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Review Article

Status Epilepticus in the Elderly☆

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SUMMARY

Status epilepticus is a life-threatening neurologic emergency. The elderly constitute the largest and fastest continuously growing population among patients with status epilepticus. The complexity of clinical presentations and difficulty in diagnosis further complicate, and possibly delay, prompt management. High clinical suspicion and proper investigation are the best tools for a prompt diagnosis. The etiology of elder-onset status epilepticus is primarily symptomatic, and cerebrovascular diseases are one of the most common causes, followed by neurodegenerative diseases such as dementia. Status epilepticus causes significant mortality among the elderly, who have the highest mortality of all age groups. These patients are very different from other age groups in many respects and clinicians should never treat them in the same manner as younger adults. Status epilepticus warrants immediate treatment to prevent irreversible neuronal damage. Decision-making regarding the choice of antiepileptic drugs (AEDs) depends on many factors such as adverse effect tolerability, drug interactions, and medical comorbidities. Balancing efficacy with the adverse effects of antiepileptic drugs is needed. The newer intravenous antiepileptic drugs, which have fewer adverse effects and drug interactions, appear to be reasonable treatment options for elderly patients. However, more evidence from clinical trials in this specific age group is required.

1. Introduction

Most generalized convulsive seizures stop quickly and spontaneously, whereas status epilepticus (SE) is a common neurological emergency that causes high mortality and irreversible neuronal damage if unsuccessfully treated. Status epilepticus is a seizure lasting more than 30 minutes or intermittent seizures without the recovery of consciousness between seizures[1]. However, based on the short duration of typical seizures (1–2 minutes)[2] and evidence of neuronal injury resulting from prolonged seizure, it was proposed that SE should be operationally defined as a seizure lasting more than 5 minutes to hasten intervention and treatment[3]. Elderly people (i.e., older than 65 years) have the highest prevalence and incidence of SE, and the prevalence further increases with advancing age. Because of the continuing aging of the worldwide population, first-line clinicians are treating an increasing number of elderly patients with SE. It is important to note that elderly patients differ from younger adults in many respects. Management of elderly patients with SE involves unique considerations regarding epidemiology, etiology, prognosis, and treatment choice. Articles included in this review were identified through searches of PubMed from 1988 until August 1, 2015, using the terms “epilepsy”, “status epilepticus,” “elderly,” and “aged.” Only papers published in English were reviewed. The final list of included articles was based on the relevance to the topics in this review article.

2. Epidemiology

One retrospective study[4] that calculated the cumulative incidence of SE reported that 0.4% of the general population will have experienced at least one episode of SE by the age of 75 years. The age-specific incidence rate of SE reflects a U-shaped curve or a bimodal distribution with peak rates among infants and the elderly. The incidence of epilepsy and SE has significantly declined in children and young adults with a concurrent increase among the elderly[5]. A landmark study conducted in Richmond, VA, USA showed an annual incidence of SE in the elderly of 86 cases per

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100,000 individuals, which was nearly twice the incidence in the general population[6]. The 70–79-year-old subgroup had an even higher annual incidence of 100 cases per 100,000 individuals. Similar results have been reported in other studies with different inclusion criteria, which reveals the fast growth and continuing rise in the annual incidence of SE in the older age group[7].

3. Clinical features and classification

Status epilepticus has a wide variety of clinical presentations and electroencephalography (EEG) features. Similar to epilepsy, several classification schemes of SE have been proposed. Status epilepticus can simply be divided into convulsive SE or nonconvulsive SE, based on the presence of clinically significant motor activity. Each group can be further divided by the consciousness level and clinical/EEG features[8]. Patients are categorized as markedly/severely impaired or as normal/mildly impaired, based on the consciousness level. With regard to clinical semiology and ictal EEG activity, patients are categorized into the generalized group or focal group. Focal seizures with or without secondary generalization are more common in elderly patients than in young adults. In the Richmond study, 26% of elderly patients were categorized as having generalized SE, whereas 29% of patients were categorized as having focal seizures and 45% of patients were categorized as having focal seizures with secondary generalization[9]. A caregiver or family member may witness an elderly patient having a generalized convulsive SE, although it is more likely a secondary generalized seizure due to a previously unrecognized focal onset seizure[10].

