Management of nonconvulsive status epilepticus

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Background
Nonconvulsive status epilepticus (NCSE) represents an important challenge to modern neurology and epileptology. It occurs in 8–37% of the general ICU population. The diagnosis and treatment of NCSE are not straightforward and depend on many variables, including the clinical setting, etiology, electroencephalographic (EEG) findings, and the clinical status of the patients. It has a wide range of differential diagnosis including posthypoxic and metabolic encephalopathies. The current treatment options are still unsatisfactory, and mortality and morbidity rates remain high.

Objective
The aim of this study was to determine which cases of convulsive status epilepticus (CSE) are more prone to proceed to NCSE.

Patients and methods
A case series clinical study was undertaken in the Inpatient Pediatric Neurology and Emergency Units, Assiut University Hospital, Assiut City, Egypt. The study included 114 patients between the ages of 1 month and 18 years who had CSE (seizures lasting >5 min). Patients were grouped using EEG results into those with and without NCSE, and retrospectively, the clinical risk factors were studied.

Results
Our study revealed that the incidence of NCSE after control of CSE is 18.4%. The most common age group affected was from 6 to 10 years (52.4%). Mixed type of convulsions (47.6%), convulsions lasting more than 10 min (52.4%), and prolonged postictal period more than 30 min (80.9%) were common among patients with NCSE. Tachycardia (57.1%), dilated pupils (81%), and impaired level of consciousness were commonly found in NCSE group. Brain atrophic changes (28.6%), hydrocephalus (4.8%), cerebral edema (9.7%), and intracranial hemorrhage (5.4%) were detected in computed tomography brain of patients with NCSE. On the contrary, normal computed tomography brain result was found in 28.6% of patients. Midazolam was used to stop convulsions in 47.6% of patients with NCSE, each of phenobarbital and phenytoin was used in 9.5%, and a combination of anticonvulsants were used in 28.57% of patients with NCSE.

Conclusion
We found that in patients with suspected NCSE in whom an EEG is requested, several clinical risk factors–seizures in the acute setting, age more than 6 years, mixed seizures, prolonged seizures (>5 min), persistent tachycardia after control of convulsions, impaired consciousness, dilated pupils, the use of benzodiazepines for control of convulsion and ongoing central nervous system infection –influence the risk of NCSE. The risk of NCSE rises as the number of risk factors increases. By focusing on these risk factors at the bedside, the clinician can prioritize patients for EEG.

Keywords:
status epilepticus, nonconvulsive, seizures

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Introduction

Nonconvulsive status epilepticus (NCSE) is defined as a persistent change in behavior and/or mental processes from baseline associated with continuous epileptiform electroencephalographic (EEG) changes but without major motor signs [1–3]. Patients with baseline coma or encephalopathy typically include patients with more than 30 min of ictal EEG activity in any given hour of recording (i.e. >50% of the record) [4]. It represents an important challenge to modern neurology and epileptology. There is a difficulty in clearly delineating the condition, its various clinical forms, and the relevant underlying pathophysiological processes. Consequently, current treatment options are still unsatisfactory, and mortality and morbidity rates remain high [2]. Unfortunately, overdiagnosing NCSE is difficult to avoid if the diagnosis is based only on EEG changes [5]. It is therefore important for the neurologist consulting a patient in the ICU to consider

a wide range of differential diagnoses including posthypoxic states, septic and various metabolic encephalopathies [6]. The diagnosis and treatment of NCSE are not straightforward and depend on many variables, including the clinical setting, etiology, EEG findings, and the clinical status of the patient [7]. Nonconvulsive SE is still underdiagnosed in critically ill patients presenting with disturbed conscious level. It occurs in 8–37% of the general ICU population [1]. It has been reported that NCSE persisted in 14% of patients after generalized CSE was controlled [8].

Aim

The aim of this study was to determine which cases of convulsive status epilepticus (CSE) are more prone to proceed to NCSE.

