales have been published that are of interest to the ED (Figure 2). The ADAN scale is a novel tool of great usefulness at the prehospital level to identify the patient at risk of SE (> 80% ADAN > 1)[15]. The Status Epilepticus Severity Score (STESS)[16] and, even better, a modified version (mSTESS)[17] predict mortality on admission (> 80% if mSTESS > 4). Finally, the RACESUR model identifies the patient at high risk of suffering an adverse outcome 30 days after discharge from the ED (> 0% if mSTESS > 2)[18].

Other variables not included in the previous scales, which in this consensus are suggested to be included in the concept of high-risk crises are: patients with first crisis, crisis in pregnancy, poor adherence to treatment (more than 24 hours without taking treatment), fever, severe psychiatric comorbidity and the presence of complications associated with the crisis (bronchial aspiration, head trauma, burns).

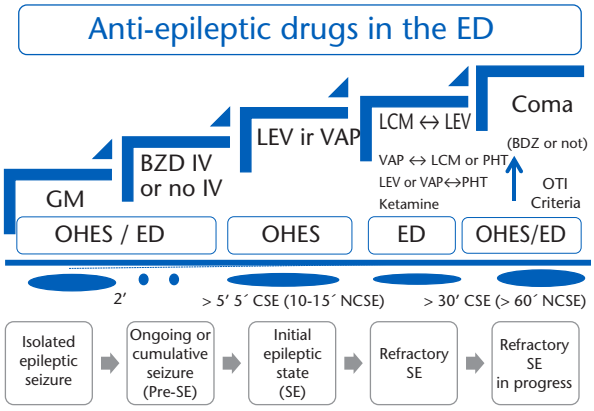

Figure 3. Summary algorithm of treatment of epileptic seizure in the acute phase.
GM: general measures; BZD: benzodiazepines (diazepam iv, midazolam no iv); OTI: orotracheal intubation; LEV: levetiracetam; VAP: valproic; LCM: lacosamide; PHT: phenytoin; CSE: convulsive status epilepticus; NCSE: non-convulsive status epilepticus (focal with coincidence alteration); OHES: out-of-hospital emergency services; ED: hospital emergency departments.

Treatment of epileptic seizures in the acute phase

Current recommendations on urgent ES treatment arise from work on patients with SE or ES in accumulation, and are summarized in the algorithm in Figure 3.

General measures

The general measures integrated in a proactive behavior of Protect, Warn and Relieve (PAS behavior) based on expert opinion and SE management guidelines aim to optimize the initial management, prevent and control possible complications in patients with ES[11]. Initial measures have been described for both non-healthcare and healthcare personnel (Table 1).

First therapeutic phase

Benzodiazepines (BZDs) are the only drugs with sufficient scientific evidence (IA recommendation) as initial treatment of the ES patient (Table 2). They have been shown to be safe and effective and respiratory complications are higher when not administered11. Early use, after 25 min of an ES and ES in accumulations, is associated with better ES control (60-80%) and lower morbimortality[19-25]. Each minute of delay in the treatment means a 5% accumulated risk for seizures lasting more than 60 min[26], and patients treated after this time present more neurological sequelae at 4 years[27]. Despite this, only 13% of patients attended by family members[28] and 20% of those attended by emergency personnel[4,22] received BZD early. The lack of training justifies these results[29].

Intravenous (IV) BZDs are the choice if venous access is available[19,23,33,34]. Diazepam (DZP) is the most recommended IV BZD because of its better level of evidence and recommendation (1A), providing as advantages a quick start of action (13 min), although its effect is short-lived (10-30 min)[35]. In the absence of lorazepam (LZP) IV in our setting, clonazepam (CNZ) IV is recommended as an alternative, with a similar and even superior profile[36]. Due to its longer lasting effect (12 h) than DZP, it is recommended for cumulative crises and maintenance. Midazolam (MDZ) IV is more suitable for the third line in continuous perfusion because it has a similar onset of action to DZP IV, but with a less lasting effect (5-10 min).

If venous access is not available, BDZ No IV is recommended. They may be as effective as BDZ IV when the total time of administration is taken into account[23,37]. Currently, approved non-IV therapies are rectal DZP and intramuscular (im) or oral MDZ (in children under 18 years). Intranasal MDZ, oral DZP or LZP are used off-label. According to current evidence, non-IV MDZ is more effective and better tolerated than rectal DZP[31,32]. BZD is being explored by both the inhaled and subcutaneous routes[30].

