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ORIGINAL ARTICLE

Adult status epilepticus at the emergency department: a retrospective chart review of a UAE tertiary care hospital

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ABSTRACT

Background: Status epilepticus (SE) is a serious neurological emergency that is associated with high mortality and morbidity. Significant data describing SE in the Middle East and North Africa regions are lacking. This study is a review of adult SE cases managed at the emergency department (ED) of Al Mafraq Hospital, Abu Dhabi, United Arab Emirates, from January 2011 to April 2016.

Methods: A retrospective chart review of adult patients, who were 18 years of age and older, and who presented to the ED with SE, between January 2011 and April 2016, was conducted. Data were collected from the electronic medical records system after obtaining institutional research ethical approval.

Results: Overall, 38 subjects were identified within the study period of 64 months. Demographic data reflected a male predominance of 74%. Multiple nationalities were involved, with the majority being the local Emiratis (34%). A previous history of epilepsy was present in 68% of the sample. More than three seizure episodes were observed in 66%. Generalized tonic-clonic seizure was seen in 79%. Single-agent anti-epileptic drug (AED) utilization was noted in 18% of the subjects (n = 7 subjects). In 58% of the subjects (n = 22), two agents were utilized to abort SE. 24% of the subjects required multiple agents to abort SE (n = 9). Various benzodiazepines were utilized as first-line agents in 89% of the subjects (n = 34), while the most utilized second-line agent was found to be phenytoin in 61% of the subjects (n = 23). Computed tomography of the head showed abnormal new findings in four out of 33 subjects. Only one subject had an abnormal lumbar puncture result. The control of seizures was possible in 53% of patients by using various benzodiazepines as first-line agents. There was a need for intubation in 58% of patients for airway protection. Therapeutic drug monitoring of relevant AEDs was carried out in 84% of subjects. During the admission for SE, one patient died.

Conclusion: The sample reflected male Emirati predominance. There was consistency in ED management with favorable outcomes. Tools to assess nonadherence in similar samples need to be further developed. We hope that this would stimulate further research in the region and mobilize resources to develop preventive strategies.

Keywords: Status epilepticus, epilepsy, medication adherence, neuroepidemiology.

Introduction

Status epilepticus (SE) is a serious neurological emergency that is associated with high mortality and morbidity [1]. It can have long-term consequences, including neuronal death, injury, and alteration of neuronal networks, depending on the type and duration of seizures [2]. Significant data describing SE in the Middle East and North Africa (MENA) are lacking. New studies within the region would result in better resource allocation in the future [3].

The aim of this study is to describe the multiple variables of the presenting characteristics of SE in the emergency department (ED) of Al Mafraq Hospital, a tertiary care hospital in Abu Dhabi, the capital of the United Arab Emirates. We hope that this will enrich the current pool of reported cases and studies within the MENA regions.

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Methods

Adult patients who were 18 years of age or older and who presented to the ED of Al Mafraq Hospital, Abu Dhabi, United Arab Emirates, with SE between 1 January 2011 and 31 April 2016 were included in the study.

Inclusion criteria were adult patients, 18 years or older with any type of seizure presentation meeting the operational definition of ≥5 minutes of continuous seizures or ≥2 discrete seizures, between which there is an incomplete recovery of consciousness [4]. Exclusion criteria were pediatric cases, subjects misdiagnosed as SE, and single seizures not meeting the SE diagnosis criteria (Figure 1).

We systematically reviewed data collected from the electronic medical records for demographic data, clinical presentation variables, associated symptoms, postictal symptoms, vital signs, glucose measurements, computed tomography (CT) brain, lumbar puncture (LP), the need for intubation, utilized anti-epileptic drugs (AED) for aborting the crisis, AED levels, and all documented chronic AED usage in those cases with prediagnosed epilepsy. Any changes in AED type or dosage in the preceding neurology appointment and therapeutic drug monitoring requested during admission were captured with an aim to assess any possible trigger and adherence issues.

Using Microsoft Excel, variables, frequencies, and percentages were reported and summarized.

