



Case Report

Carbamazepine induced leukopenia: A case series

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ABSTRACT

This is a case series of 4 patients who developed leukopenia on, controlled-release carbamazepine (CBZ-CR) monotherapy for focal seizure prophylaxis. All 4 cases (2 males and 2 females), presented to the neurology department with history of episodes of sudden onset, abnormal body movements. Patients were diagnosed as cases of focal seizures and were prescribed tablet CBZ-CR 300 mg twice a day for seizure prophylaxis. One month later patients presented for follow-up and were continuing with the treatment. Blood biochemistry parameters indicated leukopenia with total leukocyte count less than 4000 per mm³. According to World Health Organization Uppsala monitoring Centre (WHO-UMC) causality assessment, all 4 cases were classified as 'probable/likely' for carbamazepine-induced leukopenia. Carbamazepine was continued and total leukocyte count gradually recovered on 3-months follow-up.

Conclusion: Total leukocyte count should be documented before initiating carbamazepine therapy. Patients with pre-existing leukopenia should not receive carbamazepine. All patients receiving carbamazepine should be monitored for leukocyte count in addition to other blood biochemistry parameters.

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1. Introduction

'Seizure' refers to transient alteration of behavior due to abnormal, synchronous and rhythmic firing of brain neurons. Antiepileptic drugs are administered orally for seizure prophylaxis.¹

Carbamazepine is used widely for focal seizure and focal with secondary generalization seizures.² It blocks voltage-gated sodium channels, responsible for the rising phase of neuronal action potentials.² Hematological adverse effects include aplastic anemia, agranulocytosis and thrombocytopenia in 1 to 2%.^{1,3} Decrease in total leukocyte count due to CBZ use is due to inhibition of colony stimulating factor in the bone marrow.³

Incidence of leukopenia is 12% in children and 7% in adults. The leukopenia and neutropenia are more common in patients with low-normal pretreatment WBC or neutrophil

counts and need frequent monitoring. Classically, WBC count may decrease by as much as 25% and this usually occurs within first three months of treatment. Leukopenia may persist in some cases without clinical significance.⁴

Abnormality in CBZ metabolism and resultant toxic CBZ metabolites has been hypothesized as the cause of hematologic dyscrasias. The lymphocytes of CBZ hypersensitive individuals are susceptible to toxic arene oxide metabolites of CBZ in vitro. CBZ did not suppress cell proliferation or function in an in vitro study. It has been postulated that hematologic effects reported in early 1960s were due to impurities in original manufactured tablet. Refined manufacturing techniques, have decreased the impurities since then.⁴

CBZ dose needs to be decreased or discontinued if WBC count falls below 3000/mm³ or neutrophil count is below 1000/mm³ or platelet count is less than 100,000/mm³.⁵

Leukopenia usually reverses, even if CBZ treatment is continued. A risk of severe infections is there when the

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neutrophil count falls below 500/mm³.⁶

2. Case

We are reporting case series of 4 patients (2 men & 2 women), from post-graduate academic thesis, who developed leukopenia within 4 weeks of CBZ-CR intake.

The patients visited neurology OPD with complaints of abnormal body movements. Each episode lasted for 3 to 5 minutes. No family history of seizures was there in any of the 4 cases. All 4 cases were having CT scan/MRI confirmed neurocysticercosis as the cause of seizures. The patients were diagnosed as cases of focal seizures. Mean age was 39.5 years for men and 23.5 years for women.

The baseline TLC was; 4400 (42 years male), 5200 (37 years male), 4600 (27 years female) and 6400 (20 years female) per mm³. Patients had no history of drug or food allergy. They were randomly allocated to CBZ-CR 300 mg orally twice daily arm. Adverse effects like somnolence and dizziness were reported by all 4 patients. They were advised to continue the treatment.

At 1st month follow-up all 4 cases were seizure free, without any complaints. Blood biochemistry revealed normal results except for leukopenia. The TLC was 3900, 3790, 3600 and 3800 per mm³ respectively. Treatment was continued.

At 3rd month follow-up 3 patients were seizure free, while the 20 years old woman had breakthrough seizure for which her evening dose of CBZ-CR was raised to 400 mg. All blood biochemistry parameters were within normal limits. The TLC rose above 4000/mm³ for all the 4 patients. The TLC was reported as 5800, 6000, 5400 and 4800 mm³ respectively. The patients were diagnosed as cases of carbamazepine induced transient leukopenia. Treatment was continued.

At 6th month follow-up all the patients were seizure free. Also, all biochemistry parameters were within normal limits. The TLC was 5700, 6100, 5600 and 5100 per mm³ respectively.

Table 1: Treatment was continued.

Patient age & gender/TLC	42	37	27	20
	Years Male	Years Male	Years Female	Years Female
TLC baseline	4400	5200	4600	6400
TLC at 1-month	3900	3790	3800	3600
TLC at 3-months	5800	6000	4800	5400
TLC at 6-month	5700	6100	5100	5600

According to the World Health Organization Uppsala monitoring Centre (WHO-UMC) causality assessment system, the cases were classified as 'probable/likely' for carbamazepine-induced transient leukopenia.

3. Discussion

There is evidence of leukopenia due to carbamazepine use. In our study 4 patients developed transient leukopenia, 1-month after CBZ intake. They were classified as drug induced leukopenia.

Owens CW. et al.⁷(1980) reported a case of 61 years patient in which TLC was reduced to 1300/mm³ from the baseline 9600/mm³ after 48 days of treatment with CBZ. This reduction was evident on blood biochemical profile because patient was suffering from malaise, sore throat and fever. Patient was suffering from oral candidiasis secondary to drug induced leukopenia. CBZ was discontinued and TLC raised to 2700/mm³ after 8 days.

Sabotka JL. et al.⁴(1990) recommended that all patients receiving CBZ, should have CBC prior to initiation of treatment. Patients should be advised to report immediately if signs and symptoms such as infections, fever, fatigue, ecchymosis and bleeding through mucous membranes appears.

Hughes JR. et al.⁸(1995) reported 28 (21.4%) cases of leukopenia at some point during treatment out of total 131 patients receiving CBZ and 18 (13.7%) cases out of 131 in control arm (p=0.072). They also reported that decrease in TLC was associated with increase in CBZ dose.

Daughton JM. et al.⁹(2006) concluded that prompt reduction or withdrawal of CBZ is warranted based on laboratory investigations. Anti-infectious therapy may also be necessary in symptomatic cases of infection due to underlying leukopenia.

4. Conclusion

Cautious monitoring and patient education regarding adverse events are of paramount importance, after starting therapy with any drug. Keeping in mind the possibility of drug induced leukopenia, it is imperative to investigate complete blood counts before initiating CBZ therapy and follow-up regularly. Patients with pre-existing leukopenia should not be treated with CBZ.

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6. Conflict of Interest

The authors declare they have no conflict of interest.

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