Table 1. General measures in the acute phase

Non-healthcare personnel
– Keep calm and prevent injuries (loosen clothes, protect from shocks), safety side position, do not abandon the patient, take into account the duration of the crisis, clean secretions or vomit, administer rescue drugs if available, perform capillary glycemia in diabetic patient and take the temperature. It is not recommended to limit the patient's movement, force or introduce objects to open the mouth or artificial respiration.
– Notify the corresponding emergency department by phone (112/061): if the seizure lasts longer than usual or > 5 min, if the seizure is recurrent within a few minutes, if it is the first episode and if the neurological, respiratory, etc. clinic persists.
Healthcare personnel
– Opening of the airway and ensuring adequate oxygenation and ventilation. If necessary, the secretions should be aspirated and foreign bodies removed.
– Administer oxygen. Assess orotracheal intubation (OTI) if: imminent or potential compromise of the airway, altered level of consciousness (GCS < 8 points), excessive (> 40 brpm) or decreased (< 10 brpm) respiratory work, hypoxemia (pO_2 < 50, $satO_2$ < 85%) refractory to treatment or progressive respiratory acidosis (pH < 7.2, pCO_2 > 60).
– Monitoring of vital signs (respiratory rate, heart rate, blood pressure, temperature, oxygen saturation) and determination of blood glucose Administer thiamine if you have a habit of wine consumption or malnutrition, hypertonic glucose if you have hypoglycemia and rapid insulin if you have hyperglycemia.

GSC: Glasgow Coma Scale.

Second therapeutic phase

The most recent recommendations state the need to administer non-BZD antiepileptic drugs (AEDs) earlier in SE[2-4]. Delayed initiation and infratherapeutic doses are associated with increased refractoriness and poorer prognosis[38,39]. Early therapy with non-BZD AEDs is recommended after administration of BZDs in the first 15 min after initiation of any type of ES[40]. These AEDs are not recommended before or at the same time as BDZs[41] (Table 3).

Table 2. First therapeutic phase: benzodiazepines

Drugs	Dosage	Evidence	Comment
IV Benzodiazepines			
Diazepam (vial 10 mg/2 ml)	5-10 mg (0.15 mg/kg) bolus iv (dilute 1 mg/ml) or in 50 cc PSS in 2 min. (max. 5 mg/min up to 20 mg) Children: 0.3 mg/kg. Max. 5 mg (< 50 kg)	IA	Choice IV in SE
Clonazepam (vial 1 mg/ml)	1 mg iv bolus, evaluate repeat bolus after 5 min (max 0.5 mg/min, max 3 mg dose) Children: 0.05 mg/kg. Max. 2 mg	IIIB	Alternative IV in SE Cumulative seizure Safety measures
Midazolam (vial 15 mg/3 ml, 50 mg/10 ml)	1-2 mg/1 min. (0.1-0.2 mg/kg) (max. 2 mg/min up to max. 15 mg) Children: max. 4 mg (14-40 kg)	IB	Alternative IV in SE Preferable in 3rd line
Non-IV Benzodiazepines			
Midazolam (vial 15 mg/3 ml, 50 mg/10 ml)	5-10 mg IM, evaluate repeat after 10 min (max 15 mg)	II A	Choice non-IV in SE IM similar efficacy as IV
Midazolam (Buccal solution between both cheek and gum, syringe 2.5/5/7.5/10 mg) (Buccal solution or ampoules titrated with intranasal spray)	2.5 mg if child 3 m-1 year; 5 mg if 1-5 years; 7.5 mg, if 5-10 years, 10 mg if > 10 years	IIB	Choice non-IV, IM
Diazepam (Rectal Cannula 5, 10 mg)	10 (5 mg if children < 40 kg) rectally, evaluate repeat after 10 min. (max 20 mg)	IIA	Non-IV Alternative in Children Crisis in Accumulation/SE
Lorazepam (1 mg and 5 mg tablets)	1-2 mg between lip and gum	IIIB	Alternative No IV Crisis in Accumulation/SE
Clonazepam (Tablets 0.5 mg, 2 mg, oral drops 2.5 mg/ml)	0.5-1 mg between lip and gum/5-10 drops by spoonful with or without water/tea/juice	IIIB	Alternative No IV Crisis in Accumulation/SE

SE: status epilepticus; IV: intravenous; IM: intramuscular; max: maximum; PSS: physiological saline serum.

