# Carbamazepine Poisoning and Effect of Multiple-Dose Activated Charcoal

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**Abstrac**t: Introduction: Carbamazepine is commonly used in a variety of indications. Poisoning by this drug, can lead to coma, seizures, cardiac disorders and respiratory distress. The treatment of poisoning is generally supportive. Method: 68 poisoned patients with carbamazepine, who referred to poisoning ward of Loghman Hospital, from July 2003 to September 2004, were studied. These patients were investigated for demographic details, complications and types of treatment. Patients were grouped into two, receiving either single dose of activated charcoal (30patients) or multiple doses of activated charcoal (38patients). Results: 58.8%of patients were female and 41.2% were male, the average age being 24.2 years old. The most obvious clinical symptom was a decreased level of consciousness, in 69% of cases. Therapeutically, those taking multiple doses of charcoal, were about 24 hours faster in recovery from clinical symptoms and leaving the hospital than other patients. Conclusion and Recommendation: The results of this study are compatible with previous ones. Factors like education for suitable management, good care and psychiatric consult have important roles in prevention and treatment. Furthermore, administration of repeated doses of charcoal is therapeutically very important.



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**Key words:** Carbamazepine, poisoning, activated charcoal

## Introduction

One of the frequently used drugs for treatment of convulsion is carbamazepine. This drug was approved in 1968 by F.D.A for treating simple partial, complex partial, and generalized tonic-clonic sizures. Nowadays, it is also used in bipolar disorders, trigeminal neuralgia, neuroleptic pain, and many other conditions, especially in patients who already have cerebral complications and behavioral disorders; therefore, the poisoning is very common (1,2). Carbamazepine is an Iminostilbene derivative, which is chemically similar to Imipramine and constructively similar to phenytoin. It limits the repetitive firing of the brain neurons involved in seizures (3). The daily therapeutic dosage is 200 mg, and the therapeutic serum level is 4-12µg/ml (4). Poisoning can be characterized as acute or chronic; acute poisoning can be accidental or suicidal and chronic poisoning results from inappropriate dosing of the drug and poor monitoring. Because of the narrow therapeutic index, patients may manifast poisoning with a little change in the dosage (5). The poisoning symptoms appear within 1- 3 hours. But sometimes, with extended-release formulations, it takes about 30 hours. Poisoning by this drug, can lead to cerebral disorders (ranging from a mild decrease in level of consciousness to coma, headache, ataxia, convulsions, and decreased deep tendon reflexes), visual symptoms (nystagmus, ophtalmoplegia), cardiac disorders (QRS widening, heart block, arrhythmia), breathing disorders (respiratory distress, bradypnea, and apnea), digestive disorders (abdominal pain, decreased GI movements), and urinary disorders (urinary retention) (3, 4, 6).

From the laboratory viewpoint, measurement of the drug serum levels is needed. Ofcourse, according to the similarity in structure of carbamazepine with tricyclic antidepressants, false positive results are probable (7). The drug serum level more than 40 µg/ml is usually accompanied by the possibility of serious complications like coma, convulsion, breathing disorder, and cardiac complications (8). Electrolyte study is needed due to the possibility of secretion of inappropriate ADH (SIADH), hyponatremia and, rarely, hypokalemia. Acidosis is not very common, unless in case of convulsion or hypertension; there are also some reports of the increase of the liver enzymes (9).

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The treatment of poisoning is generally supportive . GI lavage has to be done. In case of respiratory distress or convulsion, symptoms must be treated. The prognosis is often good, but death can ensue convulsions or pulmonary aspiration (3, 10, 11).

Because of the its vast usage and high prevalence of poisoning with this drug, and also knowing that with good care and appropriate treatments, serious complications and mortality can be prevented, and regarding the fact that a general study in this field has never been done in Iran , the recent study was performed with the aim of investigating the prevalences, clinical symptoms, complications, and management of this poisoning in patients referring to the poisoning ward of Loghman hospital, the most important toxicology center in Iran, and comparing the results with those of similar foreign studies.

## Patients and Methods

This study was approved by the ethics commity of Tehran University of Medical sciences. All patients' records were kept confidential.

This was a randomized controlled study performed from July 2003 to September 2004 in the poisoning ward of loghman hospital, Tehran. In this study, 68 poisoned patients with carbamazepine , who were all older than 13 and whose poisoning was confirmed by clinical examination and paraclinical tests, were studied.

