ORIGINAL ARTICLE

Status Epilepticus in Children: Risk Factors and Clinical Evaluation

État de mal épileptique chez l'enfant: Facteurs de risque

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Abstract

Introduction and aim: Status epilepticus (SE) in children is a critical condition that can be life-threatening. The objective of this study was to identify factors associated with the occurrence of SE after a first convulsive seizure in children.
Methods: A retrospective study was conducted at the pediatric department of BEN AROUS regional hospital between January 2015 and December 2019.
Results: A total of 300 patients admitted for a first epileptic seizure were included in this analysis. The mean age of the patients was 33 months. Seizures were generalized in 92.7%, with tonic-clonic seizures being the most common (54.8%). SE was diagnosed as inaugural in 29% of cases. Abnormalities in EEG were observed in 36.5% of cases, while MRI revealed abnormal results in 32.8% of patients. Factors associated with a risk of SE recurrence were age younger than 1 year ($p = 0.003$), neuromotor retardation ($p = 0.001$), EEG abnormalities ($p < 0.001$), MRI abnormalities ($p = 0.001$), and abrupte discontinuation of antiepileptic treatment ($p < 0.001$). Simple febrile seizure was identified as a protective factor ($p = 0.038$).
Conclusion: The study identified that age under 1 year, neuromotor delay, and abnormalities in EEG and MRI are significant risk factors for the recurrence of status epilepticus after a first epileptic seizure in children. These findings suggest targeted preventive strategies to improve the management and prognosis of these patients.

Key words: children, Status epilepticus, risk factors, EEG abnormalities, cerebral MRI abnormalities, antiepileptic treatment.

Résumé

Introduction et objectif: L'état de mal épileptique (EME) chez l'enfant est une situation critique pouvant mettre sa vie en danger. Cette étude avait pour objectif d'identifier les facteurs associés à la survenue d'un EME après une première crise épileptique chez des enfants.
Méthodes: Une étude rétrospective a été menée au sein du service de pédiatrie de l'hôpital régional de BEN AROUS entre janvier 2015 et décembre 2019.
Résultats: Au total, 300 patients admis pour une première crise épileptique ont été inclus dans cette analyse. L'âge moyen des patients était de 33 mois. Les crises étaient généralisées dans 92,7 % et tonico-cloniques dans 54,8 % des cas. L'EME a été diagnostiqué comme étant inaugural chez 29 % des patients. Des anomalies à l'EEG ont été observées chez 36,5 % des cas, tandis que l'IRM a révélé des résultats anormaux chez 32,8 % des patients. Les facteurs associés à un risque de récurrence de l'EME étaient un âge inférieur à 1 an ($p = 0,003$), un retard neuromoteur ($p = 0,001$), des anomalies à l'EEG ($p < 0,001$), des anomalies à l'IRM ($p = 0,001$) et l'arrêt brusque du traitement antiépileptique ($p < 0,001$). La simple crise fébrile était identifiée comme facteur protecteur ($p = 0,038$).
Conclusion: L'étude a identifié que l'âge inférieur à 1 an, le retard psychomoteur, et les anomalies à l'EEG et à l'IRM sont des facteurs de risque significatifs pour la récurrence de l'état de mal épileptique après une première crise épileptique chez les enfants. Ces résultats suggèrent des stratégies préventives ciblées pour améliorer la gestion et le pronostic de ces patients.

Mots clès: État de mal épileptique, enfants, facteurs de risque, EEG, IRM cérébrale, traitement antiépileptique.

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Introduction

Status epilepticus (SE) in children is a life-threatening condition with potential short-term and long-term complications. The definition of SE has evolved over the years [1]. The most recent definition by the International League Against Epilepsy (ILAE) in 2015 describes it as "a condition resulting from either failure of the mechanisms responsible for seizure arrest or failure of their implementation which results in abnormally prolonged seizures" [2]. SE can be inaugural or occur in children with a history of seizures. Therefore, it is important to identify, from the first seizure, the associated factors with the occurrence of SE in order to implement a preventive strategy and improve the patient's short-term and long-term prognosis.

The aim of this study was to identify the associated factors with the occurrence of SE after a first epileptic seizure in children.

Methods

This was a retrospective, descriptive, analytical, and monocentric study conducted in the pediatric department of BEN AROUS regional hospital between January 1st, 2015, and December 31st, 2019. We did not include infants aged < 28 days and children with a history of epileptic seizures. We also excluded children lost to follow-up and those who were followed in other healthcare facilities. A total of 300 patients admitted for a first epileptic seizure were included in this analysis. All patients were followed up for one year after the first seizure. Patients who experienced SE were designated as SE (+), while others were designated as SE (-). Data concerning clinical and paraclinical parameters were extracted from the patients' medical records. Statistical analysis was performed using SPSS®. Chi-square test and Fisher's exact test were used for univariate analysis. Logistic regression was used for multivariate analysis.

Results

A total of 300 patients were included. The mean age was 2 years and 8 months. The majority of patients (64.3%) were between 1 and 5 years old. The sex ratio was 1.1 (159 boys and 141girls). Consanguinity rate was 14%. Family history of febrile seizures or epilepsy was reported in 21% of cases. Prematurity was reported in 4.3% of cases. Both birth asphyxia and neuromotor retardation were reported in 7.7% of cases.

