Case Report
Toxicology International, *Sept-Dec 2017 / Vol-24 / Issue-3, 309-312*
ISSN (Print) : 0971-6580
ISSN (Online) : 0976-5131
DOI: 10.22506/ti/2017/v24/i3/166496

A Child with Coma, Hypotension, Respiratory Depression and Cardiac Conduction Disturbance - Carbamazepine Poisoning

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Abstract

Previously healthy child presenting with coma, hypotension and respiratory depression is challenge to the treating clinician. The wide availability of anticonvulsants increases the risk of overdose, may be intentional or accidental. Adequate history taking is very important to clinch the diagnosis. The clinical spectrum of carbamazepine poisoning may range from drowsiness to profound coma with respiratory failure. Cardiotoxicity is rare, presents primarily as conduction disturbances. Here with we report a 14 year old boy who presented with coma, respiratory depression, hypotension and cardiac involvement. The diagnosis of carbamazepine toxicity was revealed only after adequate history taking and toxicology screening.

Keywords: Carbamazepine, Coma, Conduction Disturbance, Hypotension, Screening.

Received: 17-10-2016 **Revised:** 21-08 -2017 **Accepted:** 03-09-2017

Introduction

Carbamazepine is used as one of the primary anticonvulsants in clinical practice (1). The wide availability of the drug increases the risk of overdose, may be intentional or accidental (1). Among 1880 single exposures to carbamazepine in the year 2014, 62 patients developed major toxicity(2). Lifshitz et al reported carbamazepine poisoning in 14 children and all of them accidentally took carbamazepine prescribed for a family member (3). The clinical spectrum of carbamazepine poisoning usually involves the central nervous, cardiovascular and respiratory systems. Cardiovascular involvement is rare in children (2). We report a 14-year-old boy who presented with sudden onset coma, respiratory depression, hypotension and cardiac involvement. The diagnosis of carbamazepine toxicity was revealed only after adequate history taking and toxicology screening.

Case report

A 14-year-old developmentally normal boy brought at 11 AM with history of altered sensorium since morning 6 AM. There is no history of fever, headache, vomiting, convulsions, trauma, drug intake or unknown bite. On examination his vitals were temperature 98^0F, RR 13/minute shallow, PR 110/minute with cold peripheries, BP 80/50 mm of Hg, CFT >4seconds and SPO_2 96 %. Nervous system examination revealed GCS of 9/15,pupils normal & reactive, tone normal, reflexes not elicitable

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and without signs of meningeal irritation. Other systems examination was unremarkable. Provisional diagnosis of encephalitis/unknown poisoning with shock and respiratory depression was made. Investigations are shown in the table 1. He was started on 20ml/kg normal saline three bolouses along with stomach wash. Intubation set & ventilator kept ready. Activated charcoal was given through ryles tube. Started on inj phosphenytoin, acyclovir and ceftriaxone. With 3 bolouses still he was in hypotension, therefore inj dopamine 10microgram/kg/minute started. After increasing the dopamine infusion to 15 microgram/kg/min also, still his BP was 86/68 mm of Hg, PR 112/min with cold extremities and shallow respiration of 15/minute. Therefore inj adrenaline infusion 0.5microgram/kg/miute started. After 20 hours of admission he started regaining consiousness and by 24 hours his GCS improved to 15/15 with normal vitals and good respiratory efforts. Oral feeds given, stopped phosphenytoin & acyclovir and started tapering inotropes over 12 hours. He was discharged after 5 days.

Discussion

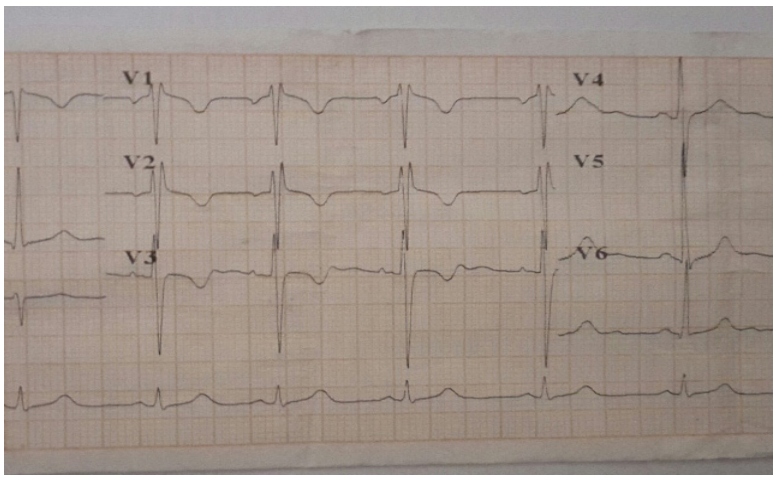
The clinical spectrum of carbamazepine poisoning usually involves the central nervous, cardiovascular and respiratory systems. After ingestion toxicity usually occurs within 1–3 hours (4). Mild poisoning usually manifests as ataxia, slurred speech, nystagmus, and tachycardia. Severe poisoning presents with coma, respiratory depression, hypotension, seizures, dysrhythmias and myocardial depression (4). Out of 30 children with carbamazepine overdose, 27% presented with coma and 10% had minor arrthymias (5). Out of 427 cases with carbamazepine overdose 40%developed coma, 13% had respiratory depression and 13% of them had fatal outcome (6). The course of carbamazepine intoxication seems to be more benign in patients aged below 15 years(6). However our child condition was critical.