Results

Within the total period of the study of 5 years and 4 months, a total of $n = 38$ subjects were identified. Subjects were in the age range from 18 to 85 years. The highest incidence was in the age group from 18 to 38 years. Male subjects constituted the majority in all age groups (n = 28 subjects, 74%) (Table 1). Nationalities data indicated the predominance of Emiratis (n = 13 subjects, 34%), followed by Indians (n = 7, 18%), Yemenis, and Pakistanis (equally contributing n = 5, 13.16%).

The frequency of seizure at presentation showed multiple seizure episodes (three or more, of variable durations) in 66% (n = 25 subjects), single episode of prolonged seizure activity in 32% (n = 12), and two episodes of prolonged seizure activity in 2.63% (n = 1).

The duration of seizures varied from prolonged seizures lasting for more than 5 minutes (n = 15, 39%) to less than 5 minutes (n = 11, 29%). The remaining 12 subjects (32%) had no documented duration.

The International League Against Epilepsy provided a revised operational classification of seizure types in 2017, with basic and expanded versions; this was based on seizure onset types, semiology of seizures, and further descriptors [5]. Based on this, we identified that 79% of the subjects had generalized onset-motor-tonic-clonic seizures (n = 30); 8% had focal onset-impaired awareness-motor onset seizures (n = 3); 8 % had focal onset-impaired awareness-motor onset-focal to bilateral tonic-clonic seizures (n = 3); and 5% had generalized onset-nonmotor (absence)-atypical seizures (n = 2). These are depicted in Table 2.

All patients had a variety of associated symptoms. Subjective fever was reported in 32% (n = 12), apart from the altered mental status reported in 24% (n = 9) of the sample. 13% had a cough (n = 5) and 11% had vomiting and headache (n = 4), respectively. Sleep deprivation