All patients presented with seizures with altered consciousness. The mean time between seizure onset and emergency consultation was 100 minutes. The mean seizure duration was 10 minutes. SE was inaugural in 87 patients (29%). Nine out of ten patients presented with generalized seizures. More than half of the patients presented with tonic-clonic seizures.

Fever was reported in 186 cases (63%). Post-critical neurological examination was normal in 246 cases (82%). The most common neurological examination abnormalities were altered consciousness with a duration of more than 30 minutes (n=39), reflex abnormalities (n=3), and intracranial hypertension syndrome (n=3).

Twenty-six percent (n=78) of patients received anticonvulsant treatment, and the most commonly used treatment regimen was two doses of diazepam (n=50) followed by one dose of phenobarbital (n=28).

Biological tests were performed in 90% of cases (n=270). The mean hemoglobin level was 10.7 g/dl. Anemia was reported in 42% of cases (n=126). One patient had hyponatremia and required specific treatment.

Computed tomography (CT) scan was urgently performed in 15% of cases (n=45). Its main indications were prolonged altered consciousness, focal seizures, and intracranial hypertension. The CT scan was pathological in 9 cases.

Cerebral magnetic resonance imaging (cMRI) was performed in 19.3% of cases (n=58). It was pathological in 19 cases and showed parenchymal abnormalities in 19% of cases (n=11).

Electroencephalogram (EEG) was performed in 38.3% of cases (n=115). Its main indications were complex febrile seizures, inaugural SE, and simple febrile seizures. EEG was pathological in 36.5% of cases (n=42) and showed generalized paroxysmal abnormalities in 21.7% of cases (n=25).

Antiepileptic treatment was initiated in 52.3% of cases (n=157), with sodium valproate being the most commonly used drug (99.4%). The main indications for treatment were inaugural SE (n=43), relapse within 24 hours (n=30), and age under 1 year (n=22).

The identified etiologies of epileptic seizures were febrile seizure (71.6%) (n=215), West syndrome (1.3%) (n=6), tuberous sclerosis (0.3%) (n=1), epilepsy (23.8%) (n=71), and hypoxic-ischemic encephalopathy (3%) (n=9).

Seizure recurrence occurred within 24 hours in 14.6% of cases (n=44) and within a year in 31.3% of cases. The average time to recurrence was 5 months and 21 days. Almost half (57%) of the recurrences were in the form of SE (18% of all first epileptic seizures). Almost half of the patients (54.2%) who experienced recurrence were not on antiepileptic medication.

The factors associated with the risk of SE recurrence were: age < 1 year (p = 0.003), neuromotor retardation (p = 0.001), EEG abnormality (p < 0.001), MRI abnormality (p = 0.001), and abrupt discontinuation of antiepileptic treatment (p < 0.001) [Table 1 and 2].

Table 2. Paraclinical markers of the occurrence of status epilepticus after the first epileptic seizure in children.

Factor	SE (-) Group (N=246)		SE (+) Group (N=54)		OR	$IC_{95\%}$	P
	N	%	N	%			
Anemia	101	41	25	50	1,03	[0,92-1,15]	0,535
EEG abnormality	21	28	21	52,5	**1,48**	**[1,06-2,06]**	**0,009**
MRI abnormality	4	13,3	15	53,6	**3,2**	**[1,3-7,8]**	**0,001**

Table 1. Clinical risk factors for the occurrence of status epilepticus (SE) after the first epileptic seizure in children (Univariate analysis)

Factor		SE (-) group (N=246)		SE (+) group (N=54)		OR	$IC_{95\%}$	P
N		%		N	%			
Sex	Female	120	48,8	21	38,9	1,07	[0,96-1,19]	0,187
	Male	126	51,2	33	61,1			
Age	< 1 year	42	17,1	21	38,9	**1,29**	**[1,07-1,54]**	**<0,001**
	1 an – 5 years	167	67,9	26	48,1	**0,85**	**[0,75-0,97]**	**0,006**
	> 5 years	37	15	7	13	0,97	[0,84-1,12]	0,69
Prematurity		9	3,7	4	7,4	1,19	[0,83-1,72]	0,26
Perinatal suffering		10	4,1	13	24,1	**1,96**	**[1,2-3,1]**	**<0,001**
Neuromotor retardation		4	1,6	19	35,2	**5**	**[2,1-12,2]**	**<0,001**
Semiology	Generalized	233	94,7	45	83,3	**1,4**	**[1,01-2]**	**0,008**
	Focal	13	5,3	9	16,7			
	Tonic	70	28,6	13	24,1	0,96	[0,86-1,07]	0,51
	Tonic-clonic	136	55,5	29	53,7	0,98	[0,88-1,1]	0,83
	Atonic	32	13,1	4	7,4	0,91	[0,8-1,03]	0,25
	Myoclonic	2	0,8	6	11,1	**3,3**	**[1,05-11,1]**	**0,001**
Duration	< 30 min	212	86,2	40	74	1,2	[0,98-1,4]	**0,036**
	≥ 30 min	34	13,8	14	26			
Inaugural SE		60	24,4	27	50	**1,3**	**[1,1-1,5]**	**<0,001**
Glasgow coma scale	≤14	29	11,8	13	24,1	1,22	[0,98-1,5]	**0,018**
	15	217	88,2	41	75,9			
Neurological examination abnormality		33	11,8	20	37	**1,38**	**[1,11-1,7]**	**<0,001**
Relapse within 24h		27	10,9	17	31,5	**1,4**	**[1,1-1,8]**	**<0,001**
Simple febrile seizure		126	51,2	5	9,2	**0,7**	**[0,67-0,82]**	**<0,001**
Complex febrile seizure		65	26,4	16	29,6	1,03	[0,91-1,16]	0,23
Epilepsy		26	10,6	12	22,2	1,2	[0,95-1,48]	**0,04**
Abrupt treatment discontinuation		6	7,1	17	45,9	**3,2**	**[1,6-6,5]**	**<0,001**