None of the non-BZDs AEDs have proven to be clearly superior compared to the rest, among other reasons because there are no studies that adequately compare them[41-44]. Nor has a recent clinical trial (Established Status Epileptic Trial, ESETT), in which the efficacy in crisis control between phosphophenytoin (fPHT), valproic acid (VPA) and levetiracetam (LEV) has been compared, demonstrated superiority of any of these AEDs[42]. Because of this, at present, the choice of non-BZD AEDs is determined primarily by the safety profile and patient characteristics[2,45].

Phenytoin (PHT) is the classic AED of choice in the SE (focal) because it is the only one with a Food and Drug Administration (FDA) recommendation with evidence level (EL) I[2,45]. However, due to its low safety profile (contraindicated in cardiac patients, enzyme inducer, complex posology or local irritation) and the appearance of alternatives, it has fallen into disuse[4]. No fPHT is contemplated in Spain since its withdrawal in 2012 due to lethal adverse reactions.

Phenobarbital (PB) was a pioneering drug in the treatment of SE, even before BDZ and PHT, but it has also been relegated to a lower safety profile[10].

VPA was approved in Europe as an alternative to PHT because of its better tolerance. It is not cardiotoxic, but because of its metabolism and interactions it is contraindicated in patients with liver or coagulopathy. It is also not recommended in women of childbearing age because of its teratogenic effects[10,45,46]. Unless contraindicated, it continues to be of choice in idiopathic generalized epilepsy (IGE) in men and women with no reproductive potential.

LEV is a broad-spectrum AED, indicated in ES of focal and generalized onset, which is not less reliable

Table 3. Second therapeutic phase: intravenous non-benzodiazepine antiepileptic drugs

Drugs	Dosage	Evidence	Comment
Phenytoin (vial 250 mg,dilute in 250 cc non-glucose saline serum, plastic container)	20-30 mg/kg 1,000 mg 30-40 min Max: 1 mg /kg/min > 20 min Bolus can be repeated 10 mg/kg In plastic container and serum	IA	
Valproico (vial 400 mg with or without diluting)	20-40 mg/kg, 1.200-2.000 mg in 5-10min Max: 6 mg/kg/min) 15-20 mg 800-1.200 mg (elerly, children y < 50 kg)	IIB	Alternative IV in SE Preferable in SE in generalized epilepsy
Levetiracetam (vial 500 mg/5 ml, dilute in 100 ccPSS/SG 5%)	30-60 mg/kg, 3,000-4,500 mg 15-20 min Max: 4,500 en adultos, 2,500 mg children	IIC	Choice IV in SE in OHES
Lacosamida (vial 200 mg/20 ml with or without diluting)	6 mg/kg, 400 mg in 15-20 min Max: 600 mg	IIIC	Choice IV in ED focal SE
Brivaracetam (vial 50 mg/5 ml, with or without diluting)	2 mg/kg, 100-200 mg, in 10-15 min Max: 3 mg/kg, 300 mg, 50 mg si < 50 kg	IV	Alternative IV in SE Adjuvant therapy

Max: maximum; IV: intravenous; SE: status epilepticus.

Table 4. Third therapeutic phase: intravenous anesthesia

Drugs	Dosage	Evidence	Comment
Midazolam (vial 15 mg/3 ml, 50 mg/10 ml)	1-2 mg/1 mins. (0,1-0,2 mg/kg) in initial bolus + tea 0,1-0,4 mg/kg/h	IB	Choice IV in SE (non-barbiturate coma)
Ketamina (vial 500 mg/10 ml)	50-1,000 mg (0.5 a 3 mg/kg) in bolus + tea 1-10 mg/kg/h	IV	Alternative IV in RSE (Coma or non-induced coma)
Propofol (vial 10 y 20 mg/ml)	3-5 mg/kg in initial slow bolus + tea 5-10 mg/kg/h	IV	Alternative IV in RSE (non-barbiturate coma)
Tiopental (vial 500 mg/10 ml)	2-3 mg/kg in 30 s bolus + tea 3-5 mg/kg/h	IV	Alternative IV in RSE (barbiturate coma)

IV: intravenous; SE: status epilepticus; RSE: refractory status epilepticus.

than the previous ones, preferred for its better pharmacological profile[7,43,48-49]. It stands out for its linear kinetics, combination of interactions, easy oral administration: IV 1:1 conversion and combination of interactions or serious adverse effects. In renal insufficiency, it requires dose adjustment. Currently, it is the most used AED[4] and it is considered as the AED of choice in many lines[43,50]. In this paper it is suggested as such, especially in OHES.

