

Management of Status Epilepticus among the Elderly

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Status epilepticus (SE) can occur in individuals of all ages and genders, but they are often found among the elderly. This rising prevalence of epilepsy in older adults is higher. SE need prompt diagnosis and treatment. However, diagnosing this condition in the elderly is often challenging due to incomplete information from the patients' medical histories. The cause of SE in the elderly group was more frequently attributed to remote symptomatic causes that were primarily due to cerebrovascular disease. Accurate and rapid diagnosis of elderly patients with SE requires that physicians have more experience. The factors affecting treatment outcomes of SE in elderly patients are as follows: 1) the length of the hospital stay, 2) the duration of the stay in the intensive care unit, and 3) the occurrence of infections during treatments. In the treatment of SE in the elderly, the selection of the most appropriate anticonvulsants is essential since patients often have comorbidities and are taking multiple medications.

Keywords: Status epilepticus; Elderly; Management

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Status epilepticus (SE) can occur in individuals of all ages and genders, but they are often found among the elderly⁽¹⁾. This rising prevalence of epilepsy in older adults is higher. Therefore, SE need prompt diagnosis and treatment. However, diagnosing this condition in the elderly is often challenging due to incomplete information from the patients' medical histories. This difficulty is particularly found in cases of non-convulsive status epilepticus (NCSE)⁽²⁾, in which older patients may present with atypical symptoms such as confusion, memory loss, and behavioral changes. The outcomes of treating SE in the elderly indicate a high mortality rate, which may be attributed to delayed diagnoses, comorbid conditions, and a greater likelihood of complications⁽³⁾.

The incidences of SE among the elderly, as reported by Somsak Tiamkao et al.⁽¹⁾, indicated a rising trend, as shown in Table 1.

The data indicated a significant annual increase in the incidence of SE, which likely correlated with the rising

prevalence of epilepsy among the elderly. Additionally, there are increased incidences of cerebrovascular disease, which is a common comorbidity in patients with SE. Frequently encountered comorbidities consist of hypertension, diabetes, and cerebrovascular disease, as illustrated in Table 2.

Patients with comorbid conditions were observed to have a higher mortality rate compared to those without. The study highlighted that chronic renal failure and central nervous system infections are significant risk factors for death in individuals with SE. Various epidemiological studies⁽⁴⁻⁶⁾ on SE among older adults have reported incidence rates of 15.5, 21.5, and 24.9 per 100,000 people in the age groups of 60 to 69, 70 to 79, and 80+, respectively. The primary cause of SE in adult patients is often associated with a prior history of epilepsy, particularly in those who have abruptly discontinued anticonvulsant medication, which can lead to the onset of SE. Other contributing factors include cerebrovascular diseases⁽⁷⁾. Approximately 50% of patients, who had experienced SE, had not had any prior history of epilepsy, with their first seizure episode being SE. These patients are at risk of developing refractory status epilepticus (RSE)⁽⁸⁾. The clinical characteristics of new onset status epilepticus (NOSE) among elderly patients differ from those observed in younger adults under 60⁽⁹⁾. The details were presented in Tables 3 and 4. Table 4 showed that elderly patients have a higher mortality rate compared to those under 60 years of age, at 16% and 2%, respectively. Regarding the seizure characteristics, they were predominantly classified as non-convulsive status epilepticus (NCSE) in 57.4% of elderly patients, while

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Table 1. The Incidences of SE among the Elderly in Thailand between 2004 to 2012

Years	Numbers	Age: 60 to 69 years	Age: 70 to 79 years	Age: ≥80 years	Rate/100,000 population
2004	113	65	33	15	1.84
2005	166	76	64	26	2.63
2006	174	78	68	28	2.67
2007	241	115	90	36	3.60
2008	356	149	149	58	5.14
2009	413	170	174	69	5.74
2010	556	216	243	97	7.40
2011	590	247	242	101	7.55
2012	717	304	264	149	8.78
Total	3,326	1,420	1,327	579	

Reference: Tiamkao S, Pranboon S, Thepsuthammarat K, Sawanyawisuth K. Status epilepticus in the elderly patients: A national data study in Thailand. *Journal of the Neurological Sciences* 2017;372: 501–5.

