First Attack of Status Epilepticus in Adults: Etiology and Risk Factors

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Abstract

Background: Status Epilepticus (SE) is a common life-threatening neurological emergency the etiology of SE varies according to age and prior history of seizures. In people known to be epileptic poor compliance and drug withdrawal are the commonest causes of SE. On the other hand in patients with no prior seizure history strokes, head traumas, CNS infections, cardiac arrests and metabolic disturbances are the most common causes.

Aim of Study: Is to study the possible etiologies and outcome of first attack of SE in adults.

Patients and Methods: This was a 6-month duration cross sectional study done at Neuropsychiatry Department, Tanta University Hospital, started from July 2016. All patients presented by first attack of SE over the age of 18 years and didn't have previous history of SE, were considered.

Results: Of 42 patients included in the study 35 (83.3%) had non refractory SE while 7 (16.7%) had RSE. 37 patients survived (88.1%) and 5 patients died (11.9%). Analysis of statistically significant and most clinically important variables showed that these factors were significantly higher in RSE, cryptogenic etiology ($p=0.024$), EEG changes ($p=0.015$). number of AEDs ($p=0.001$), duration of hospitalization ($p=0.037$), complications due to hospitalization ($p=0.015$), EMSE scores ($p=0.001$).

Conclusion: Most patients presented by SE over the age of 18 has no prior history of epilepsy. CVAs are the leading cause of de novo SE in adults followed by metabolic derangements. Refractory Status Epilepticus (RSE) is associated with prolonged duration of hospitalization and higher rates of complications compared to non-refractory SE. Complications due to seizures were the most common followed by side effects of AEDs while complications of prolonged hospitalization were the least common. EEG monitoring is an important tool both in managing and predicting the outcome of status epilepticus. STESS and EMSE scoring systems are easy to use bed side tools to help in predicting the outcome of SE.

Key Words: Status – Epilepticus – Risk factors – Etiology.

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Introduction

STATUS Epilepticus (SE) is a common life-threatening neurological emergency, it is defined as a state of continuous seizure activity for more than 5 minutes or two or more discrete seizures between which there is incomplete recovery of consciousness [1].

The etiology of SE varies according to age and prior history of seizures. In people known to be epileptic poor compliance and drug withdrawal are the commonest causes of SE. On the other hand in patients with no prior seizure history strokes, head traumas, Central Nervous System (CNS) infections, cardiac arrests and metabolic disturbances are the most common causes [2].

Seizures lasting approximately 30 to 45 minutes can cause cerebral injury especially in limbic structures such as the hippocampus, this damage is mainly a consequence of glutamate mediated excitotoxicity and doesn't appear to be due to excessive metabolic demand imposed by repetitive neuronal firing [3].

The fundamental pathophysiology of SE involves a failure of mechanisms that normally abort an isolated seizure. This failure can arise from abnormally persistent excessive excitation or ineffective recruitment of inhibition [4].

Status epilepticus is associated with high rates of mortality and morbidity that is why rapid initiation of treatment is required to control such fatal condition and ensure a better outcome for the patients. Complications of SE are either due to seizures itself, complications of Antiepileptic Drugs (AEDs) and complications of hospitalization, that's why determining the risk factors associated with refractoriness to treatment, morbidity and mortality is essential to properly manage patients with SE and improve their outcome [5].

Patients and Methods

This study was conducted in the Neuropsychiatric Department of Tanta University Hospital on 42 patients with first attack of Status Epilepticus (SE) in the period between July 2016 and January 2017. They were classified into non refractory group (35 patients) and refractory group (7 patients).

Each patient was subjected to full history taking, thorough general and neurological examination brain CT and/or MRI. Routine laboratory investigations including complete blood count, liver functions, renal functions, arterial blood gases and serum electrolytes. Specific laboratory investigations in certain cases e.g: Cerebro spinal fluid analysis. Electroencephalogram (EEG) monitoring in the first 24hrs after hospitalization. Status Epilepticus Severity Score (STESS) and Epidemiology based Mortality Score in Status Epilepticus (EMSE) were calculated for each patient.

Results

There was that no statistically significant difference between both groups as regard gender and age distribution (Table 1).

Table (1): Demographic data of both groups.