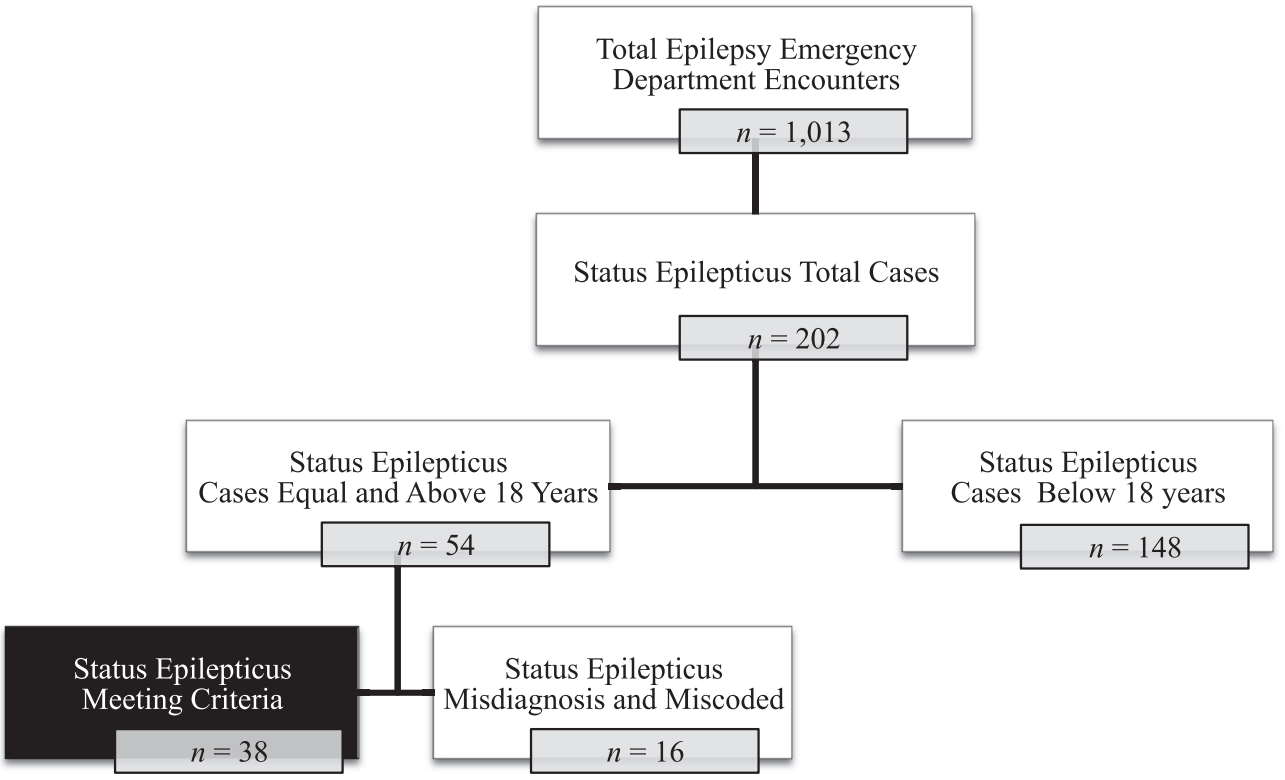

Figure 1. *Inclusion and exclusion process flowchart.*

and shortness of breath had a frequency of 8% (n = 2), respectively. Further symptoms reported each at 3% (n = 1) were tongue bites, back pain, combativeness, diarrhea, and compulsive water drinking.

Subjects with known epilepsy as part of their past medical history with and without other comorbidities constituted 68% of the sample (n = 26).

An ED management review revealed variable use of AED utilization to abort and control SE. Single-agent AED utilization was noted in 18% of the subjects (n = 7 subjects). Phenytoin was administered as a single agent in four subjects who seemed to have self-aborted in the ED (n = 4), while the remaining three subjects required only one benzodiazepine agent to abort SE, mainly diazepam (n = 1) or midazolam (n = 2) was noted.

In 58% of the subjects (n = 22), two agents were utilized to abort SE. Within this category of two agent's utilization, only 5% needed lorazepam and midazolam (n = 2), while the remaining 53% of the cases (n = 20) required a benzodiazepine drug as a first-line agent, followed by loading agents as either phenytoin, fosphenytoin, or levetiracetam.

24% of the subjects required multiple agents to abort SE (n = 9). Similarly, multiple benzodiazepines were used initially, followed by loading agents of phenytoin, fosphenytoin, and or valproic acid. Table 3 provides details of AED utilization and frequencies to abort SE in the ED.

Upon gross review of all AED utilization and frequencies, apart from the four self-aborted cases loaded with phenytoin (n = 4), all of the remaining subjects (n = 34) required benzodiazepines as first-line agents, whether used as a single agent, two agents, or multiple agents, which constituted 89% of the sample.

Lorazepam was noted to be the most utilized first-line agent in the majority of the sample (45%), yet it was never used alone, as it was always followed-up by a second-line agent to abort SE (n = 17). The most used second-line agent was phenytoin in 61% of the subjects (n = 23), yet adding to that the four encounters it was utilized in as a single agent, bring up its absolute count of utilization to 27 subjects, making it the most consistently utilized AED in 71% of all ED encounters. Table 4 provides details of AED absolute counts utilization in all ED encounters.

There was a variety of postictal symptoms. The majority had an altered sensorium (n = 36, 92%). Other reported

Table 1. *Gender and age group distribution.*

Age (years)	Female	Male	(n =)	%
18-28	5	8	13	34%
29-38	1	9	10	26%
39-48	2	4	6	16%
49-58	1	3	4	11%
>58	1	4	5	13%
Total	10	28	38	100%

Table 2. *Seizure types in the ED.*

Quality of Seizure	(n =)	%
Generalized onset - motor - tonic-clonic seizures	30	79%
Focal onset - impaired awareness - motor onset	3	8%
Focal onset - impaired awareness - motor onset - focal to bilateral tonic-clonic	3	8%
Generalized onset - nonmotor (absence) - atypical	2	5%