Table 2. Comorbidities in elderly patients with status epilepticus

Comorbidities	Numbers (percentage)
Hypertension	1,072 (32.2)
Diabetes mellitus	543 (16.3)
Previous strokes	423 (12.7)
Chronic renal failure	219 (6.6)
Traumatic brain injuries	45 (1.4)
Cirrhosis	43 (1.3)
CNS infections	38 (1.1)
Schizophrenia	24 (0.7)
Brain tumors	21 (0.6)
Psychosis	12 (0.4)
Depression	8 (0.2)

Reference: Tiamkao S, Pranboon S, Thepsuthammarat K, Sawanyawisuth K. Status epilepticus in the elderly patients: A national data study in Thailand. *Journal of the Neurological Sciences* 2017;372: 501–5.

NCSE was observed in only 29% of the younger patients. The cause of SE in the elderly group was more frequently attributed to remote symptomatic causes that were primarily due to cerebrovascular disease, which was consistent with findings from Yoshimura H et al.⁽¹⁰⁾.

Patients in both groups (those under 60 years of age and those 60 years of age and older) exhibited distinct clinical characteristics, as shown in Table 5.

The factors affecting treatment outcomes of new onset status epilepticus (NOSE) in elderly patients are limited to three: 1) the length of the hospital stay, 2) the duration of the stay in the intensive care unit, and 3) the occurrence of infections during treatments⁽⁹⁾. Additionally, a study by Yoshimura H et al.⁽¹⁰⁾ found that among patients aged 65 years and older, the causes that were related to remote symptomatic and cryptogenic factors had negatively impacted the treatment outcomes. Accurate and rapid diagnosis of elderly patients with non-convulsive status

epilepticus (NCSE) requires physicians have experience and consistently consider the possibility of NCSE. Otherwise, there will be a high risk of misdiagnosis. In a study conducted by Shavit L. et al.⁽²⁾, 14 patients exhibited symptoms of NCSE. As detailed in Table 6, 9 of the patients presented with confusion, 4 with stupor, and 1 with coma. All patients had undergone a thorough assessment to determine the cause of altered consciousness in accordance with the appropriate diagnostic guidelines. It was found that the time which was taken to diagnose NCSE had been no less than 24 hours and had ranged from 1 to 3 days. Moreover, this aligned with findings from other studies^(11,12). When patients receive an accurate diagnosis, then their conditions improve rapidly with anticonvulsant treatment. Therefore, it is essential to maintain a high index of suspicion for NCSE in cases in which patients exhibit altered levels of consciousness.

Woodford HJ et al.⁽¹³⁾ proposed a diagnostic approach for NCSE, as illustrated in Figure 1. Additionally, it was observed that the clinical symptoms of patients with NCSE, aside from changes in consciousness, had included other symptoms, as detailed in Table 7.

Consequently, when there is a suspicion that an elderly individual may be experiencing NCSE, it is essential to carry out electroencephalography (EEG), particularly continuous EEG, since it yields more precise results compared to conventional EEG⁽¹⁴⁾. Nonetheless, there are considerable constraints concerning the availability of hospitals, which are capable of performing this type of test. Moreover, the procedure requires more time to complete.

The study by Leppik IE⁽¹⁵⁾ found that the most common causes of SE in elderly patients had been cerebrovascular disease, metabolic disorders, and withdrawal from anticonvulsants, which differ from the causes observed in the adult patient group, as shown in Table 8.

In the treatment of SE in the elderly, the selection

Table 3. New Onset Status Epilepticus (NOSE) in patients under and above 60 years of age

Cause/Precipitating factors	Number of patients (total 135 patients) (%)	Number of patients >60-year-old (total 51 patients) (%)	Number of patients <60-year-old (total 25 patients) (%)
Symptomatic	122 (90)	40 (78%)	24 (96%)
Acute symptomatic	56 (41)*	23 (45)*	16 (64)*
Drug withdrawal	10 (7)	-	-
Alcohol abuse	13 (10)	4 (8)	7 (64)
Acute CNS infections	5 (4)	2 (4)	2 (8)
Metabolic/toxic	10 (7)	4 (8)	4 (16)
Acute cerebral bleeding	6 (4)	5 (10)	0 (0)
Acute cerebral infarctions	2 (1)	2 (4)	0 (0)
New cerebral neoplasms	9 (7)	5 (10)	3 (12)
Acute head injuries	1 (1)	1 (2)	0 (0)
Remote symptomatic	51 (38)*	14 (27)*	4 (16)*
Infarctions in the past	24 (18)	11 (21)	3 (12)
Cerebral bleeding in the past	5 (4)	2 (4)	0 (0)
Residual infections	1 (1)	0 (0)	0 (0)
Head injuries in the past	7 (5)	1 (2)	1 (4)
Perinatal encephalopathy	3 (2)	0 (0)	0 (0)
Known epilepsy	11 (8)	-	-
Progressive symptomatic	13 (10)*	3 (6)*	3 (12)*
Known CNS tumors		3 (6)	3 (12)
Multiple sclerosis		0 (0)	0 (0)
Cryptogenic (n=11)		11 (22)*	2 (8)*

