Survey of Convulsive Diseases in the Emergency Room: Pitfalls of Clinical Epilepsy Practice

Hiroyuki Ura[1,3], Ichiro Takumi[2], Akihiro Watanabe[3], Keiko Fukuda[3], Yuichiro Sakamoto[6], Shiro Kobayashi[4], Akira Teramoto[5], Kunihiro Mashiko[6] and Kiyomi Sadamoto[1]

[1]Department of Clinical Pathophysiology, Toho University School of Pharmaceutical Sciences
[2]Department of Neurosurgery, Nippon Medical School Musashi Kosugi Hospital
[3]Department of Pharmacy, Nippon Medical School Chiba Hokusoh Hospital
[4]Department of Neurosurgery, Nippon Medical School Chiba Hokusoh Hospital
[5]Department of Neurosurgery, Nippon Medical School
[6]Department of Emergency and Critical Care Medicine, Nippon Medical School Chiba Hokusoh Hospital

Introduction

Of the 120 million people in Japan, approximately 1.2.million are known to have epilepsy, a chronic brain disorder characterized by recurrent seizures that vary from brief lapses of attention and involuntary muscle movements to severe and prolonged convulsions. For the appropriate antiepileptic drugs to be selected, the diagnosis of convulsive disorders must be accurate. It is, therefore, critical to determine whether the patient has epilepsy and, if so, what kind or whether another convulsive disorder is responsible. To identify pitfalls of clinical epilepsy practice, particularly regarding diagnosis, we conducted a survey of convulsive disorders in the emergency room (ER) and estimated the future requirements for epilepsy pharmaceutical services in Japan.

Materials and Methods

A synthetic retrospective study was performed with ER records from January 2006 through December 2008 held at the Department of Emergency and Critical Care Medicine of Nippon Medical School Chiba Hokuso Hospital. In addition, patients who satisfied at least 1 of the following 3 criteria were selected for further examination of the complete medical records of the outpatient/inpatient clinic: (1) chief complaint of convulsion; (2) previous history of epilepsy or febrile seizure or both; and (3) diagnosis of epilepsy after emergency transportation.

Results

A total 6,924 patients were transported to the ER at Nippon Medical School Chiba Hokuso Hospital during the study period. Of these, 3,379 patients (mean age: 43.1 ± 23.6 years ; <15 years of age: 16.7%) had exogenous disorders, and 3,545 patients (mean age: 61.6 ± 20.0 years ;<15 years of age: 16.1%) had endogenous disorders (**Fig. 1**). Exogenous disorders included trauma, 78.0%; toxicosis, 8.0%; burns, 2.8%; anaphylaxis, 1.5%; heat stroke,

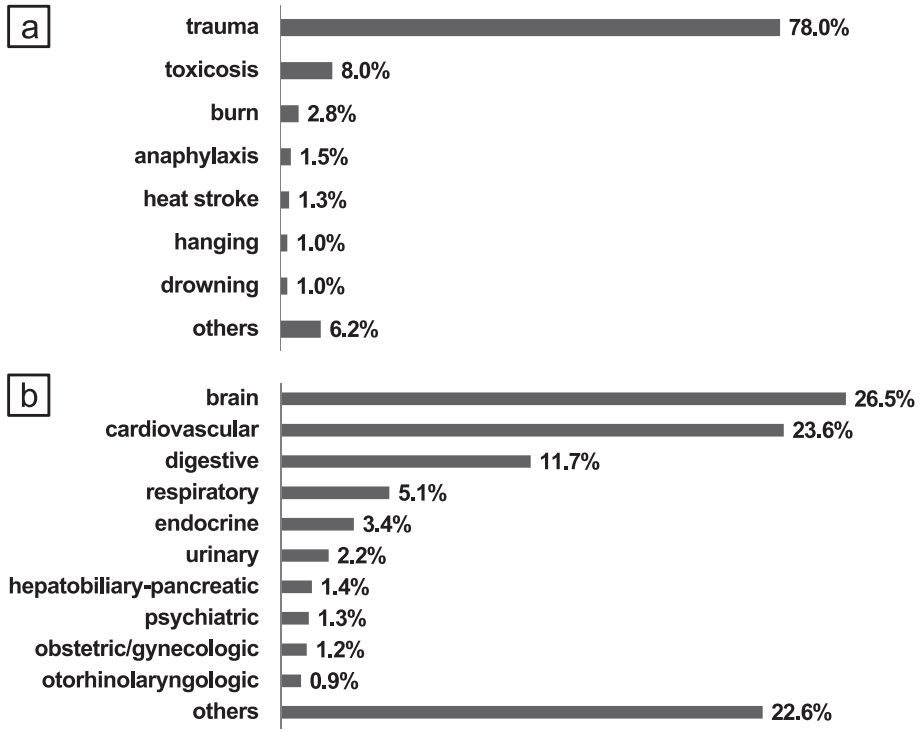

Fig. 1 Details of emergency cases of convulsive disorders (2006－2008)
a: Exogenous cases (3,379 cases)
b: Endogenous cases (3,545 cases)