Characteristics	Group A (n=35) Non-refractory	Group B (n=7) Refractory	Sig. test	p
Age (in years):				
Mean ± S.D	47.8±10.4	39.5±16.4	t	0.325
Range	20-85	18-74	1.050	
Gender:				
Male	18 (51.4%)	2 (28.6%)	χ^2	0.269
Female	17 (48.6%)	5 (71.4%)	1.222	

Acute symptomatic causes were the most common in both groups, remote symptomatic causes were more common in the non-refractory group while cryptogenic causes were more common in the refractory group. Cerebrovascular causes were the most common overall while metabolic causes were more common in the non-refractory group and unknown etiologies were more common in the refractory group with a statistically significant difference (Table 2).

The mean values of random blood glucose, blood pressure and body temperature on admission were higher in the refractory group but without any statistical significance (Table 3).

EEG abnormalities were significantly more encountered in patients with refractory status epilepticus, Lateralized Periodic Discharges (LPDs) were the most common EEG change in our study (Table 4).

Table (2): Possible etiologies among studied patients.

Etiology	Group A (n=35) Non-refractory		Group B (n=7) Refractory		χ^2	p
Acute symptomatic (n=30):						
Cerebrovascular	14	40.0%	3	42.9%	9.716	0.024*
Metabolic	9	25.7%	0	0.0%		
Drug overdose	1	2.9%	0	0.0%		
CNS infections	2	5.7%	1	14.3 %		
Remote symptomatic (n=5):						
Cerebrovascular	2	5.7%	0	0.0%		
Head trauma	1	2.9%	0	0.0%		
Non-compliant	2	5.7%	0	0.0%		
Progressive symptomatic (n=3):						
Tumors	2	5.7%	1	14.3 %		
Unknown (n=4):						
Cryptogenic	2	5.7%	2	28.6%		

Table (3): Clinical characteristics of the studied groups.

Characteristics	Group A (n=35) Non-refractory		Group B (n=7) Refractory		Sig. test	p
Blood pressure:						
Normotensive	19	54.3%	19	154.3%	χ^2	0.756
Hypotensive	6	17.1%	6	17.1%	0.559	
Hypertensive	10	28.6%	10	28.6%		
Systolic blood pressure:						
Mean ± S.D	125.1±26.8		125.1±26.8		t –0.947	0.370
Diastolic blood pressure:						
Mean ± S.D	74.2±15.6		74.2±15.6		t –0.432	0.676
Temperature:						
Normal temp.	26	74.3%	26	74.3 %	χ^2	0.738
Hypothermia	2	5.7%	2	5.7%	0.606	
Hyperthermia	7	20.0%	7	20.0%		
Mean ± S.D	37.3±0.6		37.3±0.6		t –1.351	0.210
Random blood glucose:						
Normal	29	82.9%	29	82.9%	χ^2	0.800
Hypoglycemia	2	5.7%	2	5.7%	0.446	
Hyperglycemia	4	11.4%	4	11.4%		
Mean ± S.D	201.3±102.1		201.3±102.1		t –0.234	0.819

Table (4): EEG changes in the studied groups.

EEG changes	Group A (n=35) Non-refractory		Group B (n=7) Refractory		χ^2	p
No changes	12	34.3%	0	0.0%	12.300	0.015*
Burst suppression	1	2.9%	3	42.9%		
GPDs	5	14.3%	1	14.3 %		
LPDs	10	28.6%	2	28.6%		
ASIDs	7	20.0%	1	14.3 %		

GPDs : Generalized Periodic Discharges.
LPDs : Lateralized Periodic Discharges.
ASIDs : After Status Epilepticus Ictal Discharges.

The mean number of AEDs used was significantly higher in the refractory group (Table 5).

Table (5): Number of antiepileptics used among the studied groups.

No. of antiepileptics	Group A (n=35) Non-refractory		Group B (n=7) Refractory		Sig. test	p
No drugs	2	5.7%	0	0.0%	χ^2	0.001*
One drug	6	17.1%	0	0.0%	42.000	
Two drugs	25	71.4%	0	0.0%		
Three drugs	2	5.7%	0	0.0%		
Four drugs	0	0.0%	4	57.1%		
Five drugs	0	0.0%	3	42.9%		
Mean ± S.D	1.8±0.6		4.43±0.5		t −11.572	0.001*

There was statistically significant relationship between the type of SE and the duration of hospitalization as the mean duration was higher in patients with RSE (Table 6).