Unlike convulsive SE presenting with clinically obvious tonic, clonic, or tonic-clonic movement of the extremities, nonconvulsive status epilepticus (NCSE) is much more difficult to recognize because of the lack of significant motor phenomena. There is usually only subtle twitching of the face or limbs, or nystagmoid eye movement associated with a wide range of mental statuses from mild confusion to coma. Nonconvulsive status epilepticus may arise as the initial manifestation of seizure or result from the control of convulsive SE[11]. Decades ago, NCSE in elderly patients was described in the literature. It can be successfully treated after a correct and prompt diagnosis[12]. The diagnostic challenge remains because many conditions mimic NCSE such as metabolic encephalopathy, delirium, psychosis, and drug intoxication. Patients may go undiagnosed for days, even weeks, unless finally diagnosed by EEG abnormalities. The exact prevalence or ratio of NCSE to all types of SE is difficult to determine, but it is more common in the elderly, especially in settings of critical illness. Eight percent of all comatose patients in intensive care units are diagnosed with NCSE, based on EEG monitoring[13]. This percentage may reach as high as 37% if the patient cohort is limited to individuals with otherwise unexplained altered consciousness[14]. In a prospective study focused on elderly patients with confusion of unknown origin, 16% of the patients were diagnosed with NCSE by video-EEG; none of them had a history of epilepsy[15]. Acute onset (i.e., within 24 hours) and lack of clinical response to simple commands were associated with NCSE. In another recent prospective study with continuous EEG monitoring in elderly patients presenting with delirium, 28% of patients showed EEG patterns that were compatible with NCSE but without any other reliable clinical parameters for differential diagnosis[16]. A high index of clinical suspicion and timely EEG confirmation, especially in elderly patients presenting with altered mental status, are the best and probably the only ways to diagnose NCSE.

4. Etiology

Status epilepticus can occur in people with no previous history of seizures or epilepsy, especially in elderly patients. More than 70% of elderly patients in the Richmond cohort developed SE as their first-ever seizure[7]. The underlying causes of SE in elderly patients are also different from the causes in children and young adults. The etiologies are age-dependent and largely determine the prognosis and mortality rate. The underlying cause of late-onset SE is mostly symptomatic epilepsy (recently redefined as “structural–metabolic epilepsy”)[17], as opposed to idiopathic epilepsy (recently redefined as “genetic epilepsy”) that is common in young people[18]. In the Richmond study[6], an acute cerebrovascular accident was reported as the cause of SE in 21% of elderly patients. Remote symptomatic causes, which were mostly cases of a prior stroke, contributed another 21%. Other etiologies such as hypoxia, metabolic derangement, low AED concentration, traumatic brain injury, and central nervous system infection occur at any age, and still contribute to a substantial number of cases, just as in other age groups. When acute and remote strokes were combined, cerebrovascular events represented the most important etiology in elderly SE, whereas stroke was relatively uncommon in young adults and children. Similar findings were consistently noted in many studies across different countries[19]. A retrospective study in Taiwan also indicated cerebrovascular disease as the leading cause among patients who experienced their first-ever SE after the age of 60 years[20].

The relationship between stroke and SE is complex and not well understood. Status epilepticus occurs in more than 25% of early poststroke seizures[21]. Status epilepticus may present as the first symptom of stroke or at any time during the acute phase of the stroke (i.e., within 14 days). Stroke patients with SE have higher mortality and poorer functional disability, compared to stroke patients without SE[22]. Moreover, early-onset poststroke SE is associated with a high risk of recurrent seizure[23]. Outside the acute stage, SE more commonly occurs in stroke survivors with a relatively stable neurological condition. A large retrospective study of poststroke patients with a mean age of 72 years showed that cerebral infarction within 1 year raised the seizure risk by 23-fold, compared to the risk in the general population[24]. Poststroke patients with greater disability tended to develop SE later.

Frequently under-recognized degenerative diseases such as dementia are also associated with a high risk of late-onset epilepsy. Compared to their controls, age- and sex-adjusted patients with dementia had a six-fold increased risk of unprovoked seizure[25]. A case–control study of hospitalized inpatients older than 70 years revealed nonvascular dementia as an independent predictor of SE at an adjusted odds ratio of 4.16[26]. Patients with Alzheimer's disease had an even higher odds of seizure and epilepsy than individuals with non-Alzheimer's dementia in a nationwide inpatient study[27]. A causal relationship between dementia pathology and the development of SE has been proposed but the underlying mechanism remains unclear[28].

5. Prognosis and mortality

After the first episode of SE, the overall mortality is more than 20%[9]. The mortality rate remained consistently high across different epidemiological studies using various methodologies and inclusion criteria[29]. The underlying cause of SE is the most important factor affecting its prognosis and mortality rate. Potentially fatal etiologies usually lead to unfavorable neurological outcomes. An inadequate AED level and alcohol misuse have a relatively good prognosis and low mortality rate (i.e., < 10%), whereas hypoxic brain injury is associated with a high mortality rate (i.e., 60–100%)[30]. Because of the differential distribution of SE etiologies among the elderly, the mortality rate is also different from other age groups. Unlike the U-shape curve of the age-specific incidence mentioned previously, the mortality rate of SE is low in children