The following patients were excluded from the study:

Those who had taken other drugs including anticonvulsants in addition to carbamazepine; those who had taken some unknown drug; those in whom it was not possible to confirm carbamazepine as the cause of poisoning; those who had taken this drug, but still, they did not need to be hospitalized, or those who left the hospital before the treatment process was completed.

Their clinical symptoms, were recorded since admission and complications evaluated. Eight patients were admitted to I.C.U. and the rest to the ward. One of the therapeutic protocols in these patients, was the administration of charcoal. In all patients admitted to I.C.U. and 30 patients of the ward, multiple doses of charcoal were administered, whereas the resting 30 patients -who were chosen randomly- received single doses of charcoal. The recovery time was studied in both groups. The rest of the treatment was supportive.

The sample size was measured acoording to the descriptive studies formula and the *p* value was calculated based on the number of controls with carbamazepine poisoning in Loghman Hospital, in previous years. Data was analysed by the SPSS software.

## Results

40 patients (58.8%) were female, and 28 (41.2%) were male. Their ages varied from 13 to 65, with an average of 24.2. In 66 patients, the invertal between carbamazepine consumption and referring to the hospital ranged between 0.5 and 15 hours, with an average of 7.44 hours. in 2 cases, however, this interval was not certain. The number of the pills taken varied between 6 (1.2g), to 120 (24 g), with an average of 34 pills (6.8 g). In 7 men (10.3%), and 10 women (14.7%), had a history of previous carbamazepine consumption, one case because of depression, and others due to treatment and prevention of convulsion, in cases of previous brain damage. All of these pationts had poor control of drug consumption. 28 (41.2%) patients had a history of attempted suicide by pills (21 patients; 39.9%) or autoinfliction (7 patients; 10.3%) out of which, there were 9 men and 19 women.

In 2 patients convulsion was observed, one of which happened at the time of admission; and the other after 2 hours. The second one, had a previous history of convulsion. Eight patients were sent to I.C.U including all cases with grade 3 and 4 of decrease in level of consciousness (at the time of admission); and one patient with grade 2 of decrease in level of consciousness, that after 3 hours from admission, his consciousness had worsen. Twelve patients (17.6%) needed intubation because of respiratory depression; 8 of whom were connected to ventilator, and 2 (2.9%) had convulsion. In 6 patients (8.8%), there were pneumonia, and bronchitis; and 1 patient (1.4%) had GI bleeding in second day of admission. Therapeutically, intubation had been done in all cases needed (12 patients), and in 2 cases, the convulsion was treated by diazepam. Gastric lavage and charcoal administration was done via nasogastric tubes. In 30 cases, a single dose of charcoal was given, and in other cases (including all patients with grade 3 and 4 decreases in level of consciousness), repetitive doses of charcoal were administered (100 g, every 4 hours).

The other therapeutic measures were conservative. About the duration of hospitalization, generally, the average was 51.5 hours. The average time of admission in 8 patients, in I.C.U, was 108 hours (SD: 12.9); and in the other 3 patients, who received multiple doses, it was 31 hours (SD: 8.9); in the other cases, who received

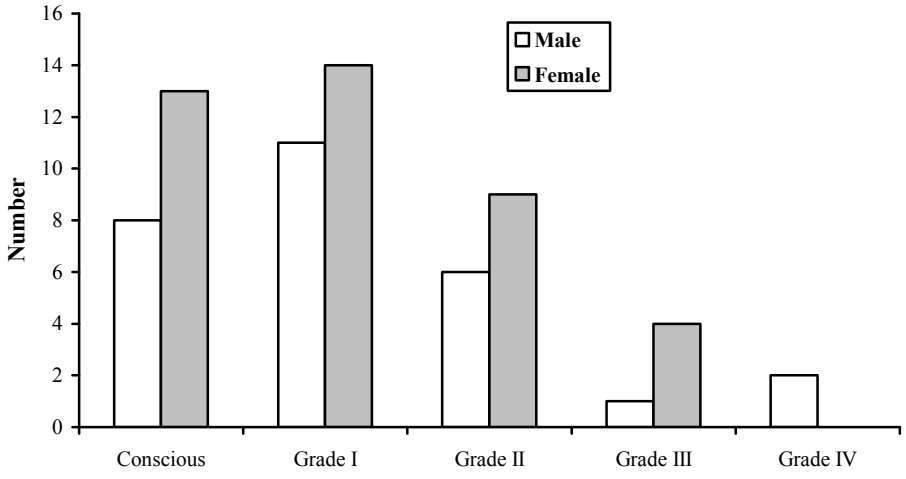


**Figure 1.** Evaluation of the level of consciousness in patients with carbamazepine poisoning, in Loghman hospital from July 2003 to September 2004

a single dose of charcoal, the average time was about 55 hours (SD: 8.5); which proved a scientific significant difference ($P$ <0.05). Psychiatric consultation was done in all of the poisoned patients.

