Seizure 18 (2009) 215–219

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Etiology of a short-term mortality in the group of 750 patients with 920 episodes of status epilepticus within a period of 10 years (1988–1997)

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ARTICLE INFO

Article history:
Received 4 July 2007
Received in revised form 3 July 2008
Accepted 10 October 2008

Keywords:
Status epilepticus
Mortality
Complications
Etiology
Antistatus therapy
Prolonged coma

ABSTRACT

Purpose: To determine the etiology of short-term mortality in patients with status epilepticus (SE).
Methods: 920 episodes of SE were recorded among 750 patients in a 10-year period. According to the clinical assessment, sequence of events that led to death in a particular case showed two major causes of death: (1) underlying disease, and (2) complications caused by convulsions, therapy or coma.
Results: Among 920 episodes of SE, 120 (13%) patients passed away. 79 patients (65.8%) died due to the underlying disease and 27 patients (22.5%) died of the combination caused by complications of underlying disease, convulsions, therapy, and/or coma. Among remaining 14 patients (11.7%), underlying disease was not the cause of death. Those 14 patients suffered complications caused by convulsions, therapy, and coma which caused death in four; therapy and coma in three; therapy in three; coma in two; and convulsions and coma in two patients, in the order already mentioned.
Conclusions: Among approximately 9 out of 10 patients with SE, death was the result of underlying disease. Although with very few patients, additional factors could provoke fatal complications of SE. In case of 1 among 10 patients complications caused by coma, therapy, and/or convulsions were the immediate cause of death. In case of such patients timely and adequate treatment could prevent death.

1. Introduction

Studies from the 19th and early 20th century indicate that SE resulted in a dramatic course and grave prognosis with a considerable rate of mortality (according to 1,2). In the last few decades, the rate of mortality has been decreasing most likely due to the improved treatment.[3] It is estimated that the SE mortality is 3.6–4.0/100,000 per year.[4] However, these figures do not explain relative contribution of various factors to mortality as well as its wide variability.

Death is a common outcome of SE caused by a severe symptomatic underlying disease. Nevertheless, death following an episode of SE caused by cryptogenic, idiopathic, or chronic non-progressive disease is exceptional.[5,6] In patients with SE that started during the hospital stay for reason other than epilepsy, the mortality rate was especially high (61%), with approximately one-third dying during SE, and two-thirds after its termination.[7]

The purpose of this study is to determine the etiology of short-term mortality in patients with SE.

2. Methods

2.1. Period of study

This study encircles a period of 10 years from January the 1st 1988 until December the 31st 1997 at the Institute of Neurology Clinical Center of Serbia, Belgrade.

2.2. Population of patients

Patients of both genders, older than 12 years with SE were included.

2.3. Management of patients

Paramedics and emergency physicians initially treated majority of patients during transfer to hospital. Approximately 20% of patients were transferred from another hospital in uninterrupted SE. Upon admission, they were initially treated by residents in emergency room (ER) and transferred to the neurology intensive care unit (ICU), which is equipped with facilities for vital function monitoring, and ventilator support supervised by neurologist. Only patients with respiratory depression (RD) were artificially

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doi:10.1016/j.seizure.2008.10.002

ventilated. In 7 patients, death occurred before they reached the ICU and they were not included in our study.

2.4. Surveillance of SE

For each SE episode vital parameters and total number of generalized tonic–clonic (GTC) seizures were observed, as well as the duration of SE, and time from the application of effective antiepileptic drug (AED) to the SE severance.

2.5. Therapeutic protocol

Patients were treated according to the standardized hospital-wide therapeutic protocol. However, during the 10-year period the protocol was occasionally violated mainly due to a periodic lack of particular AED on local market.

2.6. Definition of SE

SE is defined as "a condition in which epileptic activity persists for 30 min or longer, causing a wide spectrum of clinical symptoms",[2] and short-term mortality as death during the first 30 days following episode of SE.[10] SE cessation was clinically defined as a complete abolition of convulsions with normalization of autonomic parameters for GTC and partial motor (PM) SE, and abolishing of abnormal stereotype behavior with regaining of consciousness for non-convulsive SE. For all patients with non-convulsive SE and majority of patients remaining in coma for at least 4 h, EEG confirmed SE severance as soon as possible during regular working hours.

