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Case Report

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Carbamazepine - Induced Hypoglycaemia

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Abstract

Carbamazepine is a very important drug used for treating epilepsy, mood disorder, and trigeminal neuralgia. The most important adverse reaction related to this drug are linked to its anticholinergic effects. Most of them affect the heart, brain, and metabolic system. The incidence of hypoglycaemia has been reported rarely in literature. Although its occurrence is uncommon, yet it has the potential to lead on to drastic patient outcomes. It is very easy to treat such a condition, so it is important to recognize its symptoms at an early stage, so as to take timely corrective measures. We report a case of hypoglycaemia induced by this medication.

Keywords: Carbamazepine, hypoglycaemia, anticholinergic effects.

Introduction

Carbamazepine is a first line drug used for the treatment of epilepsy. It is also used extensively for the treatment of trigeminal neuralgia, as a mood stabilizer and for treatment of neuropathic pain syndromes. It belongs to the iminostilbene group of drugs (1). It acts by prolonging the inactive state of sodium channels, as well as preventing the repeated firing of neurons. Anticholinergic effects are also associated with intake of this drug, but these effects are observed more frequently when the quantity of intake of this drug exceeds normal therapeutic dose (2). Its water solubility is not good, which is responsible for its slow rate of oral absorption and 75% of it is protein bound. The drug is an inducer of CYP3A4. That is why its chronic use requires giving a larger amount of the drug to have the same effect.

Non-dose dependent reactions associated with the use of this drug are rash and photosensitivity and rarely more serious ones such as drug-induced lupus and agranulocytosis. An overdose of this drug leads to adverse events related to neurologic, cardiac and metabolic manifestations (1, 3, 4, 5).

Case Report

Our patient was a 23 years old male who presented to the emergency department in an unconscious state. His blood pressure on presentation was 80/50, pulse rate was 106 per minute and respiratory rate was 20 per minute. His extremities were cold, bilateral plantar was down, and pupils were bilaterally dilated and sluggishly responding to light. His deep tendon

reflexes were sluggish. The patient's relatives gave a history of overdose with carbamazepine medication two hours back. He took 25 tablets of 200 milligrams of carbamazepine, which amounted to a total dose of five grams. His relatives denied intake of any other medication. The patient was a known case of seizure disorder and was taking carbamazepine 200 mg once daily for the last 4 years. At the time of presentation to the emergency department, his random blood sugar was 116 mg/dl. Intravenous access was obtained with a large bore needle, and intravenous fluid was started, low dose vasopressors were started. Gastric lavage was done and ryles tube was inserted. Intensive care unit (ICU) call was made, he was shifted to ICU and the patient was intubated for low sensorium and put on a ventilator.

His lab reports returned with findings of carbamazepine levels of 22 micrograms/ml (normal levels being 6-12 micrograms/ml), haemoglobin of 10 gm/dl, total leucocyte count (TLC) of 9200. His liver functions tests (LFTs), renal function tests (RFTs), bleeding time, clotting time and prothrombin time index (PTI) were all within normal limits. Repeat carbamazepine levels on the second day were 19.8 micrograms per ml, and on the fourth day was 16.2 micrograms/ml.

On the second day of admission, five episodes of hypoglycaemia occurred, for which the patient was given 50% dextrose, for each of these episodes, after which patient was started on 25% dextrose which was continued for the next two days to prevent a further repeat of hypoglycaemic episodes. The patient recovered from circulatory shock after 9 days of admission, he was extubated and vasopressors were gradually stopped. Carbamazepine levels were also normalized at this time (3.64 micrograms/ml). The patient was discharged after two weeks of admission and was followed up after every two weeks. No fresh episodes of hypoglycaemia were reported for the follow up for three months.

Discussion

Carbamazepine follows first-order pharmacokinetics, which means that there is a linear relationship between drug dose, serum drug levels and manifestations of toxic effects (6).

The common adverse effects of Carbamazepine are tachycardia, hypotension, QRS interval prolongation, and ventricular extrasystoles. Sodium channel blockage is supposed to be responsible for some of the cardiovascular adverse events, especially QRS interval prolongation; which may lead to ventricular arrhythmias and hypotension (7).

Rash and photosensitivity are also documented ill effects of this medication. Acute toxicity is known to manifest by symptoms such as ataxia, nystagmus, seizures, status epilepticus, and altered sensorium (8, 9). Leucopenia and aplastic anaemia are the haematological side effects related to the use of this drug (6). Although hepatotoxicity occurs commonly with chronic use, its occurrence in the setting of acute overdose is rarely seen. Incidences of acute hypernatremia have also been reported in the literature, which is believed to occur because of the higher amount of secretion of the anti-diuretic hormone (10, 11). Our patient manifested some of the common complications of carbamazepine including hypotension, tachycardia and altered sensorium (12). In addition, repeated episodes of hypoglycaemia, one of the rarely seen complications associated with carbamazepine overdose, although it had been reported with use of valproic acid another commonly used anti-seizure drug, (13). But a few studies in the past has also shown hypoglycaemia with the use of carbamazepine too, which was also noted in our patient. The reason for the cause of hypoglycaemia is unclear. The use of valproic acid has been linked to the development of hyperinsulinemia, but no such effect has been seen with carbamazepine use. In fact, studies have shown that carbamazepine protects against the development of type 1 diabetes in non-obese diabetic (NOD) mice because of the preservation of beta cells of the pancreas. (14)

Conclusion

Carbamazepine is a widely prescribe anti-seizure medication. It is important for treating physicians and pharmacists to know that hypoglycaemia is a possible adverse effect of this medication especially in the setting of acute overdose. It can be confirmed by a simple random blood sugar test, and it can be easily treated with high concentration dextrose fluids. If undiagnosed, this condition can be potentially fatal. So, random blood sugar testing in all cases of suspected carbamazepine toxicity is highly recommended.

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