Discussion

The study included 300 patients, primarily aged 1 to 5 years. All presented with seizures with altered consciousness, with an average duration of 10 minutes and an average consultation time of 100 minutes. Status epilepticus was initial in 29% of cases. Fever was present in 63% of patients, and post-critical neurological examination was normal in 82% of cases. Radiological abnormalities were observed in 20% of CT scans and 33% of MRIs. Antiepileptic treatment was administered to 52% of patients, primarily sodium valproate. The main etiologies were febrile seizures (71.6%) and epilepsy (23.8%). Seizure recurrence occurred in 14.6% of cases within 24 hours and in 31.3% within one year. Identified risk factors for recurrence included age under 1 year, neuromotor delay, and abnormalities in EEG and MRI.

Our study of 300 patients examines the first epileptic seizures in children in Tunisia, with good national representativity. It identifies predictive factors for the recurrence of status epilepticus, allowing us to propose preventive strategies. The limitations include the retrospective and single-center nature of the study, leading to information and selection biases, and limited generalizability of the conclusions. The changing definitions of status epilepticus also caused some confusion.

In this study, age less than 1 year was identified as a predictive factor for status epilepticus (SE) recurrence (OR=4.5; CI [1.7-12.2]; p=0.003). This is explained in the literature by the higher risk of recurrence in an immature brain with a low epileptogenic threshold [3,4]. Similarly, neuromotor retardation was found to be a predictive factor for SE recurrence (OR=16.7; CI [3.2-88]; p=0.001). Neuromotor retardation was also associated with poor epilepsy control and more severe seizures, including SE [5,6].

The tonic-clonic type was the most frequent in our study, observed in 54.8% of cases, which is comparable to literature data, with rates up to 86% [7]. In the univariate analysis of our study, the myoclonic type was associated with a risk of SE recurrence, although this association was not found in the multivariate analysis. This is explained by the diverse underlying etiologies in patients with myoclonic seizures, including anoxic-ischemic encephalopathy, Dravet syndrome, agenesis of the left internal carotid artery, propionic aciduria, and undetermined cases [8].

Cerebral MRI (cMRI) was the most commonly performed radiological examination in our study, remaining the neuroradiological examination of choice for investigating a first seizure. Morphological abnormalities of the central nervous system on cMRI were significantly associated with SE recurrence in both univariate and multivariate analysis (OR=18.1; CI [3.5-94.4]; p=0.001), consistent with other studies emphasizing the value of brain imaging in suspicious cases [9].

Electrophysiological abnormalities, detected through EEG, showed a statistically significant association with SE recurrence risk (OR=4.75; CI [1.22-18.45]; p<0.001),

consistent with the literature, highlighting the importance of EEG in investigating a first epileptic seizure [10].
Additionally, simple febrile seizures accounted for 61.8% of febrile seizures, and they were identified in this study as a protective factor against SE recurrence compared to other types of seizures (OR=0.27; CI [0.07-0.9]; p=0.038). This can be attributed to their benign nature in the absence of other associated factors [11].
Regarding treatment discontinuation, a Cochrane review in 2020 analyzed the risk of seizure recurrence based on the method used. Although no statistically significant difference was found, abrupt discontinuation of treatment was significantly associated with SE recurrence risk in our study (OR=57.9; CI [14.7-227.4]; p<0.001), corroborating the findings of a previous study [12,13].

Conclusions

In children after a first epileptic seizure, age less than 1 year, neuromotor retardation, abnormalities in EEG and cerebral MRI, as well as abrupt discontinuation of anti-epileptic treatment, are significant risk factors for the evolution to status epilepticus. Considering these risk factors during evaluation and follow-up of children after their first seizure is essential to identify high-risk patients for SE. A preventive and tailored management approach, along with attentive medical monitoring, will improve short and long-term outcomes for these vulnerable patients. Future studies could further explore these findings and investigate other potential risk factors to optimize the management of status epilepticus in children.

Abrevations list:
CT : Computed tomography .
cMRI : Cerebral magnetic resonance imaging.
EEG : Electroencephalogram.
ILAE : International League Against Epilepsy.
SE : Status epilepticus.

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