Background: Carbamazepine is an iminostilbene derivative structurally related to cyclic antidepressants which implies its potential cardiotoxic properties, especially in acute poisoning. This study aimed to determine the frequency and severity of cardiovascular complications in carbamazepine intoxication and its relationship with level of consciousness.

Methods: Patients with carbamazepine intoxication referred to our department recruited using convenience sampling method. Analysis included following parameters: systolic (SBP) and diastolic (DBP) blood pressure, ECG parameters: heart rate (HR), QRS width, PR interval and corrected QT interval (QTc). Relations between features on admission, 12 and 24 hours later and level of consciousness evaluated.

Results: 77 patients (28 males, 49 females; median age 25.1) which got our criteria included in this study. QRS complexes in 9 cases (11.7%) were wider than normal and PR interval and corrected QT interval (QTc) were normal. There was no significant relationship between QT interval, QRS width and pulse rate changes with level of consciousness during 24 hours post admission, but blood pressure [systolic, diastolic and mean arterial blood pressure (MABP)] progressively decreased and PR interval changes progressively increased during this period. Further, there was negative correlation just between sever decrease of level of consciousness (coma) and blood pressure [systolic, diastolic and mean arterial blood pressure (MABP)], and positive correlation with QRS complexes widening at 12 hours after admission. There was no correlation between loss of consciousness and diastolic blood pressure, QT interval and PR interval on admission and 12 hours and 24 hours later.

Conclusion: Regarding the relationship between level of consciousness and cardiovascular changes at 12 hours after admission, particular attention on cardiovascular changes and ECG monitoring particularly in intoxicated patients with severe loss of consciousness(coma), should considered; it will lead to prevent unexpected complication, mortality and to decrease the length of hospitalization. Key words: Carbamazepine intoxication, Blood pressure, level of Consciousness, ECG parameter

1. INTRODUCTION

Carbamazepine is an iminostilbene derivative structurally related to cyclic antidepressants which implies its potential cardiotoxic properties, especially in acute poisoning. It has prescribed for many approved indications, including trigeminal neuralgia, partial seizures, and generalized tonic-clonic seizures (1). It has also been used in treating bipolar-affective disorder, alcohol withdrawal syndrome, resistant schizophrenia, pain syndromes, and restless legs syndrome. It is usually preferred to phenobarbital or phenytoin because of its powerful antiepileptic activity combined with a relative lack of adverse effects and may be especially useful for pregnant women with epilepsy.

Possibility of intentional carbamazepine poisoning increases because of it has prescribed for many approved indications and access to psychiatric patients.

Carbamazepine is absorbed slowly and erratically. Peak serum concentrations occur at 4–8 hours after administration of immediate-release tablets and up to 12–24 hours after slow-release preparations (2). Carbamazepine poisoning has a wide range of clinical manifestations, usually involving the central nervous, cardiovascular, and respiratory systems. The onset of toxicity is usually within 1–3 hours after ingestion. Mild poisoning associ-
ated with drowsiness, ataxia, slurred speech, nystagmus, and tachycardia. With severe overdose, dysrhythmias, myocardial depression, hypotension, coma, seizures, and respiratory depression may result.

Serum carbamazepine concentrations above 40 μg/mL associate with coma, seizures, respiratory depression, and cardiotoxicity (1).

Cardiovascular complications are sinus tachycardia, hypotension, myocardial depression, cardiac conduction disorders (3) and ECG parameters changes such as increase in the PR and QT intervals and QRS complex widening (1).

The frequency of cardiovascular manifestations is controversial in different studies. Sinus bradycardia, supraventricular tachycardia, QRS widening, tachycardia and the increase in all ECG parameters mentioned in some references, but as a whole, cardiovascular manifestation rarely reported.

Hypotension, QRS widening and QT prolongation are much less common than in TCA poisonings (4, 5) while in another reference, QRS width to more than 100 ms in 15% of cases and QT prolongation to more than 42 ms in 50% of cases is reported (1).

Apfelbaum et al (6) showed significant cardiovascular toxicity be rare in CBZ poisoning and no correlation between ECG changes and serum carbamazepine level. Ciszowski et al. (6) failed to find any significant correlation between CBZ plasma level and any of the studied parameters but they mentioned Positive correlation between SBP and DBP and negative correlation between QRS and HR (7).