* p<0.05

Reference: Maltera MP, Nassa RD, Kaluschke T, et al. New onset status epilepticus in older patients: Clinical characteristics and outcome. *Seizure* 2017; 51:114-20.

of the most appropriate anticonvulsants is essential since patients often have comorbidities and are taking multiple medications for those conditions. Therefore, the suitable anticonvulsants must possess the following characteristics:

1) The mechanism of action should correspond to the factors causing the SE.

2) There should be no drug interactions with the medications that are being used to treat comorbidities.

3) The medication should be available in an intravenous formulation.

4) The half-life should be greater than 24 hours.

5) It should be safe to use for patients with comorbidities, such as cerebrovascular disease, hypoxic brain injuries, and other common comorbid conditions.

The study by Rohrer A et al.⁽¹⁶⁾ involving 75 elderly patients with SE examined the use of various anticonvulsants. It was found that lorazepam and midazolam had been used as the first-line medications in 57% and 32% of cases, respectively. Levetiracetam had been used as the second-line anticonvulsant in 51% of cases, as detailed in Table 9.

When treating elderly patients, one must be cautious of low serum albumin levels. Therefore, highly protein-

bound anticonvulsants, such as phenytoin and sodium valproate, which have over 90% protein binding, may result in higher levels of free drug form and may potentially lead to drug concentrations exceeding therapeutic levels. Anticonvulsants that affect heart function or blood pressure, such as phenytoin, should be used with caution in the elderly due to side-effects like arrhythmias and hypotension. Consequently, if a patient had coexisting heart disease, care should be taken when using phenytoin. Additionally, elderly patients may have comorbidities, such as renal or liver disease, necessitating caution with anticonvulsants that have side-effects that affect liver and renal function. Anticonvulsants, such as levetiracetam and lacosamide, do not affect the liver and are not related to the metabolism of other anticonvulsants, whether through inhibition or induction. The first-line anticonvulsants (lorazepam or midazolam) are administered intravenously, which is similar to the treatment for general status epilepticus. The available second-line anticonvulsants consist of four options: fosphenytoin/phenytoin, sodium valproate, levetiracetam, and lacosamide. Phenobarbital is not commonly used due to its significant effects as a respiratory depressant. Care should be taken when phenytoin, phenobarbital, and lacosamide

Table 4. The clinical characteristics of patients with New Onset Status Epilepticus in patients under and above 60 years of age

	Above 60 years/total 87 patients (%)	Under 60 years/total 48 patents (%)	p value
New onset status epilepticus	51 (59)	25 (52)	0.48
Good treatment outcomes	39 (45)	34 (71)	0.004*
Mortality	16 (18)	1 (2)	0.006*
Female	56 (64)	20 (42)	0.01*
Characteristics of status epilepticus			0.002*
GTCSE	29 (33.3)	30 (63)	
CPSE	41 (47.1)	14 (29)	
CPSE with coma	9 (10.3)	0 (0)	
SPSE	8 (9.2)	4 (8)	
Causes			0.43
Symptomatic	76 (87)	46 (96)	
Acute	34 (39)	22 (46)	
Remote	33 (38)	18 (38)	
Progressive	9 (10)	6 (14)	
Cryptogenic	11 (11)	2 (4)	
Comorbidities	15 (17)	5 (10)	0.32
Treatments			
First-line medications:			0.06
Benzodiazepine	71 (81)	45 (94)	
Anticonvulsants	12 (14)	1 (2)	
Anesthetics	4 (5)	2 (4)	
The dosage of the first-line medication was correct	62 (71)	34 (71)	1
Subsequent treatment was appropriate	59 (68)	36 (75)	0.44
Refractory status epilepticus	44 (51)	20 (42)	0.37
Duration of status epilepticus: hours			0.50
<1	23 (26)	17 (35)	
1 to 24	35 (40)	15 (32)	
>24	29 (34)	16 (33)	
Intensive Care Unit (ICU)	85 (97)	45 (94)	0.35
Average duration in the ICU (SD)	7.5 (10.7)	7.6 (15.2)	0.95
Endotracheal intubation	33 (38)	19 (40)	0.90
Infection during treatment	39 (45)	15 (31)	0.14
Average length of hospital stay (SD)	14.7 (12.5)	12.1 (15.9)	0.30