Table 3. *AED utilization and frequencies used to abort SE in the ED.*

Number of agents used		AED	(n =)
Single agent (18%, n = 7) Midazolam Phenytoin		Diazepam	1
		2	
		4	
Two agents (58%, n = 22)	5% (n = 2)	Lorazepam and midazolam	2
	53% (n = 20)	Lorazepam and phenytoin	7
		Diazepam and phenytoin	4
		Midazolam and phenytoin	5
		Lorazepam and fosphenytoin	1
		Diazepam and fosphenytoin	1
		Midazolam and fosphenytoin	1
		Lorazepam and levetiracetam	1
Multiple agents (24%, n = 9) Lorazepam, diazepam, and phenytoin Diazepam, midazolam, and phenytoin Lorazepam, midazolam, and fosphenytoin Diazepam, phenytoin, and valproic acid		Lorazepam, midazolam, and phenytoin	3
		1	
		2	
		2	
		1	

postictal symptoms were drowsiness (3%, $n = 1$), altered coordination (3%, $n = 1$), and lethargy (3%, $n = 1$). Table 5 provides details of all the clinical parameters as well as the ED interventions and investigations conducted.

At the time of presentation, 16% ($n = 6$) of the patients were febrile with a temperature equal to or higher than 38°C; upon correlation with associated symptoms reported, five of these subjects had reported subjective fever.

Random glucose readings were documented for 95% of the subjects ($n = 36$). Hyperglycemia was noted in 55% ($n = 21$) of patients with a glucose level higher than 7.7 mmol/l. None of the subjects was hypoglycemic; the lowest glucose level was 4.3 mmol/l. Meningeal signs were not reported in any of the cases. ED intubation to protect airway was reported in 58% ($n = 22$) of the patients.

CT of the head was carried out in 87% of the subjects on presentation to the ED ($n = 33$). Previous abnormal chronic changes were reported in 12 subjects, of whom four had newly added acute findings. The CT was reported as normal in 21 subjects (63%).

LP was carried out in 10 subjects (26%). The LP results were seen as normal in nine subjects (24%). One patient died during their current admission of SE ($n = 1$, 3%); the cause of death was aspiration pneumonia with associated sepsis.

Single AED (monotherapy) used for chronic control of seizure was noted in 10 subjects (26%), utilizing levetiracetam, phenytoin, topiramate, and carbamazepine (Table 6). The remaining sample ($n = 13$, 34%) with documented AED control in their medical records were on two or multiple AEDs for seizure control. Fifteen subjects (40%) had no evidence of prior AED use.

Levels of relevant AEDs were observed in 84% ($n = 32$) of patient encounters during admission.

To analyze possible nonadherence or compliance factors in these subjects, we defined it as the number of AED refill appointments attended for the previous 3 consecutive months or more before presentation. Only $n = 9$ subjects (24%) met the suggested definition, out of whom $n = 1$ (3%) had documented missed three to six refill appointments and $n = 6$ (16%) had more than six missed refill appointments in the records. In $n = 4$ subjects (11%), it has been documented as possible caregiver underdosing and noncompliant dose administration. We noted that $n = 5$ subjects (13%) had documented a change in AED type or dosing preceding their ED presentation at their latest neurology appointment.

Discussion

This study examined all the relevant parameters and multiple variables involved at the presentation of adult SE in the ED in Al Mafraq Hospital, Abu Dhabi, United Arab Emirates, for a period of 64 months.

Table 4. *AED absolute count utilization in the all ED encounters.*

AED (n =) %	Single agent use	Part of multiple agents' use	Absolute total agents' use in all ED encounters	
Lorazepam	0	17	17	45%
Diazepam	1	9	10	26%
Midazolam	2	15	17	45%
Phenytoin	4	23	27	71%
Fosphenytoin	0	5	5	13%
Levetiracetam	0	1	1	3%
Valproic acid	0	1	1	3%

Table 5. *ED presentation and management review.*

Clinical parameters and interventions		(n =)	%
Temperature >38°C (n = 38)	Febrile	6	16%
	Afebrile	34	84%
Random glucose measurement (n = 36)	Hyperglycemia > 7.7 mmol/l	36	95%
	Hypoglycemia < 4.3 mmol/l	0	0%
	Undocumented	2	5%
ED intubation	Intubated	22	58%
	Not intubated	16	42%
CT brain with no contrast (n = 33)	Normal CT brain	21	55%
	Previous abnormal chronic changes with newly added acute findings.	4	11%
	Previous abnormal chronic changes with no new findings.	8	21%
	No CT done	5	13%
LP (n = 10)	Normal result	9	24%
	Abnormal result	1	2%
	Not done	28	74%

