

Carbamazepine Intoxication Requires not only Elevated Serum Levels, but also Symptoms of Overdose

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Dear Editor,

We were interested to read the article by Hazra et al. on a retrospective observational study of the charts over a 10-year period of 1,965 patients taking carbamazepine (CBZ).¹ In this cohort, 70 patients (3.5%) had CBZ serum levels above the upper reference limit.¹ Mild intoxication (>51 µmol/L) was observed in 44 patients and moderate toxicity (>85 µmol/L) in 26 patients.¹ An isolated overdose was found in 89% of patients, a mixed overdose in 11%.¹ The most common symptoms of CBZ intoxication were gastrointestinal symptoms and sensory disturbances.¹ Two-thirds of these patients required hospitalization. Four patients required mechanical ventilation and six patients received activated charcoal.¹ The study is appealing, but some points should be discussed.

The first point is that CBZ intoxication was defined only on the basis of CBZ blood levels and not on clinical criteria. Therefore, we should know how many of the 70 patients had no symptoms attributable to the elevated CBZ levels. It would also be interesting to know how many of them had symptoms of intoxication but had CBZ levels in the normal range. Carbamazepine levels above the upper reference limits do not necessarily mean intoxication. Many epilepsy patients taking high doses of CBZ have high CBZ blood levels or levels above the upper range without clinical or laboratory evidence of intoxication, but with good seizure control. Switching to another seizure medication or reducing the CBZ dose may not be a good choice for these patients.

The second point is that the observation period was quite long, so it is important to know whether the methods used to measure the CBZ concentration or the reference limits changed during this long period. It is also important to know whether all CBZ samples were analyzed in the same laboratory or in different laboratories with different technical equipment, different reference limits and different experienced laboratory technicians.

The third point is that the cause of the chronic intoxication was not specified. We should know in how many patients the chronic intoxication is due to overdose, in how many to liver or kidney failure, in how many to enzyme induction in the liver (co-medication) and in how many to increased gastrointestinal absorption.

The fourth point is that the outcome of those who were hospitalized was not reported. It was only stated that none of the 70 hospitalized patients died. We should know whether any of the hospitalized patients had long-term side effects or whether all hospitalized patients recovered completely and after what time.

The fifth point is that CBZ intoxication is not only characterized by gastrointestinal symptoms (e.g., nausea, vomiting), central

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nervous system (CNS) symptoms (e.g., nystagmus, agitation, hallucinations, seizures, ataxia, altered mental status, coma) and cardiac manifestations (e.g., arrhythmias), but also with mydriasis, neuromuscular impairments, anemia, urinary retention, tremor, restlessness, hyperreflexia or dystonia.²

In summary, it can be said that this interesting study has limitations that relativize the results and their interpretation. Removing these limitations could strengthen the conclusions and reinforce the message of the study. All open questions need to be clarified before readers can uncritically accept the conclusions of the study. The definition of CBZ intoxication should not only be based on CBZ serum levels but also on clinical symptoms. We therefore suggest that only patients with CBZ levels above the upper reference limit and symptoms attributable to high CBZ levels should be considered intoxicated. Patients who tolerate elevated CBZ levels above the upper limits without symptoms should not be classified as intoxicated.

AVAILABILITY OF DATA AND MATERIAL

All data are available from the corresponding author.

Completing Interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contribution

JF was responsible for the design and conception, discussed available data with coauthors, wrote the first draft, and gave final approval.

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