Patients and methods

A case series clinical study was undertaken in the Inpatient Pediatric Neurology and Emergency Units, Assiut University Hospital, Assiut City, Egypt. The study included 114 patients (68 boys and 46 girls) between the ages of 1 month and 18 years who had CSE (seizures lasting >5 min). Patients with unstable medical conditions requiring acute intervention were excluded from the study. All cases included in the study were subjected to the following: history, which included name, age, sex, and residence of studied patients; type of convulsion; duration of convulsion; and duration of postictal period; clinical examination was done for all cases, which included heart rate (HR) after control of convulsion, pupils, Glasgow coma scale (GCS), muscle tone, tendon reflexes, and Babiniski reflex; investigations included lumbar puncture and computed tomography (CT) brain done for selected patients and EEG done for all patients. Ethics committee approval no 17100042.

Statistical analysis

Data were collected and analyzed by computer program IBM SPSS (version 24.0) (SPSS Inc., Chicago, Illinois, USA). Data were expressed as number, percentage, mean, and SD. Mann–Whitney test was used to determine the significance for numeric variable. χ^2 was used to determine the significance for nonparametric variable. Pearson correlation was used for numeric variable in the same group.

Results

The study was conducted on 114 patients who had CSE at Pediatric Neurology and Emergency Units of Assiut University Children Hospital. The patients were grouped according to age into four groups: less than 1 year, from 1 to 6 years, from 6 to 10 years, and more than 10 years. It was observed that the most common group to proceed to NCSE is 6–10 years (52.4%) as compared with non-NCSE, which is more common in smaller age groups, that is, 1–5 years (43%) and in patients aged less than 1 year (41.9%). Nonconvulsive SE was found to be more common in females (61.9%) than in males (38.1%), but non-NCSE group had more males (64.5%) than females (35.5%). Most NCSE cases were from rural areas (85.7%).

The commonest type of convulsions to be followed by NCSE is the mixed type (generalized and focal), which represents 47.6%, next in order is the generalized convulsions (42.9%), and the least to be followed by NCSE is the focal one (9.5%). Patients with prolonged convulsions (>10 min) are more prone to NCSE (52.4%). Most patients with NCSE (80.9%) had a prolonged postictal period (>30 min). Examination of patients was done after termination of convulsion. Patients with NCSE were found to have tachycardia (57.1%) and less common normal HR (42.9%). It was found that 71.4% of patients with NCSE had slight impairment of consciousness (GCS 13–15), 19% had GCS 9–12, and 9.5% had GCS 3–8. Most (81%) patients with NCSE had dilated pupils.

Normal CT result was found in 28.6% of NCSE cases and in 32.3% of non-NCSE cases. Overall, 28.6% of NCSE and 12.9% of non-cases had brain atrophy; 4.8% of NCSE and 3.2% of non-NCSE cases had hydrocephalic changes; 4.8% of NCSE and 9.7% of Non-NCSE cases had brain edema; and none of NCSE cases and 5.4% of non-NCSE cases had intracranial hemorrhage. Midazolam was used in 10 (47.6%) patients with NCSE, each of phenobarbital and phenytoin used in two (9.5%) patients each, and a combination of anticonvulsants were used in

Table 1 Type of convulsions according to different age groups (*n*=114)

Age (years)	Focal convulsions [*n* (%)]	Generalized convulsions [*n* (%)]	Mixed convulsions [*n* (%)]	Total
<1	10 (24.39)	18 (43.9)	13 (31.7)	41
1-5	4 (8.88)	34 (75.55)	7 (15.55)	45
6-10	2 (9)	10 (45.45)	10 (45.45)	22
>10	1 (16.66)	2 (33.33)	3 (50)	6
Total	17 (14.9)	64 (56.14)	33 (28.94)	114

six (28.57%) patients with NCSE. Overall, 18.4% of studied patients had NCSE in EEG.

It was observed that the most common type of convulsions in patients less than one year is the generalized one (43.9%), followed by the mixed type (31.7%) and the least is the focal type (24.39%). In the second age group (1–5 years), the generalized convulsion also is the most common type (75.55%), followed by the mixed type (15.55%) and the least is the focal one (8.88%). Regarding the third age group (6–10 years), both the generalized and mixed types occurred in equal proportions (45.45%). In the last age group (>10 years), the generalized type also is the commonest type (56.14%), followed by the mixed one (28.94%), and the least is the focal one (14.9%) (Table 1).