SE=status epilepticus; GTCSE=generalized tonic clonic SE; CPSE=complex partial SE; SPSE=simple partial SE

*p<0.05.

Reference: Maltera MP, Nassa RD, Kaluschke T, et al. New onset status epilepticus in older patients: Clinical characteristics and outcome. *Seizure* 2017; 51:114-20.

are used in patients with heart disease. If the patient’s blood pressure was not stable, phenytoin and phenobarbital should be avoided, and sodium valproate should be avoided in patients with liver disease⁽¹⁷⁾.
If there was impaired renal function, the dosing of levetiracetam must be adjusted based on renal function⁽¹⁷⁾. The recommended maintenance dosage should be as follows: 1) 500 to 1,000 mg every 12 hours when the creatinine clearance is between 50 to 80 mL/min/1.73 m²; 2) 250 to 750 mg every 12 hours when the creatinine clearance is between 30 to 50 mL/min/1.73 m²; or 3) 250 to 500 mg

every 12 hours when creatinine clearance is less than 30 mL/min/1.73 m². In cases of end-stage renal disease, the dosage should be 500 to 1,000 mg every 24 hours, with an additional 250 to 500 mg given after each session of hemodialysis.
For lacosamide, no dosage adjustment is required if the creatinine clearance is greater than 30 mL/min/1.73 m². If the creatinine clearance was between 15 to 30 mL/min/1.73 m², the dosage should be adjusted to 150 mg every 24 hours, and then reduced to 75 mg every 24 hours if the creatinine clearance was less than 15 mL/min/1.73 m². Additionally, 25 to 150 mg should be given after each hemodialysis session at

Table 5. Distinct clinical characteristics among under and above 60-year-old patients

	Above 60 years/total 87 patients (%)	Under 60 years/total 48 patents (%)	p-value
New onset status epilepticus	20 (39)	15 (60)	0.14
Good treatment outcomes	9 (18)	1 (4)	0.15
Mortality	35 (69)	9 (36)	0.01*
Female			0.004*
GTCSE	14 (27)	17 (68)	
CPSE	27 (53)	6 (24)	
CPSE with coma	6 (12)	0 (0)	
SPSE	4 (8)	2 (8)	
Etiology			0.16
Symptomatic	40 (78)	23 (92)	
Acute	24 (47)	16 (64)	
Remote	14 (27)	4 (16)	
Progressive	2 (4)	3 (12)	
Cryptogenic	11 (22)	2 (8)	
Comorbidities	11 (22)	4 (16)	0.76
Treatments			
First-line medications:			0.06
Benzodiazepine	38 (75)	23 (92)	
Anticonvulsants	9 (17)	0 (0)	
Anesthetics	4 (8)	2 (8)	
The dosage of the first-line medication was correct	36 (71)	15 (60)	1
Subsequent treatment was appropriate	34 (67)	16 (64)	1
Refractory status epilepticus	25 (49)	12 (48)	1
Duration of continuous seizures: hours			0.53
<1	11 (22)	8 (32)	
1 to 24	21 (41)	7 (28)	
>24	19 (37)	10 (40)	
Intensive Care Unit (ICU)	49 (96)	24 (96)	1
Average duration in the ICU (SD)	9.4 (13.1)	7.2 (9.9)	0.42
Endotracheal intubation	22 (43)	14 (56)	0.34
Infections during treatment	28 (55)	8 (32)	0.09
Average length of hospital stay (SD)	17.3 (13.8)	12.9 (10.2)	0.13

SE=status epilepticus; GTCSE=generalized tonic clonic SE; CPSE=complex partial SE; SPSE=simple partial SE

*p<0.05

Reference: Maltera MP, Nassa RD, Kaluschke T, et al. New onset status epilepticus in older patients: Clinical characteristics and outcome. *Seizure* 2017; 51:114-20.

approximately 50% of the recommended dose. Lacosamide should not be used in patients with severe liver disease, and those using medications that are metabolized by CYP3A4 or CYP2C9 inhibitors should have their dosages reduced.