Table 6. *Long-term epilepsy AEDs medication history.*

AEDs		(*n* =)
Single AED (*n* = 10)	Levetiracetam	4
	Phenytoin	4
	Topiramate	1
	Carbamazepine	1
Two AEDs (*n* = 11)	Levetiracetam and phenytoin	4
	Levetiracetam and topiramate	3
	Levetiracetam and lacosamide	1
	Levetiracetam and CArbamazepine	1
	Valproic acid and lamotrigine	1
	Valproic acid and clonazepam	1
Multiple AEDs (*n* = 2)	Levetiracetam, phenytoin, and baclofen	1
	Levetiracetam, clonazepam, and phenobarbital	1

Internationally, the incidence of SE is 10 to 58 patients per year per 100,000 population; the frequency is estimated to be 50 patients per year per 100,000 population; and the mortality rate is estimated to be 2.7% to 22% [6-9]. Locally, fundamental descriptive data regarding SE in Arab countries is underreported, although it is expected to be higher in prevalence [3,10].

On conducting a literature review for similar adult SE studies within the region, it was noted that most articles focused on epilepsy and pediatric SE [7,9-10]. This study presents the first of its kind, describing an adult SE sample from a country in the Arabian Gulf, MENA region.

The Federal Competitiveness and Statistics Authority posited that UAE's population was 9,304,277 in 2017, out of which approximately more than 80% were expatriates [11]. Our data revealed the predominance of male Emirati subjects despite a strong expatriate community presence in the country.

The younger age groups experienced a greater risk. It is noted that 68% (n = 26) of the sample was identified with previous epilepsy. A majority (60% n = 23) was observed as having documented single or multiple AED usage. This encourages further probing into the possible causes and triggers of SE within these groups, including risks, causes of AED nonadherence, and caregiver's role in AED administration.

Reported analysis of preceding neurology appointments, refill medications, and AED type or dosage adjustments noted in this article may not be a direct indicator of a patient's compliance and adherence to administration of the AED. Similar studies have attempted to investigate nonadherence to AED by analyzing medical records [12-14]. There is a need for development of further tools to assess nonadherence issues to strategize prevention and improve resource allocations.

An ED management review demonstrated a consistent approach across almost all cases, with favorable outcomes in all except n = 1 (3% expired), due to aspiration pneumonia complications with associated sepsis.

The main limitation of this study is its retrospective nature, inappropriate coding, and pre-hospital management inaccessible data, which made it challenging to quantify and assess factors contributing to AED nonadherence. The recognition of such factors is imperative for preventive measures, correct management, and direction of prospective care.

Conclusion

SE is an underreported neurological emergency in Arab countries. Adding to the pool of literature within the region would help further research and resources to develop preventive strategies. On review of the collected cases, our sample reflected the predominance of young male Emiratis. Furthermore, the majority of the subjects had a favorable outcome, with a consistent approach in managing patients till discharge. Adherence is considered a major risk factor for SE, and it should be analyzed further with more developed tools that are consistent with the region of focus, to assess patients' compliance, or caregiver's adherence to AED administration.

List of abbreviations

AED Antiepileptic Drug
CT Computed Tomography
ED Emergency Department
LP Lumbar puncture
MENA Middle East and North Africa
SE Status Epilepticus

Conflict of interest

The authors declare that there were no conflicts of interest encountered in conducting this study.

Funding

None.

Consent for participation

Owing to the study design, the condition of informed consent was waived off.

Ethical approval

Ethical approval was obtained from the Medical Research and Ethics Committee at Al Mafraq Hospital, dated 18th of October 2016, reference letter MAF-REC_05/2016_01.

Data sharing

All data pertaining to this article are contained within or published as an online supplement. With the aim of facilitating full openness and transparency of data, anonymized data will be shared on request from any qualified investigator via a publicly accessible repository.

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