Discussion

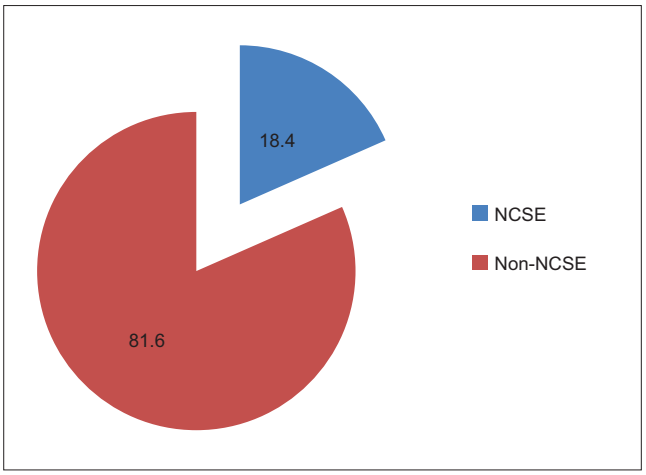
In the present study, once CSE was controlled, EEG was done for all cases. Patients were grouped using EEG results into those with and without NCSE, and retrospectively, the clinical risk factors were studied. A total of 114 patients had convulsive seizures in our study, and all occurred either just before or during the hospitalization.

Our study showed that the incidence of NCSE after CSE was terminated (Fig. 1) was 18.4%. The incidence reported in a previous study was 16%; this means that seizures in the acute setting are a strong independent risk factor of NCSE [9].

The true frequency of NCSE is often underestimated for a number of reasons: first, some cases of CSE evolve into NCSE and may not be classified as such; second, in many clinical situations, NCSE requires EEG for diagnostic confirmation, and if EEG is not available, case ascertainment will be incomplete; and third, physicians who are suspecting NCSE and who are aware of the existing studies on NCSE may opt to treat the suspected patients with NCSE before the EEG is obtained if risk factors are present, and this may abort the NCSE before the EEG is performed, causing an underestimate of NCSE incidence [10].

The ability to obtain EEG after CSE is controlled requires a significant investment in equipment, personnel, and physician resources. There is a need to triage patients based on bedside clinical features at the point of EEG request into those with high or low risk of NCSE in order to prioritize such requests [11]. Inappropriate EEG for low-risk patients leads to wastage of time and resources and delays EEG for high-risk patients. Unfortunately, the sensitivity and specificity of bedside clinical features is unsatisfactory owing to the protean manifestations of NCSE. We

Figure 1



Electroencephalography findings in the studied patients.

Table 2 Electroencephalography according to personal data (*n*=114)

Personal data	EEG [*n* (%)]		*P*
	NCSE (*n*=21)	Non-NCSE (*n*=93)	
Age (years)			
<1	2 (9.5)	39 (41.9)	0.000*
1-5	5 (23.8)	40 (43.0)	
6-10	11 (52.4)	11 (11.8)	
>10	3 (14.3)	3 (3.2)	
Sex			
Male	8 (38.1)	60 (64.5)	0.047*
Female	13 (61.9)	33 (35.5)	
Residence			
Rural	18 (85.7)	83 (89.2)	0.936
Urban	3 (14.3)	10 (10.8)	

EEG, electroencephalography; NCSE, nonconvulsive status epilepticus. *= significant *P* value.

Table 3 Electroencephalography according to pattern of convulsions (*n*=114)

Pattern of convulsion	EEG [*n* (%)]		*P*
	NCSE (*n*=21)	Non-NCSE (*n*=93)	
Type of convulsion			
Generalized	9 (42.9)	55 (59.1)	0.110
Focal	2 (9.5)	15 (16.1)	
Mixed	10 (47.6	23 (24.7	
Duration of convulsion (min)			
1-5	2 (9.5)	43 (46.2)	0.008*
6-10	8 (38.1)	22 (23.7)	
>10	11 (52.4)	28 (30.1)	
Postictal			
No postictal period	1 (4.8)	0 (0.0)	0.002*
<30 min	3 (14.3)	47 (50.5)	
≥30 min	17 (80.9)	46 (49.5)	

EEG, electroencephalography; NCSE, nonconvulsive status epilepticus. *= significant P value.

therefore studied EEG to identify bedside clinical risk factors for NCSE to use as predictive risk factors [12].