Lacosamide (LCM) is a new generation AED, with indication in focal seizures and seizures with evolution to tonic-clonic bilateral, which is characterized by a more physiological inhibition of sodium channels than PHT (51) and an efficacy not less than fPHT[52]. In SE it is more effective the earlier it is administered[53,54]. Recently, a possible synergistic effect of LCMLEV has been reported[55]. It is preferred to avoid in combination with other AEDs inhibitors of sodium channels (PHT, carbamides) and in patients with AV blocks in the ECG[54]. This study suggests that AEDs are the choice for focal SE in the ED.

Brivaracetam (BRV) is a new IV AED of the LEV family, which shows greater affinity for the SV2A protein and greater liposolubility, with potential for greater efficiency and speed of action. It has demonstrated efficacy in SE in small series[56-58]. The FDA has approved it for monotherapy but in the European Union, it is indicated for adjuvant therapy.

Topiramate (TPM)[45,59] and perampanel (PER)[60] are broad-spectrum AEDs that are considered an alternative to the above, but must be administered by orally or nasogastric tube.

Third therapeutic phase

They are used in patients with RSE after failure of the previous two lines of treatment, especially in patients with CSE lasting more than 30 minutes. Sometimes, they are used early. The low level of consciousness and hemodynamic instability in patients with CSE was associated with the need for induced coma in OHES[21]. On the other hand, in non-convulsive RSE, without altering the level of consciousness, the strategy is more conservative, avoiding as far as possible the induction of coma[2,10,45]. Barbiturate and non-barbiturate anesthetics are used (Table 4). There is no evidence of superiority of one over the other. The choice depends on the patient's situation and above all on professional experience[10,11,61,62]. If there is hemodynamic instability, non-barbiturate coma is preferred, with BZD (MDZ in perfusion) or propofol at low doses[2,10,45,63]. If rapid sequence intubation (RSI) is decided, it is recommended to use non-barbiturate inducers (etomidate or propofol) and to avoid myorelaxants because of the risk of masking an RSE[21].

Ketamine has recently been restored as an anesthetic that can be useful in RSE and SRSE because of its antiNMDA action with neuroprotective effect in patients with or without induced coma[64]. Although it has traditionally been considered as a third line treatment, recent studies suggest considering its administration in an early manner even in the initial phases of the SE[65]. In this study, it is being proposed as the AED of choice in third line, both in OHES and ED, and as an alternative in induced coma.

Clinical Scenarios

Often, ES patients are treated in the ED. Half of them arrive after previous care by OHES and the other half are accompanied by family members or caretakers[4]. The following is a summary of a series of practical aspects of interest in emergency care on which a series of recommendations are established, including a proposal for a crisis code.

1. Patient with known epilepsy and recovered seizures

Pre-hospital care by caretakers/family members:
- Apply general measures as non-healthcare personnel (Table 1).
- Notify OHES when the seizure is different from usual, when they suspect injury to the patient or in the presence of other risk factors for urgent ES.
- Administer BZD (oral/intranasal/oral) in cumulative seizures (if isolated CGTC administrate according to the pattern of her/his usual neurologist) and additional dose (advance next intake) of usual AEDs (not BZD); provide information on the semiology of the seizure and chrono-metric time.

OHES (Figure 4):
- If the patient has a seizure different from the usual ones, OHES should be notified and the need for evaluation and transfer to the hospital will be decided by the emergency coordination center.