In cases where the third-line medications are anesthetics⁽¹⁷⁾, including propofol, pentobarbital, thiopental, and midazolam, there is insufficient data to determine which drug should be used first. The choice should primarily be based on their half-lives. Therefore, thiopental and pentobarbital should not be selected as the first-line agents. The goal of administering these third-line medications is to achieve burst suppression. The dosage should be increased

every 3 to 5 minutes until the electroencephalogram (EEG) shows burst suppression. If the target had not been achieved, bolus doses may be administered. Once burst suppression has been achieved, intravenous administration should continue for at least 24 hours. Afterward, the dosage should be gradually reduced. For example, propofol should be decreased by 20% every 3 hours, and midazolam should be decreased by 50% every 3 hours. For thiopental and pentobarbital, the medications can be discontinued immediately without tapering, unless the patient has difficult-to-control seizures, in which case the anesthetic should be gradually reduced. The treatment of RSE should

Table 6. The clinical characteristics of patients with non-convulsive status epilepticus and treatment outcomes

14 Patients	Number
Prodromal symptoms	
Coma	1
Confusion	9
Stupor	4
Duration before diagnosis (days)	1.8±0.9
Time period (days)	1 to 3
Specific part of brain seizures	
Focal-temporal	3
Diffuse	11
Old cerebrovascular lesions identified from computed tomography (CT) brain scans, number	7
Duration of continuous seizures (days)	2.3±1.3
Anticonvulsant treatments	14
Phenytoin	10
Valproic acid	4
Treatment responses	14
Complete	5
Partial	8
No response	1
Treatment outcomes	14
Discharged	11
Mortality	3

Reference: Shavit L, Grenader T, Galperin I. Nonconvulsive status epilepticus in elderly a possible diagnostic pitfall. *European Journal of Internal Medicine* 2012;23:701-4.

Table 7. The neurological abnormalities of those patients with non – convulsive status epilepticus

Symptoms	Percentage (n=23)*
Myoclonus/subtle jerking	30
Aphasia/interrupted speech	26
Automatisms	26
Staring	22
Perseveration/echolalia	17
Increased tone/catalepsy	13
Nystagmus/eye deviation	13
Emotional lability	9
Disinhibition	9
Anosognosia	9
Others	17

Reference: Woodford HJ, George J, Jackson M. Non-convulsive status epilepticus: A practical approach to diagnosis in confused older people. *Postgrad Med J* 2015;91:655–61.

involve the administration of one or two anticonvulsants in conjunction with the anesthetic, and after the anesthetic has been completely withdrawn, the anticonvulsants must continue to be administered.

Once seizure control has been achieved⁽¹⁸⁾, it is

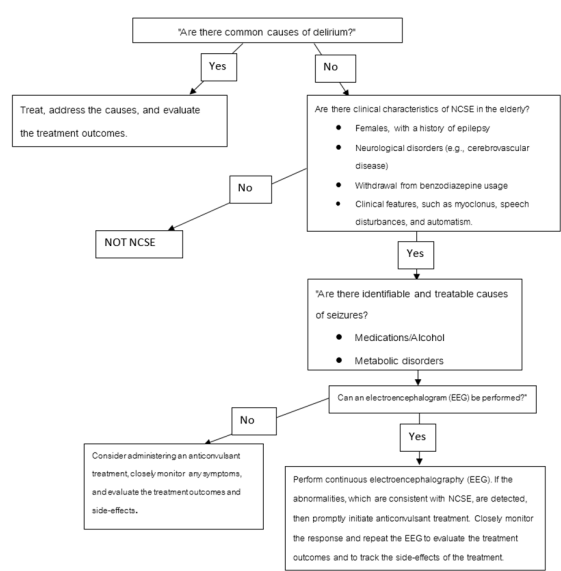


Figure 1. The diagnostic approach for non – convulsive status epilepticus.
NCSE=non – convulsive status epilepticus
Reference: Woodford HJ, George J, Jackson M. Non-convulsive status epilepticus: A practical approach to diagnosis in confused older people. *Postgrad Med J* 2015;91:655–61.

