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Original Article

Retrospective Analysis of Anticonvulsant Exposures Admitted to Department of Emergency Medicine in Dokuz Eylül University Hospital

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Abstract

Purpose: To evaluate demographic characteristics, clinical signs and symptoms, treatment methods and clinical outcomes of anticonvulsant exposures in cases who were admitted to the Department of Emergency Medicine of in Dokuz Eylül University Hospital (DEUH) between 2000 and 2010 and reported to the Dokuz Eylül University Drug and Poison Information Center (DEUDPIC).

Methods: Age, sex, type of the anticonvulsant agents, route and causes of the exposure, clinical signs and symptoms, recommended and applied treatment methods and outcomes were recorded on a standard data forms, then entered into a computerized database program (Ruber). The chi-square test was used in the statistical analyses.

Results: Seventy seven patients (45 women, 32 men) whose data were fully accessible were studied. Exposures were found to mostly occur due to acute (50.6%) and intentional (77.9%). Patients presenting with anticonvulsant exposure, were most commonly admitted (32.5%) to the DEUH within two hours after the ingestion. The most common causes of poisoning were identified as carbamazepine (32.5%) and valproic acid (23.4%). On clinical evaluation, 36.4% of the patients did not develop any clinical signs or symptoms, and 7.8% of the patients developed severe clinical signs and symptoms. Most of the severe cases (66.7%) resulted from carbamazepine ingestion. Also, 88.3% of the cases were found to have recovered and were discharged from the hospital without sequelae, no death occurred. The mean length of stay was 19.6±25.6 hours.

Conclusion: Carbamazepine intoxication ranked first among the intoxications due to anticonvulsant exposures. In this case, the length of follow up in the emergency department may be prolonged, particularly as a result of the anticholinergic effects of carbamazepine that may delay the onset of clinical manifestations.

Keywords: Anticonvulsant, exposure, poisoning, emergency department, Drug and Poisoning Information Centre

INTRODUCTION

Nowadays, anticonvulsants are used in the treatment of many neurological and psychiatric conditions such as fibromyalgia, migraine, chronic pain, bipolar disorder, and epilepsy, in particular (1). Side effects are common due to their narrow therapeutic index, particularly if used at large doses for suicidal purposes or as in case of a misuse. Based on the data from the Poison Information Centres (DPIC) of the United States of America (USA); 2.2% of the cases of poisoning that were reported in 2014, were related to anticonvulsants (2). The Edinburgh Poisoning Unit in Scotland reported that anticonvulsant overdoses account for at least 3.4% of the applications to their unit (3). In our country, there are limited data on the patients who were admitted to the emergency department due to anticonvulsant exposures.

The aim of this study was to evaluate demographic characteristics, type of anticonvulsant medications, route and the reason for the exposure clinical signs and symptoms, treatment methods and clinical outcomes of anticonvulsant exposures (except benzodiazepines) treated in the emergency department of Dokuz Eylül University Hospital (DEUH) between 2000 and 2010 and reported to the Dokuz Eylül University Drug and Poison Information Center (DEUDPIC). The results of this study will reveal the current incidence of anticonvulsant overdoses and will provide diagnostic and therapeutic guidance in the management of anticonvulsant overdoses.

METHODS

This study was approved by the Institutional Ethics Committee of the Dokuz Eylül University School of Medicine. In this cross-sectional and descriptive study, all admissions to the emergency department of Dokuz Eylül University Hospital (DEUH) due to anticonvulsant

exposures that were reported to the Dokuz Eylül University Drug and Poison Information Center (DEUDPIC) between 01.01.2000 and 31.12.2010 were included in the assessment. In our emergency department, all poisoning patients admitted to DEUH are consulted with DEUDPIC after the completion of their physical examination and they are managed according to the protocol for poisoned patients. Ecause of the data on the cases of anticonvulsant exposure have been reached through the electronic filing system of the hospital data management system (HBYS) and/or via data records from the hospital archive files which have been recorded on the database of DEUDPIC and/or DEUH registration data base of the emergency department, inform consents were not obtained. Patients who were under the age of 18 and patients whose file information was inaccessible were excluded from the study.