2.7. Classification of SE

In collaboration with the attending physician one of us (D.V.S.) classified SE according to clinical and, if available, EEG criteria.

2.8. Criteria for etiology of death

The etiology of death was determined for each patient. In each case of death, two types of etiologies and their combinations were determined: (1) severe underlying disease, and (2) complications caused by convulsions, therapy, and/or coma with no signs of severe underlying disease. Criteria for differentiation between etiologies depended on clinical assessment of the sequence of events that led to death in each particular case. If several etiologies contributed to death, their combination was considered as the principal cause. If complication of the severe underlying disease contributed to death, it was regarded as the most important, because neither SE nor other complications would have appeared in absence of the underlying disease.

2.9. Diagnosis of underlying disease

Diagnosis of underlying disease was made by the integration of clinical data and the results of complementary examination. Available anamnestic data were collected, and detailed physical, neurological examinations and CT scans were performed on all patients. Brain MRI was performed on approximately 1 among 3 patients according to availability at the time of study. ECG, EEG, blood biochemistry, complete blood count and chest X-ray, CSF examination, VDRL, various serological, toxicological, and bacteriological and virusological (mainly antibody titers for Herpes simplex I and II viruses, and HIV) tests were used frequently. Other tests were performed when that was justified. In majority of deceased patients, clinical presentation of underlying diseases was obvious and fulfilled the criteria for the diagnosis of particular type of disease. According to prevalent prognosis, different etiologies were classified as severe (that could lead to death) or benign (that usually do not lead to death).

2.10. Definition of complications caused by convulsions

Complications of vigorous convulsions resulted from powerful and protracted muscle contractions and comprised tongue bite, rhabdomyolysis, physical injuries, and RD.

2.11. Definition of complications caused by therapy

Antistatus therapy complications were related to intravenous application of the AED. RD, apnea, and cardiac arrest were complications caused by therapy only in cases when they occurred immediately (approximately within 10 min) following intravenous application of the antistatus drug. Criteria for RD were decrease of ventilator effort, cyanosis and direct demonstration of the increase of pCO_2 and decrease of pO_2 in arterial blood. Apnea was diagnosed as severance of breathing with no tendency for spontaneous recovery during at least 30 s.

2.12. Definition of complications caused by coma

Coma was the consequence of the underlying disease, prolonged convulsions, or late complication of antistatus therapy. Regarding the fact that coma causes complications not because of its etiology, but only because of its duration, it was recognized as the independent morbogenic factor. Complications that were caused by coma were consequence of prolonged immobility and included bedsores, infections, venous thromboses and embolism, or corneal perforation. The longer the duration of coma the more serious were the complications. Although coma complications were among the most serious, majority were preventable or curable.

2.13. Statistical tests

The following statistical tests were used in: Chi square test; Mann–Whitney's test; signed rank sum test; Friedman's test; Kruskal–Wallis' test; non-parametric Spearman's correlation, Student's t test; analysis of variance; and normal and binomial distribution test.

3. Results

3.1. Whole population

During a 10-year period, there were 920 SE episodes among 750 patients. Two patients had more than 10 SE episodes, 9 had 5–9, 24 had 3–4, 42 had 2 and 673 (73.1%) patients had a single SE episode. In case of 873 (94.9%) episodes, SE started before the admission to hospital and in 47 (5.1%) cases after the admission. Six hundred and two (65.4%) episodes were intercurrent and 318 (34.6%) were initial. SE was classified as GTC (725, 78.8%), PM (98, 10.7%), non-convulsive (93, 10%) or myoclonic (4 patients, 0.5%). EEG was performed in 102 (11%) episodes during and in 761 (82.7%) after the termination of SE. Among patients who died (120 of them) EEG was performed with 73 patients (60.1%).

3.2. Treatment of SE

Majority of patients (60.6%) were treated with more than one AED. Initial AEDs were intravenous diazepam (591) and