Table 8. Causes of status epilepticus in adults and the elderly

Causes	Elderly (%)	Adults (%)
Strokes	52.3	17.5
Undetermined	4.6	21.5
Metabolic	20.9	11.3
Antiseizure drug withdrawal	9.6	20.2
Alcohol-related	5.4	14.2
Traumatic brain injuries	9.3	2.3
Dementia	9.3	0.0
Cancer	8.6	5.5
Central nervous system infections	2.9	6.2
Systemic infections	6.3	0.0
Hypoxemia	5.3	0.0

Reference: Leppik IE. Status epilepticus in elderly. *Epilepsia* 2018; 59(S2): 140-3.

important to identify the underlying causes. The causes of SE in the elderly differ from those in adults, as previously mentioned. Common metabolic causes should be investigated, including hypoglycemia/hyperglycemia, hypocalcemia, hyponatremia, hypomagnesemia, uremia, hypoxia, hypercapnia, and carbon monoxide exposure. The levels of anticonvulsants should be measured since they may be below the therapeutic level (sub-therapeutic level). Alcohol levels should also be assessed. In addition, a review of the use of medications, such as beta-lactams, quinolones, isoniazid, and theophylline, should be screened

Table 9. The anticonvulsants used to treat 75 elderly patients with status epilepticus

Total number 120 patients (75 patients ≥60-year-old)	1st order, Total patients (≥60-year-old)	2nd order, Total patients (≥60-year-old)	3rd order, Total patients (≥60-year-old)	4th order, Total patients (≥60-year-old)	5th order, Total patients (≥60-year-old)	6th order, Total patients (≥60-year-old)	7th order, Total patients (≥60-year-old)
Lorazepam	57 (34)	23 (11)	2 (2)				
Midazolam	32 (22)	7 (4)	1	4 (4)	3 (3)	2 (2)	1
Diazepam	11 (6)	1 (1)					
Clonazepam	1						
Levetiracetam	17 (10)	51 (24)	21 (12)				
Phenytoin		2 (2)	4 (3)	4	6 (2)	1	
Valproic acid		2 (1)	4 (1)	10 (9)	3	2 (1)	1 (1)
Lacosamide		5 (4)	23 (12)	8 (3)	1 (1)	1 (1)	
Topiramate				6 (3)	3 (3)		
Propofol		2 (2)	2 (1)	1 (1)	3 (2)	4 (4)	2 (2)
Ketamine				1 (1)	3 (3)	5 (3)	2 (2)
Thiopental	1 (1)	3 (2)	2 (2)	1	3 (1)		1 (1)
Phenobarbital				1			1
Retigabine				1	1 (1)	1	
Magnesium				1			1 (1)
Electroconvulsive therapy							1
Perampanel						1	

Reference: Rohrachner A, Reiter DP, Brigo F, et al. Status epilepticus in the elderly—A retrospective study on 120 patients. *Epilepsy Research* 2016; 127:317-23.

for, as well as toxic substances. Once the control of seizures has been established, a computed tomography (CT) scan of the brain should be performed with urgency in all cases. A lumbar puncture to analyze cerebrospinal fluid should be considered on a case-by-case basis and should be performed only when there is suspicion of an infection in the central nervous system.

Elderly patients with liver dysfunction as a comorbidity have been found to have a higher risk of developing continuous seizures if they had cirrhosis compared to elderly individuals without cirrhosis. However, if the liver dysfunction was mild, it did not significantly affect the occurrence of continuous seizures⁽¹⁹⁾.

Conclusion

The diagnosis of SE among elderly patients should always start with considering the condition. In cases in which patients are exhibiting altered levels of consciousness, have a history of epilepsy, are female, and are showing abnormal eye movements, one should always consider the possibility of NCSE. Treatments must involve selecting anticonvulsants that do not interact adversely with the medications that are being used for comorbid conditions. Furthermore, in cases with liver and renal dysfunction, the medications must be safe for liver and renal function.

What is already known on this topic?

SE needs prompt diagnosis and treatment. However, diagnosing this condition in the elderly is often challenging due to incomplete information from the patients' medical histories.

What this study adds?

The diagnosis of SE among elderly patients should always start with considering the condition. In cases in which patients are exhibiting altered levels of consciousness, have a history of epilepsy, are female, and are showing abnormal eye movements, one should always consider the possibility of NCSE.

Conflicts of interest

The authors declare no conflict of interest.

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