Table (6): Relationship between possible etiology and outcome.

Hospitalization duration	Group A (n=35) Non-refractory	Group B (n=7) Refractory	Sig. test	p
Mean ± S.D	5.5±4.4	10.7±5.2	t −2.508	0.037*

The complications due to fits were the most common in both groups but significantly higher in Group A while the complications related to hospitalization were more common in Group B but without statistical significance. Also the survival rate was higher in Group A but with no statistical significance (Table 7).

Table (7): Outcome of both studied groups.

Variables	Group A (n=35) Non-refractory		Group B (n=7) Refractory		χ^2	p
Complications:					12.300	0.015*
Related to fits	28	80.0%	4	57.1%		
Related to drugs	14	40.0%	1	14.3%		
Related to hospitalization	4	11.4%	2	28.6%		
Survival:						
Death	3	8.6%	2	28.6%	2.225	0.136
Survival	32	91.4%	5	71.4%		

The mean score of EMSE in Group B was significantly higher than Group A, while there was no statistically significant difference between the 2 groups as regard STESS scores (Table 8).

Table (8): STESS and EMSE scores among both studied groups.

	Group A (n=35) Non-refractory	Group B (n=7) Refractory	t	p
EMSE:				
Mean ± S.D	74.8±26.1	128.0±21.5	−5.756	0.001*
Range	21-125	104-171		
STESS:				
Mean ± S.D	3.2±1.1	3.6±1.0	−0.974	0.355
Range	1-5	3-5		

Discussion

In the present study regarding socio demographic data both groups didn't show any significant difference although the mean age was higher in the group with non refractory status epilepticus (Group A) and that was in accordance to the study done by Power et al., [6].

Regarding etiology acute symptomatic causes were the most common in both groups, remote symptomatic causes were more common in the non-refractory group while cryptogenic causes were more common in the refractory group with a statistical significance (*p*-value 0.024) this can be explained by the study of Khawaja et al., [7] which showed that New Onset Refractory Status Epilepticus (NORSE) is highly associated with cryptogenic etiology.

Regarding clinical data on admission the mean values of random blood glucose, blood pressure and body temperature were higher in the refractory group but without any statistical significance but Hay et al., [8] reported a significant relation between hyperthermia and refractoriness to treatment this may be attributed to the larger number of patients in their study especially those with CNS infections and unknown etiologies because of to the neurotoxic effect of hyperthermia on brain cells which is almost always associated with poorer outcome.

In the present study EEG abnormalities were significantly more encountered in patients with refractory status epilepticus (*p*-value 0.0 15), LPDs were the commonest characteristic finding in EEG of studied patients representing 28.6% of all cases (12 patients) while burst suppression were the least common, we didn't find any significant association between the type of EEG pattern and refractoriness to treatment although Kang et al., [9] reported that periodic epileptic discharges either LPDs or GPDs are associated with RSE and poor outcome.

According to our study both the number of AEDs used and the duration of hospitalization were significantly higher it patients with RSE similar results were reported by Tsai et al., [10] in their study.

Regarding outcome we found that complications due to fits were the most common in both groups but significantly higher in the non refractory group (*p*-value 0.015) while the complications related to hospitalization were more common in the refractory group but without statistical significance. The complications encountered during our study are to somehow similar to those discussed by Hocker et

al., [11] in their review on the systemic complications of SE in which complications due to seizures itself were the most common, also the survival rate was higher in the non refractory group but with no statistical significance.

In our study the mean score of EMSE in the refractory group was significantly higher than the non refractory group (p-value 0.001), while there was no statistically significant difference between the 2 groups as regard STESS scores, there isn't enough studies discussing the relation between STESS and EMSE scores and refractoriness to treatment, but Goyal et al., [12] and Giovannini et al., [13] reported that both EMSE and STESS have an important role in predicting the outcome of SE including morbidity and mortality with EMSE being more sensitive.

Conclusion:

Most patients presented by SE over the age of 18 has no prior history of epilepsy. CVAs are the leading cause of denovo SE in adults followed by metabolic derangements. Refractory Status Epilepticus (RSE) is associated with prolonged duration of hospitalization and higher rates of complications compared to non-refractory SE. Complications due to seizures were the most common followed by side effects of AEDs while complications of prolonged hospitalization were the least common. EEG monitoring is an important tool both in managing and predicting the outcome of status epilepticus. STESS and EMSE scoring systems are easy to use bed side tools to help in predicting the outcome of SE.