Table 1 Previously administered antiepileptic drugs for patients with epilepsy treated in the ER

Classification	Localization-related epilepsy	Generalized epilepsy	Undetermined/Uncertain epilepsy
Valproate	17	1	9
Phenytoin	7	0	2
Carbamazepine	4	0	4
Zonisamide	4	0	3
Phenobarbital	3	0	3
Diazepam	1	0	0
Clonazepam	0	1	0
Acetazolamide	0	0	1

1.3%; hanging, 1.0%; drowning, 1.0%. The endogenous disorders included injuries related to the following systems: brain, 26.5%; cardiovascular, 23.6%; digestive, 11.7%; respiratory, 5.1%; endocrine, 3.4%; urinary, 2.2%; hepatobiliary-pancreatic, 1.4%; psychiatric, 1.3%, obstetric/gynecologic, 1.2%, otorhinolaryngologic, 0.9%, and other, 22.6%. A total of 130 patients (n=151; mean age: 53.1 ± 22.0 years; <15 years of age, 8.6%) received a diagnosis of epilepsy after arrival at the ER: these included 96 patients with localization-related epilepsy, 9 with generalized epilepsy, and 25 with either undetermined epilepsy or epilepsy with an uncertain classification. Antiepileptic drug monotherapy was started in 42 patients with epilepsy. The antiepileptic drugs prescribed at the start of treatment were carbamazepine (n=15), phenytoin (n=13), and valproate (n=8) for 36 patients with localization-related epilepsy, and valproate (n=6) for patients with other types of epilepsy (3 with generalized epilepsy, 3 with undetermined epilepsy). **Table 1** lists the antiepileptic drugs previously administered to patients for whom we had information (43 patients, 61 agents); 28 patients had localization-related epilepsy, 2 had generalized epilepsy, and 13 had undetermined epilepsy or epilepsy of uncertain classification. Among the patients with localization-related epilepsy, valproate had been prescribed for 17 (63.0%), phenytoin for 7 (25.0%),

and carbamazepine for 4 (14.3%).

We measured serum levels of antiepileptic drugs in 28 patients, and a total of 34 data was obtained. 14 (41.2%) had blood concentrations that were less than the therapeutic drug concentration range, 19 (55.9%) had concentrations within the therapeutic range, and 1 (2.9%) had a concentration higher than the therapeutic range.

Discussion

In this study, the majority of patients in the ER with epilepsy had localization-related epilepsy, a result that we attribute to the low percentage of pediatric patients. Generalized epilepsy usually presents in childhood, and our study showed that patients with localization-related epilepsy who had previously been treated with valproate accounted for a large number of the patients with localization-related epilepsy in the ER. These findings suggest that it may not always be appropriate to prescribe valproate for the treatment of localization-related epilepsy, although this may simply reflect the possibility that the prescription rate of valproate for treating localization-related epilepsy is high in Japan. Indeed, valproate is one of the drugs most commonly used to treat localization-related epilepsy. However, some studies outside Japan have shown that carbamazepine is significantly more effective in the treatment of localization-related epilepsy than is valproate[1], and Japanese guidelines for the treatment of epilepsy also recommend carbamazepine as the initial agent for localization-related epilepsy. Consequently, the use of valproate for treating localization-related epilepsy should be re-evaluated.

Our results also indicate that many epileptic seizures can be attributed to inadequate serum levels of antiepileptic drugs. Also, because the concentration range of therapeutic drugs varies between patients, serum levels of antiepileptic drugs can be used to monitor the adverse effects associated with drug adherence. Pharmacists should, therefore, play a more active role in epilepsy treatment by examining each pharmacological factor to facilitate treatment and to ensure that epilepsy is less intractable.

References

1. Marson A, Williamson P, Clough H, Hutton J, Chadwick D: Carbamazepine versus valproate monotherapy for epilepsy: a meta-analysis. Epilepsia 2002; 43: 505–513.