A poisoning form was simultaneously filled out, when a case of poisoning was reported to the DEUDPIC. In addition, a "Standard Data Form for Anticonvulsant Overdoses" which was specifically prepared for emergency admissions is filled out, when a patient was admitted to the emergency department of DEUH due to an anticonvulsant exposure. The data on the forms were recorded to a Microsoft Access 2000 (9.0.2812, written by Sedat Capar, 2001) computer program. Data regarding admission dates (day, month, year), demographics (age, gender), overdose information [route and underlying cause of the exposure, elapsed time after the exposure, circumstances associated with the overdose (intentional, unintentional and unknown)], clinical signs and symptoms, type and plasma levels of anticonvulsants, laboratory results (ECG, laboratory findings), recommended and applied treatment methods outcome information (clinical state, clinical outcome, and length of hospital stay) were evaluated. Clinical signs and symptoms were assessed according to the EAPCCT/IPCS Poisoning Severity Score (asymptomatic, mild, moderate or severe) (4).

Statistical Analysis

Study data were recorded on a standard program "Statistical Package for Social Sciences for Windows 15.0" (SPSS Inc.; 15.0, Chicago, IL, USA). t-test was used in the comparison of the means. The chi-square test was used in the comparison of the defined variables $p<0.05$ values were considered as statistically significant.

RESULTS

Between 01.01.2000 and 31.12.2010, 110 cases of anticonvulsant exposures (except benzodiazepines) were reported to the Dokuz Eylül University Drug and Poison Information Center (DEUDPIC) by the emergency department of Dokuz Eylül University Hospital (DEUH). Twenty four patient files were unavailable due to the missing registration data. Nine cases were excluded from the study since the poisoning data were missing in patient files. Seventy seven cases whose overdose data were fully accessible through archive files were included in the study.

Out of these 77 patients 45 (58.4%) were female and 32 (41.6%) were male, female/male ratio was 1.41/1. Overall mean age was 35.1±19.0 years while the mean age of female patients was 31.1±17.1 years (range: 18 to 87 years) and the mean age of male patients was 40.8±20.4 years (range: 18-82 years) (Table 1).

Table 1. The demographic characteristics of anticonvulsant exposures

Age	Female No (%)	Male No (%)	Total No (%)
18-29	29 (64.4)	12 (37.5)	41 (53.2)
30-39	6 (13.3)	6 (18.8)	12 (15.6)
40-49	4 (8.9)	4 (12.5)	8 (10.4)
50-59	3 (6.7)	2 (6.3)	5 (6.5)
60-69	-	4 (12.5)	4 (5.2)
>69	3 (6.7)	4 (12.5)	7 (9.1)
Total	45 (100.0)	32 (100.0)	77 (100.0)

Table 2. Causes of anticonvulsant exposures

Cause of poisoning	Female No (%)	Male No (%)	Total No (%)
Intentional	39 (86.7)	21 (65.6)	60 (77.9)
Unintentional	5 (11.1)	10 (31.3)	15 (19.5)
Unknown	1 (2.2)	1 (3.1)	2 (2.6)
Total	45 (%100)	32 (%100)	77 (%100)

During the study period, the annual number of emergency admissions due to an anticonvulsant expose was highest during 2009 (13.0%, n=10) and its incidence was highest in summer (29.9%, n=23). The anticonvulsant exposure-related emergency admissions were most frequent during August (14.3%, n=13).

Admissions most frequently occurred between 8:00 PM and 12:00 PM (41.6%; 32 cases) with 21 females (46.7%) and 11 males [34.4%]). When the time of admission compared between men and women, the admissions in the evening (20:00-23:59) and other admissions during the daytime did not significantly differ between male and female patients (χ^2=0.7123, $p<0.05$).