Referring to mentioned study (7) and in the view of Tibballs et al (8) study which they figured out the level of consciousness has a stronger correlation with the severity of poisoning in contrast to CBZ plasma level and because In all hospitals there is no possibility of measuring plasma levels of carbamazepine, this study aimed to find out the frequency and severity of cardiovascular complications in carbamazepine poisoning and its relationship with level of consciousness.

2. METHODS

In a cross-sectional study, patient with CBZ poisoning based on history referred to our clinical toxicological department recruited using convenience sampling method.

Exclusion criteria were co-ingestion cardioactive drugs, such as TCA, Digoxin, beta-blockers or type I antiarrhythmic drugs, any history of cardiovascular disease and death on admission.

Analysis included following parameters: systolic (SBP) and diastolic (DBP) blood pressure, ECG parameters: heart rate (HR), duration of QRS complex, PR interval and corrected QT interval (QTC). These measurements repeated twice daily. Level of consciousness based on GCS divided into 3 categories [severe with a Glasgow Coma Scale (GCS 3-4), moderate (GCS 5-8), mild or normal (GCS 9-15)]. Relations between mentioned parameters on admission, 12 and 24 hours later and level of consciousness evaluated.

Standard descriptive analysis performed. Statistical significance accepted if P was less than .05. Values are expressed as mean±SD. ANOVA Repeated measure, fried man, x2 and paired sample t-test used to define the correlation between variables.

3. RESULTS

Seventy-seven patients 49 female (%63.6) and 28 male (%36.4) met inclusion criteria. Mean age 25.1 ± 8.1 years. Number of carbamazepine tablets (200 mg) ingested was 5 and 100 and the average number was 27.3 ± 21.3.

The frequency of ECG changes on admission and after 12 hours show on table 1. There was no significant change on QRS width and QT interval in the first 12 hours (P>0.05) but PR interval significantly increased (P=0.014). ANOVA Repeated Measure test showed that systolic, diastolic and mean arterial BP significantly decreased on the first 24 hours of hospitalization (P values were 0.027, <0.001 and 0.001 respectively).

Unlike any of the patients presented with bradycardia on admission 13 patients (16.9%) had tachycardia and this
Relationship of Cardiovascular Complications with Level of Consciousness in Patients with Acute Carbamazepine Intoxication

MED ARH. 2012; 66(2): 9-11 • ORIGINAL PAPER

4. DISCUSSION

A significant correlation exists between the changes in systolic, diastolic and mean arterial blood pressures and carbamazepine toxicity. A significant decreases noted in all three features during the first 24 hours of admission. This follow some others studies (4, 7).

Although PR interval increase in first 12 hours was as other studies (4) but it was on the contrary of others findings (1, 6). There was no change do served in the width of QRS complex in the first 12 hours. Finding matches by other previous studies (6, 9) but it not supported by others (1, 4).

Unlike the study of Apfelbaum and colleagues (6), there was no significant change in the QT interval in the first 12 hours of hospitalization, but this was in harmony with (1, 4). Gradual decrease level of consciousness was significant, and this supported by others (1, 4).

There is no similar study about the correlation between the change in the level of consciousness with the changes in QRS width, QT intervals and PR intervals on admission and after 12 hours. There was no relationship between different level of consciousness and systolic and mean arterial blood pressure decrease and on admission, but this finding was significant after 12 hours, supporting findings in other study (4).

There was no significant compellation between loss of consciousness and the changes in pulse rate (tachy and brady cardia) on admission, but this was significant after 12 hours that is compatible with others report (1, 4).

5. CONCLUSION

Considering maximum CBZ concentration reaches after 12 hours, and since the relationship between the level of consciousness with pulse rate, systolic and mean arterial blood pressures, and QRS width on the 12th hour of admission determined, close cardiovascular monitoring of patients presented with decreased levels of consciousness (especially patients in coma) in order to decrease the morbidity and mortality and duration of hospitalization strongly recommend.

Conflict of interest: none declared.

REFERENCES