In the present study (Table 2), 14 (66.7%) patients of NCSE group were above 6 years, which was significantly higher than those of non-NCSE group (P = 0.00). Previous studies found that NCSE is more common in children above 10 years [9]. The percent of convulsions lasting more than 5 min (Table 3) in NCSE cases was 90.5%, which was significantly higher than that of non-NCSE group (53.8%) (P = 0.008).

The percentage of patients with NCSE with a postictal period more than 30 min (Table 3) was 80.9%, which was significantly higher than that of non-NCSE group (59.5%) (P = 0.002), and this is similar to previous studies that suggested a prolonged postictal period of more than 30 min as a risk factor for NCSE [12].

The percentage of patients with NCSE presenting with impaired consciousness (GCS <13) (Table 4) was 28.5%, which is higher than that of non-NCSE group (21.4%), confirming the results of a previous study that suggested 'impaired consciousness' as a sign of NCSE. Previous studies showed that ongoing central nervous system (CNS) infection is a risk factor for NCSE [13], and this is similar to our study, which showed that the percent of CNS infection in patients with NCSE (Table 5) is 42.86% and it was higher than non-NCSE cases (22.85%). Studies showed that brain hypoxia is a strong risk factor for NCSE, and this is consistent with our study, which found brain hypoxia in 61.86% [14].

The percent of patients with NCSE whose convulsions were stopped by midazolam (Table 6) was 47.6%, which was higher than non-NCSE cases (22.58%), and this is consistent with a previous study that suggested that benzodiazepines can cause NCSE.

Our study identified novel risk factors that have not been identified in the past, such as sex, dilated pupils, and persistent tachycardia after control of convulsions. In the present study (Table 2), 13 (61.9%) patients with NCSE were females, which was significantly higher than that of non-NCSE cases (P = 0.026).

The diagnosis of NCSE ideally must consist of a combination of clinical and EEG features, and thus, the following criteria are suggested for the diagnosis: first, clear and persistent clinical change in behavior (manifested as changes in cognition, memory, arousal, and behavior). The word 'clear' would imply that an adequate description of behavior before the onset of NCSE is available for comparison. 'Persistent' is another arbitrary term which means the episode must last at least 30 min. Second, the presence of EEG changes. Third, the absence of clinical seizures [15].

Table 4 Electroencephalography according to general examination (*n*=114)

General examination (after convulsions)	EEG [*n* (%)]		*P*
	NCSE (*n*=21)	Non-NCSE (*n*=93)	
Heart rate			
Normal	9 (42.9)	48 (51.6)	0.566
Tachycardia	12 (57.1)	43 (46.2)	
Bradycardia	0 (0.0)	2 (2.2)	
GCS			
3-8	2 (9.5)	8 (8.6)	0.560
9-12	4 (19.0)	10 (10.8)	
13-15	15 (71.4)	75 (80.6)	
Pupils			
Dilated	17 (81.0)	45 (48.4)	0.007*
Constricted	4 (19.0)	48 (51.6)	

EEG, electroencephalography; GCS, Glasgow coma scale; NCSE, nonconvulsive status epilepticus.

Table 5 Electroencephalography according to computed tomography findings (*n*=114)

CT findings	EEG [*n* (%)]		*P*
	NCSE (*n*=21)	Non-NCSE (*n*=93)	
Not done	7 (33.3)	34 (36.6)	0.781
Normal	6 (28.6)	30 (32.3)	0.743
Atrophy	6 (28.6)	12 (12.9)	0.097
Hemorrhage	0 (0.0)	5 (5.4)	0.582
Hydrocephalus	1 (4.8)	3 (3.2)	0.562
Edema	1 (4.8)	9 (9.7)	0.686

CT, computed tomography; EEG, electroencephalography; NCSE, nonconvulsive status epilepticus.

Table 6 Electroencephalography according to anticonvulsant used of convulsions (*n*=114)

Anticonvulsant used	EEG [*n* (%)]		*P*
	NCSE (*n*=21)	Non-NCSE (*n*=93)	
Combination	6 (28.57)	25 (26.88)	0.148
Midazolam	10 (47.6)	21 (22.58)	
Not given	1 (4.76)	10 (10.75)	
Phenobarbital	2 (9.5)	14 (15.05)	
Phenytoin	2 (9.5)	23 (24.73)	

EEG, electroencephalography; NCSE, nonconvulsive status epilepticus.