Acute exposure was the main type of anticonvulsant exposures in 50.6% of cases (n=39), followed in frequency by acute on chronic exposure (33.8%, n=26).

Intentional exposures (suicide attempt) were more common (77.9%) than the unintentional exposures (accidents, misuse, 19.5%) and intentional exposures were more common in females (65.0%, n=39) when compared to the males (35.0%, n=21). In addition, the underlying causes of two exposures were unknown (0.01%) (Table 2).

Most of the anticonvulsant exposures were intentional (95.2%) in 18-29 age group. The intentional anticonvulsant exposure rates were 91.7% in the 30-39 age group, 87.5% in the 40-49 age group and 60.0% in the 50-59 age group, respectively. No cases of intentional anticonvulsant overdose occurred in the 60-69 age group and in patients older than 69 years of age. When underlying causes of poisoning were compared, the rate of intentional exposure was higher in the 18-49 age group than those older than 50 years of age (χ^2=8.360, $p<0.01$ for females and χ^2=15.139, $p<0.0001$ for males).

Patients were admitted to the emergency department most commonly (32.5%) during the first two hours after the exposure. The rate of clinical improvement in patients who were admitted within two hours after the anticonvulsant exposure was significantly higher than those who were admitted >2 hours after the exposure (χ^2=4.638, p<0.05) (Table 3).

Anticonvulsants (except benzodiazepines) ingested by the patients were categorized as phenytoin, carbamazepine, valproic acid, oxcarbazepine, gabapentin, lamotrigine, phenobarbital, primidone and topiramate (Table 4). Among the co-ingestion medicines, the most commonly co-ingested medicines were antidepressants (n=21), while anxiolytics (n=12) ranked second.

In the analysis of the anticonvulsants by the underlying cause of overdose; among the patients who ingested carbamazepine, the overdose was intentional in 75% (n=21), and unintentional in 21.4% (n=6), while these rates were 95.0% (n=19) and 5.0% (n=1) for valproic acid and 35.7% (n=5) and 64.3% (n=9) for phenytoin respectively. The ingestion of oxcarbazepine was intentional in all cases of exposure (n=9). The clinical signs and symptoms was improved in 76.0% of cases who exposed carbamazepine alone. This ratio was 44.5% (n=8), 92.3% (n=12) and 66.6% (n=6) for valproic acid, phenytoin and oxcarbazepine, respectively. Out of 6 patients showing severe poisoning symptoms, 4 (66.7%) had ingested carbamazepine alone, one (16.7%) had ingested valproic acid alone, and one patient (16.7%) had ingested oxcarbazepine alone (Table 5). In the comparisons of clinical signs and symptoms by the anticonvulsants ingested by the patients; the rate of the development clinical signs and symptoms of overdose was higher in patients who had taken multiple different anticonvulsants in combination, in comparison to the patients who took carbamazepine, valproic acid, phenytoin, or oxcarbazepine alone (χ^2=4.196, p=0.0405) (Table 6). In patients who were admitted to the emergency department, due to anticonvulsant overdose, the amounts of the anticonvulsant agents ingested by the patients were classified into three groups: toxic, non- toxic and unknown amounts. Based on this classification, 46.8% (n=36) of the patient had taken the agent at toxic doses, while 29.9% (n=23) had ingested non-toxic amounts. The amount of the anticonvulsant agent was unknown in eighteen patients (23.4%). Among the patients who ingested toxic amounts of anticonvulsants, clinical signs and symptoms were mild in 33.3% (n=10) of the patients, moderate in 46.7% (n=14), and severe in 20.0% (n=6) (Table 6).