There was only one case of death, who had taken 120 pills, followed by a sudden decrease in level of consciousness (grade 3). He was taken to the hospital 6 hours after suicide commitment and had been sent to I.C.U, but unfortunately died after 18 hours of hospitalization.

**Table 1.** Investigating the condition of 8 carbamazepine-poisoned patients, admitted to I.C.U, in Loghman hospital, from July 2003 to September 2004.

| No. | previous drug consumption | previous suicide attempt | Amount of consumption (tablet) | Level of consciousness | Serum level of drug (µg/ml) | Complication | Hyponatremia | Duration of admission (day) |
|---|---|---|---|---|---|---|---|---|
| **1** | + | + | 65 | Grade II | 50 | respiratory | + | 5 |
| **2** | - | - | 120 | Grade IV | >60 | respiratory-GI bleeding | + | dead after 2 days |
| **3** | - | + | 80 | Grade III | >60 | respiratory | - | 4 |
| **4** | - | + | 100 | Grade IV | >60 | - | - | 9 |
| **5** | + | - | 60 | Grade III | >60 | - | + | 4 |
| **6** | + | + | 70 | Grade III | >60 | - | - | 5 |
| **7** | - | - | 100 | Grade III | >60 | respiratory | - | 7 |
| **8** | - | - | 70 | Grade III | >60 | respiratory | + | 6 |

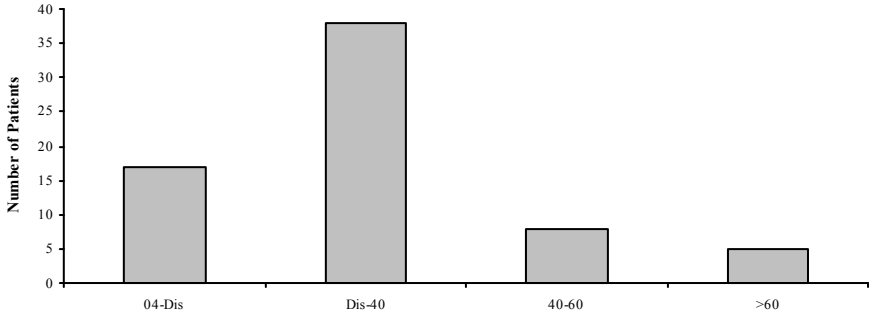


**Figure 2.** The serum levels of carbamazepine in the poisoned patients in Loghman hospital, from July 2003 to September 2004

## Discussion

A comparison between the present study and the others shows some similarities, and some differences. Feldman and his colleagues did the study on 77 carbamazepine-poisoned patients -36 women (46.7%), and 41 men (53.3%) (12). Also, in the study done by Isbister and his colleagues in the Hunter center, in New Castle (UK), 103 patients poisoned with carbamazepine were included -59 male (57%), and 44 female (43%) (13). In our study, we had 68 patients, 28 of whom (% 41.2) were male, and 40 (58.8%) were female.

The rate of poisoning with this drug, in our country, is higher for women. This may stem from of the higher rate of suicide by poisoning in Iranian women. Regarding the age, Feldman and Isbister reported an average age of 31.5 and 32, respectively (12, 13). In our study, this was 24.2 years. It is shown in our study that the average age, was younger which can be because of many factors, such as the general younger population in Iran, when compared to the other countries. About 25% of patients had taken the medicine before. Most of them took it, for convulsion. For other cases, they had bought it from the drugstores without any prescriptions or had taken other people's medicine, and this shows the importance of keeping the medicine, and delivering it, especially for those who suffer from convulsion and depression.