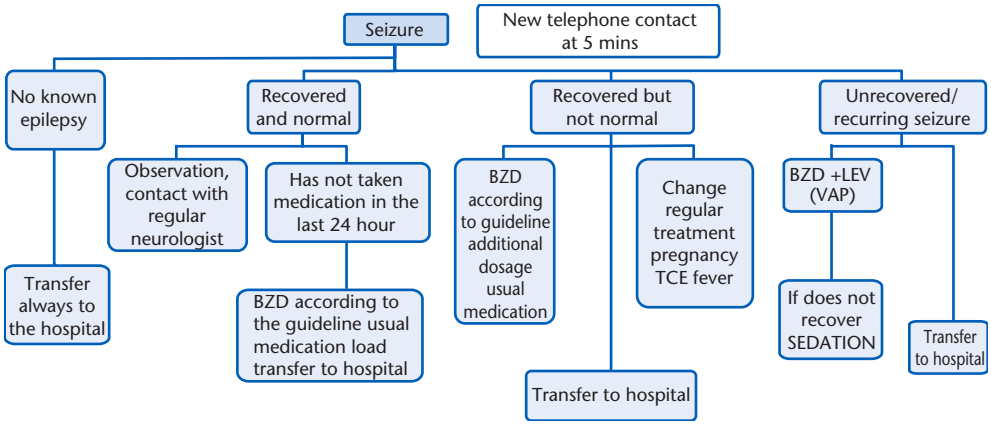

Figure 4. Out-of-hospital management. BZD: benzodiazepines; LEV: levetiracetam; VAP: valproic.

Care in the ED (Figure 5):
- It is recommended that prior notice of ED-OHES be given by contacting the neurologist on duty and that early attention (< 60 min) be given jointly with ED physicians in patients with: a) urgent ES (see definition), and b) ES other than usual.
- Take an exhaustive clinical history, perform general (laboratory, ECG, radiological) and specific (individualized CT scan, urgent video EEG monitoring (vEEG) of at least 30 min) complementary tests (laboratory, ECG, radiological) with the intention of identifying causes and preventing complications[2,3,10,12].
- In the treatment, general and pharmacological measures of the first therapeutic phase are taken into account (BZD IV/IM if they have not been administered before in the case of cumulative seizures), without forgetting to administer their usual medication (evaluate IV load dose if available).
- If subclinical or subtle seizures with EEG criteria are detected, follow the recommendations of the following sections.
- If the patient remains asymptomatic and without seizures, hospitalization or discharge from the ED will be decided according to previous assessment with early follow-up, especially in high-risk patients[18].

2. Patient with known epilepsy and persistent or unrecovered seizures (SE)

Pre-hospital care by caretakers/family members:
- Consider the above measures (general, BZD no IV, common AED no BZD and information) always and early warning to the OHES.

OHES (Figure 4):
- From the emergency coordinating center, it is identified as an emergency or non-delayable emergency and a resource capable of advanced life support and transfer to the ED (optimal start time < 30 min) would be sent with prior notice to the hospital (neurology + ED).
- BZD is administered (if not done earlier) and non-BZD AEDs (LEV, VAP) and the third therapeutic phase will be initiated in CSE (anesthetics, considering ketamine in an early manner). In EENC it is recommended to avoid coma.

ED care (Figure 5):
- Joint priority care (resuscitation or < 15 min) by ED physicians and neurologists is recommended. The ED is an emergency that requires an exhaustive assessment as above, including anamnesis, general (laboratory, ECG, radiological) and specific (CT, vEEG) tests already mentioned in the previous scenario as well as immediate treatment. If no EEG is available 24 hours a day, it should be performed as soon as it is available. If no EEG is available at the center, and there is a high suspicion of SE, a transfer to a center where EEG is available within that time frame or 24 hours a day should be considered.
- In the event that the patient shows neurological focus (deficit symptoms such as language alteration or hemiparesis with homolateral oculocephalic deviation), stroke codes will be assessed and multimodal CT scans will be performed. Up to 20% of stroke codes by ES are pseudo stroke (66). Certain findings in the multimodal CT (67) and in the vEEG would allow a more accurate diagnosis.
- Depending on the findings of the vEEG, adjust treatment:
  a) if ES with tonic-clonic evolution and EEG criteria of SE (CSE) with decreased level of consciousness/coma, administer non-BZD AEDs in bitherapy and evaluate early transfer to intensive care unit (ICU);
  b) if focal seizures and persistence of subclinical or subtle seizures with alteration of the level of consciousness and EEG criteria of SE (NCSE); or c) if recurrent focal seizures refractory to treatment without alteration of the level of consciousness, administer non-BZD AEDs and maintain monitoring with vEEG until response. In cases b and c, priority will be given to bitherapy with non-BZD AEDs and transfer to ICU will be assessed if hemodynamic instability or respiratory compromise appears, maintaining monitoring with vEEG. Otherwise, and preferably after an initial improvement, hospitalization in neurology.