While only carbamazepine, valproic acid, phenytoin and phenobarbital measurements can be made in the DEUH laboratories, serum levels of the other anticonvulsants cannot be measured. In our study, the measurements of anticonvulsant levels could be made in 72.7% of the patients (n=56, carbamazepine, valproic acid, phenytoin and phenobarbital). The measurements indicated toxic levels in 76.8% (n=43) of those who underwent anticonvulsant level testing, and non-toxic levels in 23.2% (n=13). 81.4% of the patients with toxic levels, developed signs and symptom while 18.6% were asymptomatic. The presence of clinical sign and symptoms was higher in cases with toxic levels than the non-toxic levels.

Table 3. Distribution of clinical outcome of anticonvulsant exposures by duration

Duration (hour)	Asymtomatic No (%)	Mild No (%)	Moderate No (%)	Severe No (%)	Total No (%)
<2	15 (60.0)	6 (24.0)	3 (12.0)	1 (4.0)	25 (100.0)
2-6	3 (16.7)	6 (33.3)	7 (38.9)	2 (11.1)	18 (100.0)
>6	4 (50.0)	1 (12.5)	3 (37.5)	-	8 (100.0)
Unknown	6 (23.1)	11 (42.3)	6 (23.1)	3 (11.5)	26 (100.0)
Total	28 (36.4)	24 (31.2)	19 (24.7)	6 (7.8)	77 (100.0)

Table 4. Distribution of major anticonvulsants involved in anticonvulsant exposures

Drug	Female No (%)	Male No (%)	Total No (%)
Carbamazepine	13 (29.0)	12 (37.6)	25 (32.5)
Valproic acid	16 (35.6)	2 (6.3)	18 (23.4)
Phenytoin	4 (8.9)	9 (28.1)	13 (16.8)
Oxcarbazepine	5 (11.1)	4 (12.5)	9 (11.7)
Gabapentin	2 (4.4)	1 (3.1)	3 (3.9)
Lamotrigine	2 (4.4)	-	2 (2.6)
Phenobarbital	1 (2.2)	-	1 (1.3)
Primidone	-	1 (3.1)	1 (1.3)
Topiramate	1 (2.2)	-	1 (1.3)
Other anticonvulsants along with carbamazepine	1 (2.2)	1 (3.1)	2 (2.6)
Other anticonvulsants along with valproic acid	-	1 (3.1)	1 (1.3)
Other anticonvulsants along with phenytoin	-	1 (3.1)	1 (1.3)
Total	45 (100.0)	32 (100.0)	77 (100.0)

Table 5. Distribution of major anticonvulsants by clinical outcome

	Clinical outcome				
Anticonvulsants	Asymtomatic No (%)	Mild No (%)	Moderate No (%)	Severe No (%)	Total No (%)
Carbamazepine	6 (24.0)	7 (28.0)	8 (32.0)	4 (16.0)	25 (100.0)
Valproic acid	10 (55.6)	4 (22.2)	3 (16.7)	1 (5.6)	18 (100.0)
Phenytoin	1 (7.7)	8 (61.5)	4 (30.8)	-	13 (100.0)
Oxcarbazepine	3 (33.3)	4 (44.4)	1 (11.1)	1 (11.1)	9 (100.0)
Other	8 (66.7)	1 (8.3)	3 (25.0)	-	12 (100.0)
Total	28 (36.4)	24 (31.2)	19 (24.7)	6 (7.8)	77 (100.0)

It was determined that overdosed anticonvulsants were their own medication in 68.8% (n=53) of the patients while 22.1% (n=17) of the patients did not ingest their own medications and 9.1% (n=7) of the patients did not know if it was their medications or not.

