"Carbamazepine: A Comprehensive Review of Pharmacology, Adverse Effects And Contraindication"

T.N. VINESHA YADAV, R.D. PONMUDI, K. THIRUMULA NAIK

Pharm.D Intern, Associate Professor, Department Of Pharmacy Practice, Krishna Teja Pharmacy College, Tirupati, India

Abstract: Bipolar illness and neuropathic pain can both be effectively treated with the use of the antiepileptic medicine carbamazepine (CBZ), which is also a common AED. As a result of its agonistic actions on GABA receptors, it may also modify synaptic transmission and boost sodium channel inactivation. The pharmacokinetics of carbamazepine are characterised by high plasma protein binding, excellent bioavailability, and self-metabolism resulting in enhanced clearance. The primary metabolite, carbamazepine-epoxide (CBZ-E), has completed generation and undergoes two steps of elimination. It can be tough to establish dose-response correlations since the pharmacodynamic interactions of carbamazepine with other AEDs might be complicated. In especially with AEDs that induce enzymes, carbamazepine has a number of medication interactions. Consequences of carbamazepine include fatigue, nausea, vomiting, reduced blood cell counts, hypersensitivity responses, and other symptoms including dizziness and involuntary muscular movements. however, these adverse reactions are often dose-related and less frequent when using monotherapy. A patient should avoid using carbamazepine if they have a certain medical history or are taking another medicine at the same time.

Index Terms - Carbamazepine (CBZ), Antiepileptic drug (AED), Gamma aminobutyric acid (GAMA), Oxcarbazepine (OXC), Eslicarbazepine acetate (ESL), Epilepsy, Schizophrenia, Trigeminal neuroglia, Mania, Bipolar disorder.

I. INTRODUCTION
Carbamazepine (CBZ) is one of the most well-known antiepileptic drugs (AEDs), both domestically and abroad. Since both neurologists and non-neurologists are very familiar with its spectrum of efficacy, advantages, and limitations, it is one of the most frequently utilised AEDs. More contemporary AEDs of the second generation, such as the two different but structurally related medications oxcarbazepine (OXC) and eslicarbazepine acetate (ESL), have become available since the mid-1990s. This suggests that clinicians have several choices when it comes to this family of AEDs, coupled with other CBZ formulations (Carbatrol, Tegretol-XR), and generic formulations.

Carbamazepine was initially developed as a potential antidepressant. It is a well-known mood stabiliser that can be used to treat both mania and bipolar illness. The majority of guidelines currently recognise it as a second-line mood stabiliser that is beneficial in the treatment and prevention of both stages of bipolar affective disorder. The primary uses of the drug carbamazepine (CBZ) are the management of epilepsy and neuropathic pain [1]. As effective at treating seizures as phenytoin and valproic acid. For absence seizures or myoclonic seizures, which are well-treated by the drug valproate, it is ineffective.

II. INDICATION
The FDA has given the drug carbamazepine approval to treat acute manic and mixed episodes of bipolar I disorder, trigeminal neuralgia, and epilepsy. A systemic evaluation has shown that carbamazepine extended-release is effective in treating people with acute manic or mixed episodes of bipolar I mania. Carbamazepine is used for schizophrenia patients who are resistant to treatment. All three types of patients with schizophrenia—those with violent episodes, schizoaffective disorder, and schizophrenia—have reacted effectively to simple, well-planned trials. Both the pleasant and the bad symptoms are lessened in people with schizophrenia [1].
III. PHARMACOLOGY

MECHANISM

Action on synaptic transmission and increase of sodium channel inactivation by lowering high-frequency repeated action potential firing are the two main mechanisms of action that have been proposed. Since it has been demonstrated that carbamazepine potentiates GABA receptors composed of the alpha1, beta2, and gamma2 subunits, it is a GABA receptor agonist. Its effectiveness in treating bipolar illness and neuropathic pain may be due to this mechanism.

PHARMACOKINETICS

Carbamazepine has a high affinity for plasma proteins. The bioavailability of a drug is 75–85%. The rate and amount of absorption were unaffected by food. The main metabolite, carbamazepine-epoxide (CBZ-E), is completely generated. Carbamazepine's ability to self-metabolize results in an increase in clearance, a decrease in serum half-life, and a continuous drop in blood levels. In order to maintain a consistent plasma concentration, the daily dosage must be raised. Severe liver disease may lead to disordered pharmacokinetics.

Carbamazepine elimination by epoxidation and hydroxylation in hepatic biotransformation. About 15 hours pass between two phases of elimination. It is unlikely that buildup of the parent medication or the epoxide metabolite will occur because only 1% of carbamazepine is excreted in urine undamaged. In renal disease or during dialysis, dose modification is not required.

PHARMACODYNAMICS

It is difficult to establish scientifically how pharmacodynamic interactions involving AEDs work since it is difficult to define dose-response correlations in a clinical setting.

INTERACTIONS

Valproic acid, tiagabine, ethosuximide, lamotrigine, topiramate, oxcarbazepine and its active monohydroxy-derivative (MHD), zonisamide, felbamate, and many benzodiazepine medications are all affected by the use of enzyme-inducing AEDs (carbamazepine, phenytoin, phenobarbital, and primidone).

IV. ADVERSE EFFECTS AND CONTRAINDICATION

The use of carbamazepine treatment is thought to be secure and efficient. Vertigo, Involuntary muscle movement, drowsiness, nauseousness, emesis, anorexia, decreased white blood cells and decreased blood platelet count, hypersensitive responses, are known adverse events with carbamazepine medication. Generally speaking, many side events are dose-related and happen less frequently with monotherapy than with combination therapy with other antiepileptic drugs. Patients with atrioventricular block, acute intermittent porphyria, severe hepatic impairment, tricyclic antidepressant allergies, bone marrow destruction, concurrent therapy with monoamine oxidase inhibitors, or voriconazole shouldn't use carbamazepine.

V. CONCLUSION

Antiepileptic medicine carbamazepine is a well-known and often used medication with a wide range of effectiveness. Trigeminal neuralgia, acute manic and mixed episodes of bipolar I disorder, epilepsy, and neuropathic pain can all be effectively treated with it. The drug's modes of action include sodium channel inactivation and regulation of synaptic transmission. High protein binding, excellent bioavailability, and self-metabolism are characteristics of carbamazepine's complicated pharmacokinetics. It has pharmacodynamic interactions with other AEDs, therefore care should be taken while providing particular medications concurrently. In general, adverse effects are dose-related and more seldom happen with monotherapy. However, there are certain restrictions and safety measures for using carbamazepine in particular patient groups. In general, carbamazepine remains a significant therapeutic choice for the treatment of epilepsy, bipolar disorder, and neuropathic pain. However, to guarantee its safe and efficient usage, thorough monitoring and individualised treatment considerations are required.