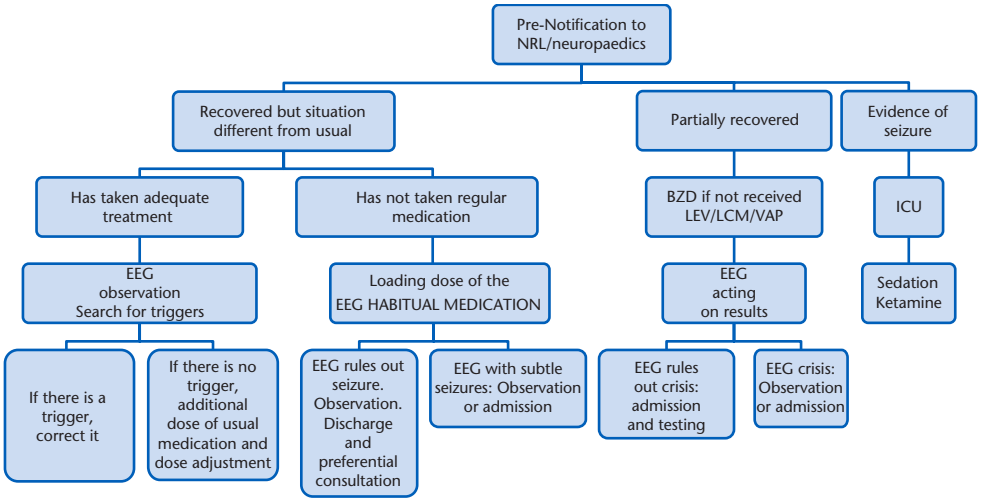

Figure 5. Hospital management. NRL: neurology; EEG: electroencephalogram; BZD: benzodiazepines; LEV: levetiracetam; LCM: lacosamide; VAP: valproic; ICU: intensive care unit.

3. Patient with unknown epilepsy

In these cases we will proceed as previously referred and the patient should always be transferred to the hospital, not only to ensure adequate control of the seizures, but also to rule out acute pathology and perform diagnostic studies, which may require hospitalization.

4. Towards the seizure code

Based on all of the above, a change in ES patient care is hereby proposed, which begins by referring to the "seizure code" instead of the "status code". This shows the intention of optimizing time to avoid arriving at the SE, acting early in the face of potentially serious attacks. The new concept of urgent ES, which is the inclusion criterion for the crisis code (Table 5), includes situations that are potentially serious and can lead to an SE. According to the new definitions of ES, it is necessary to act efficiently and early in the first 30-60 mins in order to avoid irreversible changes.

In the implementation of the seizure code, in addition to redefining concepts, diagnostic techniques such as vEEG have been included in the early assessment and treatment lines have been agreed upon. The intention is to unify criteria, emphasizing the need for greater pre-hospital (family/caretakers and OHES) and hospital (ED, neurology, others) coordination.

As a last consideration, this document opens the door to an interdisciplinary work and future collaborations that make possible "the seizure code" in our healthcare field[68], improving the prognosis of patients with urgent ES[69].

Table 5. Seizure code

Inclusion criteria
– Focal or generalized SE. – Likely NCSE (low level of consciousness or confusion without cause). – Cumulative ES. – "Pseudoictus" (neurological deficit symptoms discarded ictus code, ADAN > 1). – High-risk seizures (Figure 1).
Exclusion criteria
– Terminal illness with expectation of less than 6 months. – Previous situation of high dependence (mRankin = 4-5 or Barthel Index < 60).
Procedure
– Transfer with prior notice to neurology/neuropediatrics to center with neurologist on call and availability of emergency vEEG monitoring. – Extra and intrahospital urgent care according to flow charts. – Prioritize access to diagnostic tests (multimodal CT) and results by central services involved in the diagnosis..

SE: status epilepticus; NCSE: non-convulsive status epilepticus (focal with coincidence alteration); ES: epileptic seizure; CT: computed tomography.

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