On admission, 42.9% (n=33) of the patients had concomitant medication ingestion. Antidepressants were the most common additional medicines (n=21, 63.6%), while anxiolytics (n=12, 36.3%)

Table 6. Distribution of anticonvulsant amounts by clinical outcome and gender

	Anticonvulsant amounts							
	Toxic		Non-toxic		Unknown		Total	
Gender	Available* No (%)	None* No (%)	Available* No (%)	None* No (%)	Available* No (%)	None* No (%)	Available* No (%)	None* No (%)
Female	18 (60.0)	4 (66.7)	2 (40.0)	11 (61.9)	7 (50.0)	3 (75.0)	27 (55.1)	18 (64.3)
Male	12 (40.0)	2 (33.3)	3 (60.0)	7 (38.9)	7 (50.0)	1 (25.0)	22 (44.9)	10 (35.7)
Total	30 (100.0)	6 (100.0)	5 (100.0)	18 (100.0)	14 (100.0)	4 (100.0)	49 (100.0)	28 (100.0)

*Clinical signs and symptoms

Table 7. Distribution of recommended and applied treatments attempts

	Recommended		Applied	
Treatment methods	No	(%)	No	(%)
Observation and supportive treatment	13	16.8	17	22.0
Gastric lavage alone	2	2.6	2	2.6
Activated charcoal alone	34	44.2	31	40.3
Gastric lavage and activated charcoal	25	32.5	26	33.8
Discharged	3	3.9	1	1.3
Total	77	100.0	77	100.0

ranked second. In the assessment of the substances (alcohol and/or recreational drugs) that were ingested concurrently with anticonvulsant agents, concurrent alcohol intake was observed in 9.1% (n=7) of the patients. Also, 74.0% (n=57) of the patients did not take any additional drug while drugs concurrently taken with anticonvulsants were unknown in 16.9% (n=13) of the cases.

No clinical signs and symptoms were observed in 36.4% (n=28) of the subjects receiving anticonvulsants while clinical signs and symptoms were mild in 31.2% (n=24), moderate in 24.7% (n=19) and severe in 7.8% (n=6). There were no statistically significant differences between male and female patients in the severity of the clinical signs and symptoms associated with anticonvulsant ingestion (χ^2=0.2984, p>0.05).

In patients who were admitted to the emergency department after having ingested an overdose of any anticonvulsant the Glasgow Coma Scale (GCS) score was ≥14 in 80.5% (n=62) of the patients and ≤10 in 10.4% (n=8) of the patients. When GCS scores were evaluated in relation to the anticonvulsant ingested by the patient and the treatment administered in the emergency department of DEUH; in patients with a GCS score of ≥11, the treatment consisted of observation and supportive care alone and no gastrointestinal system (GI) decontamination methods (gastric lavage or activated charcoal or both) were implemented. In all patients with a GCS score of ≤10, a gastrointestinal decontamination method was applied.

In the assessment of ECG findings of the overdosed patients, ECG was considered normal 78.0% (n=32) of the patients, while ECG was considered abnormal in 22.0% (n=9) of the patients with the most common abnormality being sinus tachycardia (77.8%, n=7). In one patient, the QRS distance seemed to be prolonged (QRS>100ms) and in another one ECG abnormality progressed to supraventricular tachycardia. The assessment of the abnormal ECG findings by the anticonvulsant ingested by the patients revealed that 44.4% (n=4) of the ECG abnormalities were associated with carbamazepine ingestion and 22.2% (n=2) were associated with valproic acid ingestion

For the patients who referred to the emergency department of DEUH due to an anticonvulsant overdose and/or consulted with DEUDPIC, treatment recommendations include; supportive observation gastrointestinal decontamination methods (vomiting, gastric lavage, activated charcoal), antidote treatment, enhanced elimination (hemodialysis, hemoperfusion) and others. Observation and supportive treatment were suggested in 16.8% (n=13) of the poisoned patients, GIS gastrointestinal decontamination was used in 79.3% (n=61), and 3.9% (n=3) were discharged from the hospital after giving advices. None of the patients underwent hemodialysis and hemoperfusion (Table 7).

Most of the patients (61.0%) who were admitted to the emergency department of DEUH, were monitored in the emergency department, 7.8% inpatient and 7.8% of the patients were referred to another health care facility, 13.0% were monitored in the intensive care unit and 10.4% left the emergency department on their own will. Most of the patients (88.3%, n=68) who were admitted to the emergency department of DEUH due to anticonvulsant exposure, improved and discharged from the hospital and clinical outcomes were unknown in 11.7% (n=9) of the patients. The patients recovered without sequelae and no overdose-related death occurred.