Lifshitz et al reported carbamazepine poisoning in 14 children and all of them accidentally ingested carbamazepine prescribed for a family member like in our child. At the time of admission due to inadequate history the diagnosis of carbamazepine poisoning in seven children was not made and was revealed only on toxicology screen (3). In our child also we could not account for coma in a previously healthy child, therefore one of the diagnosis kept was unknown poisoning. On history taking one family member was on carbamazepine and phenobarbitone tablets for seizure disorder. This significant history along with serious clinical condition made us to ask for toxicology screen. Toxicology screen revealed carbamazepine levels (CLIA) of 7.75µg/mL which is normal [Therapeutic range= 4-12 µg/mL] & phenobarbitone levels of <0.40µg/mL [Therapeutic range=15-40µg/mL]. Probably he had ingested more number of carbamazepine tablets and few phenobarbitone tablets. But clinically he was in coma with respiratory depression and hypotension. Children are at risk for serious morbidity of carbamazepine overdose at lower serum concentration when compared to adults and the serum levels alone are not accurate predictors of risk in children (7). Due to delayed absorption of carbamazepine, the carbamazepine levels may peak as late as 72 hours(2).

Majour cardiovascular manifestations include sinus tachycardia, hypotension, myocardial depression and conductive disorders (4). Cardiovascular effects are rarely observed in children (2,8). ECG abnormalities due to carbamazepine overdose include bradycardia, sinus tachycardia, supraventricular tachycardia, wide QRS, long QRS complex, atrioventricular block, long PQ segment, long QT segment and ventricular fibrillation (2,4,8). Ciszowski et al observed PQ prolongation in 21% and QRS widening in 60%with with carbamazepine toxicity (8). Study by Apfelbaum et al concluded that significant cardiovascular toxicity is rare and there was no correlation between ECG changes and serum carbamazepine levels (9). Although arrhythmias are rare in children our child ECG revealed right bundle branch block (RBBB) which became normal after 2 days [Table 1](2).Cardiovascular conduction disturbances occur due to blocking the sodium channels in the cardiac conducting system and are not related to the plasma level of carbamazepine (2,8,9).

In our child hypotension is probably it is due to CNS involvement rather than due to cardiac involvement. Hypotension responded to two inotropes and fluids. A significant correlation exists between the blood pressure [both in systolic & diastolic] and mean arterial blood pressures with carbamazepine toxicity (4). During the first 24 hours of carbamazepine toxicity there was significant decrease in blood pressure (4). Out of 427 cases with carbamazepine overdose, lowering of BP occurred only in 2% in a study by Schmidt et al (6). Hypotension can be associated with either therapeutic or toxic blood levels of carbamazepine (8).

Table 1: Investigations

Hb12.8gm/dl, TLC, 16110/mm^3 [N 86 % ,L 9 %], Platelets 2.72 lakhs/mm^3
Blood urea 18 mg/dl,Serum creatinine 0.7 mg/dl, Sodium 135mEq/L,Potassium 3.8mEq/L
Total Calcium 9.5 mg/dl,Ionoized calcium 1.21 mg/dl,Magnesium 1.5 ng/dl,Blood sugar 118 mg/dl
Total bilirubin 0.2 mg/dl, Direct 0.15 mg/dl,SGOT 45 U/L,SGPT 18 U/L ,Alkaline Phosphatase 603 U/L,Total protein 7.03 gm/dl ,Albumin 3.86 gm/dl PT control 14.2 seconds, Patient 17 seconds,INR 1.25 APTT 33 seconds
CPK-MB 21.55[Normal=1 to 7ng/ml],Troponin-T=0.005ng/ml [Normal=0.0001-0.0249]
CSF analysis normal, Peripheral smear for Malarial Parasite negative, CRP 1.5mg/L
pH 7.28,pCO_2 36.9 mmHg, pO_2 223mm Hg ,BE --8.5 mmol/L, HCO_3 17 mmol/L, Lactate 1.0mmol/L
Echocardiography normal study MRI Brain normal study EEG normal
ECG revealed RBBB (right bundle branch block) features with T wave inversion ,PR=0.12sec,QT=0.34sec

Toxicology screen Carbamazepine levels=7.75µg/mL [Therapeutic range =4-12 µg/mL] Phenobarbitone levels= <0.40µg/mL[Therapeutic range=15-40 µg/mL]

During the management, watch for shock and respiratory depression in the first 24 hours (2,4). In fact, the initial carbamazepine level may be misleading and the serum levels may not always directly correlate with the clinical picture like in our case (2). The severity of toxicity is should be assessed based on clinical features and ECG findings rather than carbamazepine plasma concentrations (2,8). Our child carbamazepine levels were within therapeutic range, but he was in deep coma with respiratory depression, hypotension and cardiac involvement [conduction disturbances]. Patel et al observed that 3.5% had initial carbamazepine concentrations within the therapeutic range (4-12 µg/mL) and 1.3% had initial subtherapeutical carbamazepine levels (<4 µg/mL) before rising to levels>12 µg/mL. They also noted that several cases with initial therapeutic or subtherapeutic levels deteriorated to became comatose and required ventilator (10).

To conclude carbamazepine toxicity should be suspected in a child who presents with coma, that too when any family member is on anticonvulsant therapy. We should watch for shock, cardiac conduction disturbances

and respiratory depression. The severity of toxicity is assessed and monitored based on the clinical picture not the serum carbamazepine concentration.

Conflict of Interest

None Declared

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