Conflicts of interest:

No conflicts of interest declared.

Authors' contributions:

All authors had equal role in design, work, statistical analysis and manuscript writing. All authors have approved the final article work.

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النوبات الصرعية المستمرة للمرة الأولى فى البالغين:
الأسباب وعوامل الخطورة

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تعتبر النوبات الصرعية المستمرة من الحالات الطارئة المرتبطة بالجهاز العصبى والتى قد تمثل خطورة على حياة المريض، ويتم تعريفها بأنها حالة من النوبات الصرعية المستمرة لمدة أكثر من ٥ دقائق أو أكثر من نوبتين صرعيتين متتاليتين دون إستعادة كاملة للوعى فيما بينهم. يتراوح معدل حدوث النوبات الصرعية المستمرة بين ٢٠ و٤٠ حالة لكل ١٠٠٠٠٠ شخص سنويا وتكون النسبة أعلى فى الفئات العمرية الأكبر سنا حيث يمكن أن تصل إلى ٦٠ حالة لكل ١٠٠٠٠٠ شخص سنويا. أظهرت الدراسات أن ٤٠–٦٠٪ من حالات النوبات الصرعية المستمرة ليس لديهم تاريخ مرضى سابق لأى نوبات صرعية ولا تزال عوامل الخطورة المرتبطة بحدوث هذه الحالة فى البالغين لأول مرة غير واضحة بشكل كاف، لذلك فإنه من الضرورى دراسة كافة العوامل التى تؤدى لحدوث مثل هذه الحالة حتى يصبح بالإمكان تلافيها والتعامل مع الآثار المترتبة بشكل أكثر كفاءة.

الهدف من الدراسة: يهدف هذه البحث إلى دراسة الأسباب وعوامل الخطورة المتعلقة بالنوبات الصرعية المستمرة التى تحدث للمرة الأولى فى البالغين.

المرضى وطرق البحث: أجريت هذه الدراسة على ٤٢ من المرضى البالغين الذين يعانون من النوبات الصرعية المستمرة للمرة الأولى والذين تم إستقبالهم وعلاجهم بقسم الأمراض العصبية والنفسية بجامعة طنطا فى الفترة الزمنية من يوليو ٢٠١٦ حتى يناير ٢٠١٧، وقد تم فحص جميع المرضى سريريا وعلاجهم حسب البروتوكول الخاص بالنوبات الصرعية المستمرة وتم عمل كافة الفحوصات الإشعاعية والمعملية ورسم المخ الكهربائى المطول لكافة المرضى للوصول إلى سبب النوبات. كما تم أيضا إستخدام مقياس شدة النوبات الصرعية المستمرة والمقياس الخاص بمعدلات الوفاة فى النوبات الصرعية المستمرة STESS and EMSE وتم تقسيم المرضى إلى مجموعتين المجموعة الأولى ضمت المرضى الذين إستجابوا لخطى العلاج الأول والثانى (النوبات الصرعية المستمرة غير المستعصية) وعددهم ٣٥. المجموعة الثانية ضمت المرضى الذين لم يستجيبوا لخطى العلاج الأول والثانى (النوبات الصرعية المستمرة المستعصية) وعددهم ٧.

الخلاصة: النوبات الصرعية المستمرة من أخطر الحالات الطارئة المرتبطة بالجهاز العصبى ويصاحبها العديد من الإضطرابات الوظيفية وحالات الوفاة. نسبة كبيرة من حالات النوبات الصرعية المستمرة فى البالغين ليس لديهم أى تاريخ مرضى سابقة لنوبات سابقة وتعتبر إضطرابات الأوعية الدموية المخية وإضطرابات الأيض هى أكثر الأسباب شيوعا فى تلك الحالات. رسم المخ الكهربائى المطول من أهم الوسائل التى تساعد فى علاج النوبات الصرعية المستمرة بشكل مثالى والتنبؤ بمآلها. مقاييس شدة النوبات الصرعية المستمرة والمقياس الخاص بخطر الوفاة فى النوبات الصرعية المستمرة STESS و EMSE من الوسائل البسيطة وسهلة الإستخدام للتنبؤ بمآل النوبات الصرعية المستمرة.