The mean length of stay of the patients who were admitted to the emergency department of DEUH due to an anticonvulsant exposure was 19.6±25.6 hours. The mean length of stay of female patients was 16.2±18.6 hours and the mean length of stay of male patients was 24.3±32.7 hours.

DISCUSSION

Our study provided data on the demographic characteristics, circumstances associated with overdoses, clinical signs and symptoms and outcomes of the anticonvulsant overdoses, in patients who were admitted to the emergency department of Dokuz Eylül University Hospital (DEUH) due to an anticonvulsant exposure (77 patients, except benzodiazepine).

Anticonvulsant agents affect the central nervous system by different mechanisms. They have a wide range of applications such as epilepsy, mood disorders, pain syndromes and are now widely used all over the world (1). Poisonings resulting from high-dose exposures may result in serious life-threatening clinical signs and symptoms. Based on the data obtained from all Poison Information Centres (DPIC) of United States (US), 2577557 poisonings were reported in 2014 and anticonvulsant agents were responsible for 2.2% of these cases (2). In a study conducted in Scotland, 618 (3.4%) out of 18010 cases of poisoning reported to the Edinburgh Poisoning Unit were the cases of poisoning with at least one anticonvulsant agent (3). In our country, there are limited data on the patients who are admitted to the emergency department due to anticonvulsant exposure. Between 1993 and 1995, 3.7% of the poisonings were associated with anticonvulsants and carbamazepine was responsible 44.3% of the cases of anticonvulsant poisonings that were reported to the Dokuz Eylül University Drug and Poison Information Center (DEUDPIC) (5). According to the retrospective evaluation of emergency admissions to Ege University Hospital between 2006 and 2007; 4% of 608 cases of poisoning were anticonvulsant overdoses (6). According to the retrospective evaluation of 245 patients admitted to the intensive care unit of Cumhuriyet University Hospital due to acute prescription drugs overdoses, all patients deliberately ingested relevant drug to commit suicide and 6.4% are poisoned with anticonvulsants (7).

Suicide attempts have been reported to increase in certain months and seasons in many countries. Although, Verstraete and Buylaert reported that there is no seasonal variation in the cases of acute overdose, other sources have reported that the cases of overdoses tend to occur especially in summer and in June and July in particular (5, 8, 9, 10). Similarly, in our study, the highest number of anticonvulsant related emergency admissions occurred in the summer (most often in August rather than June).

In a study conducted in Ankara Hacettepe University Hospital, the highest number of hospital admissions occurred between 6:00 PM and 12 PM (38%) in 1098 patients who were admitted to the hospital due to a prescription drug overdose and poisoning. 52% of the patients were admitted during the first two hours after the ingestion (11). In another study reported from our country, 51% of the poisoned pediatric patients were admitted to the emergency department within in the first two hours after the ingestion and 82% were admitted within the first six hours (12). Consistent with other studies in the literature, our study showed that patients intoxicated with an anticonvulsant agent were admitted to the emergency departments most commonly during the first 2 hours after the ingestion.

Like all over the world in our country as well, poisoning is more common among young adults. In a study conducted by Ozkose and Ayoglu (13) on acute poisoning, more than half of the poisoned patients were under the age of 25 and the average age was 26 years. According to the data of Poisoning Center of Uludağ University, most poisonings occur between the ages of 14-25 years (14). In two studies which performed in our country, intentional medication intakes were found to be higher in the younger population (6, 15). In an ongoing survey in Iran lasting for about 7 years poisonings were most commonly observed between the ages of 6-17 years during the childhood and in the 18-29 age group among the adults, and it was emphasized that the overall average age was about 22 years (16). In line with these findings, anticonvulsant agent intakes were more frequent between the age of 23-44 years, in a study conducted by Nixon et al. (3) In our study, anticonvulsant exposures were more common in the 18-29 age group and high-dose exposure to an anticonvulsant, is largely (95%) intentional.