In Isbister's study, the average time between taking the medicine, and referring to the hospital, and admission, was 4.16 hours 13, and in our study it was 7.44 hours. The reasons for this divergence could be various, (e.g. the limited number of the poisoning clinics, and the time/distance to such clinics). The average amount of drug consumption in this study was 6.8 g, the maximum amount being 24 g. All patients who had taken more than 15g had a serious poisoning condition, with a necessity to be sent to I.C.U; and none of the poisoned patients who had took a less amount faced decrease in level of consciousness more than grade 2, only one case, with 19 g, and grade II of decrease in level of consciousness, had been referred; his alertness condition worsen, and was sent to I.C.U. Also based on a study, done in the Louisville University (US), there is coordination between the amount of the drug taken and the intensity of symptoms of poisoning (14).

In the study of the clinical symptoms, the most important finding was the effect of carbamazepine on C.N.S, *i.e.* a decrease in level of consciousness (3). Also in our study, the most common clinical finding was decrease in level of consciousness at the time of admission, in 69.1% of all cases (from grade 1 to 4). In Saymour JF's study in Australia, convulsion was observed in 24% of all cases (15). In our study, 2.9% of patients had convulsion. This difference may be because in Saymour study, those with more serious poisoning were studied (12g, against 6.8 g). Based on Feldman's study, there is a direct relation between the serum levels (higher than 40 μg/ml), and the clinical symptoms (12). In our study, 12 patients had respiratory distress, and high grades of decrease in level of consciousness, all of which had a serum level higher than 40μg/ml. In levels less than 40 μg/ml, no direct relation was found between the intensity of the clinical symptoms and the serum level ($P < 0.05$). In Isbister's study, 26% of the poisoned patients with carbamazepine were admitted to I.C.U (13). In our study, 8 patients (11.7%) were sent there, of whom all had ingested high amounts of this drug, and the serum level was higher than 40 μg/ml. Most of the complications in this study were observed in these patients, who needed mechanical ventilation, because of respiratory depression. The reason for the difference in the rate of admission in I.C.U was limited number of beds in the I.C.U, in Loghman Hospital. If there were

more beds, more patients would be admitted there. Based on the study done from 1993 to 1997 in the US, 4.2% of poisoned patients had serious complications (6). In our study, 17.6% of patients had respiratory distress, which needed intubation. Pneumonia and brounchitis were observed in 8.8% of all cases, which included 5 intubated patients. Two (2.9%) cases experienced convulsion, both of whom were sent to I.C.U, and in one of them, also G.I. bleeding occurred.

Therapeutically, in all of the patients GI lavage and charcoal administration were done via nasogastric tubes. In 38 cases, including all who were sent to I.C.U, and 30 patients with normal level of consciousness or grade 1 and 2 of decrease in level of consciousness admitted in ward, multiple doses of charcoal and sorbitol were given (100g chorcoal every 4 hours up to 24 hours) and in the other 30 patients (with normal level of consciousness or decrease in level of consciousness with grade 1 and 2), a single dose of charcoal was administered. The average time of admission in I.C.U was 108 hours (SD: 12.9) and in other 30 patients who had received multiple doses, this time was about 31 hours (SD: 8.9). In the group receiving a single dose of charcoal, this value was about 55 hours (SD: 8.5) being statistically significant ($P < 0.05$). Based on the studies in America, and Mexico, the prescription of the multiple doses of charcoal accelerates the improvement and recovery of carbamazepine poisoned patients (16, 17). The rest of the therapeutic measures were supportive. The pH of their blood was set to normal by prescribing bicarbonate; in cases of convulsion, diazepam was prescribed and in cases of respiratory distress, intubation, and if needed mechanical ventilation, were performed.

In the study that was performed from 1993 to 1996 in America, the mortality caused by this poisoning was less than 1% (6). In our study, only one patient died (1.4%), and since the general number of the patients in our investigation were less than that mentioned in the foregoing study, there could not be found a significant difference between these two studies. The dead patient had a sudden decrease in level of consciousness with grade 3 at the time of admission, and had taken 120 pills; he had referred to the hospital 6 hours after consumption of the drug. This patient was immediately intubated and was sent to I.C.U, and had GI bleeding, supraventricular arrhythmia, and convulsion.

Generally, for preventing such kinds of poisoning, it is necessary for the physicians to take good care, especially in prescribing accurate amounts of drug during treatment. Drug prescription should merely be done by physicians. Administration of the repetitive doses of activated charcoal should be considered, as it decreases the hospitalization period and accelerates the improvement of patients. Psychiatric consultation must be done in all of the poisoned patients with this drug.

Also, it is necessary to increase and better equip poisoning clinics in Iran.

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