Conclusion

We found that in patients with suspected NCSE in whom an EEG is requested, several clinical risk factors – seizures in the acute setting, age more than 6 years, mixed seizures, prolonged seizures (>5 min), persistent tachycardia after control of convulsions, impaired consciousness, dilated pupils, use of benzodiazepines for control of convulsion and ongoing CNS infection – influence the risk of NCSE. The risk of NCSE rises as the number of risk factors increases.

By focusing on these risk factors at the bedside, the clinician can prioritize patients for EEG.

Recommendations

(1) Nonconvulsive SE should be suspected in cases of CSE and prolonged post-ictal period (>30 min), especially when associated with one or more of the following risk factors: age more than 6 years, mixed convulsions, convulsions lasting more than 5 min, rapid HR after termination of convulsions, dilated pupils, ongoing CNS infection, and brain atrophy in CT brain.
(2) The diagnosis of NCSE ideally must consist of a combination of clinical and EEVG features.
(3) EEG is a simple and safe method and should be done in every case suspected to have NCSE.
(4) Our study identified novel risk factors that have not been identified in the past (age, mixed convulsions, convulsions lasting >5 min, rapid HR after termination of convulsions, and dilated pupils). We hope that future investigators can explore these risk factors to confirm or refute its association with NCSE.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Shah AM, Vashi A, Jagoda A. Review article: convulsive and non-convulsive status epilepticus: an emergency medicine perspective. Emerg Med Australas 2009;21:352-366.
2 Riggio S. Psychiatric manifestations of non convulsive status epilepticus. Mt Sinai J Med 2006; 73:960–966.
3 Trinka E, Cock H, Hesdorffer D, Rossetti AO, Scheffer IE. A definition and classification of status epilepticus report of the ILAE task force on classification of status epilepticus. Epilepsia 2015; 56:1515–1523.
4 Brophy GM, Bell R, Claassen J. Guidelines for the evaluation and management of status epilepticus. Neurocrit Care 2012;17:5-7.
5 Towne AR, Waterhouse EJ, Boggs JG, Garnett LK, Brown AJ, Smith JR, De Lorenzo RJ. Prevalence of non convulsive status epilepticus in comatosed patients. Neurology 2000; 54:340–345.
6 Drislane FW. Presentation, evaluation, and treatment of non convulsive status epilepticus. Epilepsy Behav 2000; 1:301–314.
7 Holtkamp M, Othman J, Buchheim K, Meierkord H. Predictors and prognosis of refractory status epilepticus treated in a neurological intensive care unit. J Neurol Neurosurg Psychiatry 2005b; 76:534–539.
8 Knake S, Rosenow F, Vescovi M. Incidence of status epilepticus in adults in Germany. A prospective, population-based study. Epilepsia 2001; 42:714–718.
9 Berg AT, Scheffer IE. New concepts in classification of the epilepsies: entering the 21st century. Epilepsia 2011; 52:1058–1062.
10 Kaplan PW. No, some types of non convulsive status epilepticus cause little permanent neurologic sequelae (or: 'the cure may be worse than the disease'). Neurophysiol Clin 2000b; 30:377–382.
11 Benbadis S, Tatum W. Prevalence of non convulsive status in comatosed patients. Neurology 2000; 55:1421–1422.
12 Meierkord H, Holtkamp M. Non-convulsive status epilepticus in adults: clinical forms and treatment. Lancet Neurol 2007; 6:329–339.
13 Husain AM, Horn GJ, Jacobson MP. Non-convulsive status epilepticus: usefulness of clinical features in selecting patients for urgent EEG. J Neurol Neurosurg Psychiatry 2003; 74:189–191.
14 Swisher CB, Shah D, Sinha SR, Husain AM. Base line EEG pattern on continuous ICU EEG monitoring and incidence of seizures. J Clin Neurophysiol 2015; 32:147–151.
15 Brenner RP, Hirsch L, Drislane FW, So E, Kaplan PW, Jordan KG. The ACNS subcommittee on research terminology for continuous EEG monitoring: proposed standardized terminology for rhythmic and periodic EEG patterns encountered in critically ill patients. J Clin Neurophysiol 2005; 22:128–135.