Regarding the gender distribution among poisoned patients, there were differences between the age groups. The majority of the paediatric patients under the age of 6 were males. The rate of female patients were relatively higher in other age groups (53%) (15). The assessment of the childhood poisoning by gender distribution revealed that anticonvulsant overdoses were relatively more prevalent among the boys under the age of 10 years (52%), and among the girls older than 10 years of age (79%) (12). According to the data of The World Health Organization (WHO), suicide attempts are more common in men than women (17). The results of two studies conducted in our country, indicated that the rate of attempted suicide was higher among females than it was among males (6, 15). Anticonvulsant agent poisonings were examined in a study of Nixon et al. (3), and it was reported that, the rate of females patients who had taken an overdose of any anticonvulsant was 57.5% in the study sample. In line with the similar studies in the literature, more than half of the patients who took an overdose of an anticonvulsant agent were females in our study.

In a study of Akkas et al. (11), 11% of all poisonings occurred concurrently with alcohol intake. This result was similar to the results of Kiyan et al. (6) (9.2%). In our study, 9% of the cases of anticonvulsant overdose were associated with alcohol intake. In our study, 43% of the patients who referred to the emergency department due to an anticonvulsant overdose had also ingested an additional drug concurrently (antidepressants or anxiolytics, most commonly). In the study of Nixon et al. (3) anticonvulsant were taken in combination with antidepressants in 65% of the cases of anticonvulsant overdose, and were taken most frequently in combination with benzodiazepines.

Most of the researches on anticonvulsant poisoning have indicated that carbamazepine and valproic acid are the most common anticonvulsant agents that cause anticonvulsant intoxications (3). In line with this result, carbamazepine and valproic acid were the most common causes of anticonvulsant poisoning in our study. Since these agents are the most commonly used anticonvulsants, this result is not surprising. The third most common anticonvulsant taken as overdose was phenytoin. In the study of Nixon et al. (3), the most frequently used anticonvulsant was lamotrigine. In contrast with this result, non classified anticonvulsant poisoning was the most common anticonvulsant poisoning, other than these three medications according to the data reported by the American Association of Poison Control Center Unit (2). In recent years, increased use of the new generation anticonvulsants for the treatment of epilepsy and, differences of anticonvulsant prescribing habits of physicians, could have brought the most

commonly used different anticonvulsant medication.
In this study on the patients who were admitted to the emergency department of DEUH due to anticonvulsant overdose, only blood carbamazepine, valproic acid, phenytoin and phenobarbital levels could be measured in the DEUH laboratories, serum levels of the other anticonvulsants could not be measured. Therefore, anticonvulsant agent levels could be measured in about 73% of the patients. The measurements indicated toxic levels in about three quarters of the patients who underwent anticonvulsant level testing, and non-toxic levels in about one-third. The severity of clinical signs and symptoms associated with toxic serum levels were significantly higher than those associated with non-toxic levels. Clinical signs and symptoms were evaluated in a large part of the phenytoin exposed cases (86%) and, approximately one third of the carbamazepine exposed cases. Clinical signs and symptoms were less severe in the valproic acid and oxcarbazepine users in comparison to other anticonvulsants. These results are not surprising for drugs with a narrow therapeutic range such as phenytoin and carbamazepine, since overdoses may easily produce toxic effects while more serious poisoning may develop when used in combination with other anticonvulsant agents.

A variety of treatment modalities are used in the treatment of anticonvulsant overdose. Gastrointestinal decontamination methods used in a study conducted by Caravati include, vomiting induction using ipecac syrup (58%), activated charcoal alone (9%), gastric lavage combined with activated charcoal (7%), and ipecac syrup combined with activated charcoal (3%) (18). In a survey conducted by Andıran et al. (12), it was stated that mechanically induced vomiting was used in 20% of the cases of poisoning. Most patients received nonspecific supportive therapy and general decontamination methods have been used in a high percentage of patients (gastric lavage in 48%, activated charcoal in 55%, repeated doses of activated charcoal in 30%), enhanced elimination methods such as hemodialysis were used in only eight patients (1.6%) (12). In contrast to the study of Caravati et al. (18), induced vomiting was not used as a treatment modality in a study conducted by Andıran et al. (12). These results are important in terms of complications that may occur, American and European Poison Information Centers toxicity studies are being published in accordance with the gastrointestinal decontamination applications. In our study, gastrointestinal decontamination was used in about 79% of the patients, and supportive observation was used in about 17% of the patients. When considering that one third of the patients were admitted to the emergency department within two hours after the ingestion, gastric lavage and activated charcoal might be used in all of these patients. The Poison Information Centers in the United States and the European Union issued intoxication, gastric lavage and administration of activated charcoal guide, the proposal does not comply with gastrointestinal decontamination applications (19, 20). Even in cases of disability or death developments in purchasing toxic doses, it considered that decontamination methods and supported treatment are effective.

The length of hospital stay in case of an anticonvulsant overdose depends on the type of the drug, ingested amount of anticonvulsant, occurrence of clinical signs and symptoms. In a study about poisonings performed in our country, 15% of cases were discharged from hospital within 1 to 12 hours, 47% within 13 to 24 hours and 38% after 48 hours, respectively (21). In our study, the average length of stay in the emergency department was about 20 hours. In addition, the length of hospital stay was 8 to 24 hours in about 45% of the cases. Our results are consistent with other researchers reported from our country. In our study, the fact that the short duration of hospital stay under 24 hours in the patients with anticonvulsant overdose who were admitted to the DEUH emergency department, prevented further increases in hospital costs and unnecessary bed occupancy in the emergency department. Anticonvulsants generally have a narrow therapeutic index and create serious poisoning symptoms. In our study the analysis of the treatment outcomes revealed that most patients (88%) recovered and discharged from the hospital. In the study of Nixon et al. (3), in the patients who were poisoned with anticonvulsant, 78.3% of the patients were discharged from the hospital. In addition, 61% of the patients in our study were observed in the emergency department, 8% of the patients were hospitalized and 8% were referred to another health care facility, 13% were monitored in the intensive care unit, 10.4% left the emergency department on their own will.

In our study, the number of anticonvulsant exposures was limited. Our poisoning rate may be lower than the actual anticonvulsant exposure rate. These must be interpreted as minimum frequencies because of the limitations of retrospective data gathering. Also, the measurements of anticonvulsant levels were measured in 72.7% of the patients due to limitations of our laboratory measurements facilities. These data may be limitations of our study.

In conclusion, patients who admitted to the Dokuz Eylül University Hospital emergency department because of anticonvulsant overdose had mainly ingested carbamazepine, valproic acid and phenytoin. In three quarters of cases, the reason of exposure to high doses of an anticonvulsant agent were intentional (suicide, abuse) ingestion. There are no clinical signs and symptoms in one-third of the patients. When considering that one third of the patients were admitted to the emergency department within two hours after the ingestion, gastric lavage and activated charcoal might be used in all of these patients. In addition, the length of the stay in 45% of the cases was found 8 to 24 hours. The length of observation is particularly important with carbamazepine, since the onset of the clinical signs and symptoms may be delayed due to the anticholinergic effects of carbamazepine. Therefore a prolonged period of observation is recommended for carbamazepine overdoses. The Drug and Poison Information Centre (DPIC) has an important role in terms of recommendations and guidance in the reduction of hospital observation period in anticonvulsant overdoses and provides recommendations for appropriate decontamination methods.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Dokuz Eylül University School of Medicine.

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

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