Carbamazepine: Wonder Drug Against Neuralgia

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Introduction:

Neuralgia (Greek neuron, "nerve" + algos, "pain") is pain in the distribution of a nerve or nerves, as in intercostal neuralgia, trigeminal neuralgia, and glossopharyngeal neuralgia.[1]Under the general heading of neuralgia are trigeminal neuralgia (TN), atypical trigeminal neuralgia (ATN), occipital neuralgia, glossopharyngeal neuralgia and post-herpetic neuralgia (caused by shingles or herpes).[2]Carbamazepine is the primary agent for treatment of trigeminal and glossopharyngeal neuralgias.[3]

Carbamazepine

Carbamazepineis an anticonvulsant and specific first choice drug for treating trigeminal neuralgia.It is related chemically to the tricyclic antidepressants. It istypically used for the treatment of seizure disorders and neuropathic pain.[4]

History

Carbamazepine was discovered by chemist Walter Schindler at J.R. Geigy AG (now part of Novartis) in Basel, Switzerland, in 1953.[5,6] It was first marketed as a drug to treat epilepsy in Switzerland in 1963 under the brand name "Tegretol"; its use for trigeminal neuralgia (formerly known as Tic douloureux) was introduced at the same time.[5]

Mechanism of Action:

Carbamazepine stabilizes the inactivated state of voltage-gated sodium channels, making fewer of these channels available to subsequently open. This leaves the affected cells less excitable until the drug dissociates. Carbamazepine is also a GABA receptor agonist, as it has also been shown to potentiate GABA receptors made up of alpha1, beta2, and gamma2 subunits.[7] This mechanism may contribute to its efficacy in neuropathic pain and manic-depressive illness. Laboratory research has further demonstrated that Carbamazepine is aserotonin releasing agent and possibly even a serotonin reuptake inhibitor.[8,9,10]

Pharmacokinetic Properties

Carbamazepine is absorbed slowly and erratically after oral administration. Peak concentrations in plasma usually are observed 4-8 hours after oral ingestion, but may be delayed by as much as 24 hours, especially following the administration of a large dose. Approximately 75% of Carbamazepine binds to plasma proteins and concentrations in the CSF appear to correspond to the concentration of free drug in plasma.[3]

Dosage

Carbamazepine should be started as a single daily dose of 100 mg taken with food and increased gradually (by 100 mg daily in divided doses every 1-2 days) until substantial (>50%) pain relief is achieved. Most patients require a maintenance dose of 200 mg qid. If treatment is effective, it is usually continued for 1 month and then tapered as tolerated.[11]

Adverse Effects

Acute intoxication with Carbamazepine can result in stupor or coma, hyperirritability, convulsions, and respiratory depression. During long term therapy, the more frequent untoward effects of the drug include drowsiness, vertigo, ataxia, diplopia, and blurred vision. The frequency of seizures may increase, especially with overdose. Other adverse effects include nausea, vomiting, serious haematological toxicity (aplastic anemia, agranulocytosis), and hypersensitivity reactions (dangerous skin reactions, eosinophilia, lymphadenopathy, splenomegaly). A late complication of therapy with Carbamazepine is retention of water, with decreased osmolality and concentration of Na^+ in plasma, especially in elderly patients with cardiac disease.[3]

Precautions

Before initiating therapy, a detailed history and physical examination should be made. Carbamazepineshould not be used in those with a history of bone marrow problems as it causes eosinophilia, thrombocytopenia and neutropenia. Use during pregnancy may cause harm to the foetus. Epidemiological data suggest that there may be an association between the use of Carbamazepine during pregnancy and congenital anomalies (e.g., craniofacial defects, cardiovascular malformations, and anomalies involving various body systems); however stopping it in pregnant women with seizures is not recommended. Its use during breastfeeding is not recommended. Care should be taken in those with liver problems because it might cause hepatotoxicity including cholangitis, granuloma formation, fever and hepatocellular necrosis.[4]

Drug Interactions

Several drugs decrease the metabolism of Carbamazepine, thereby increasing its serum level: calcium channel blockers, cimetidine, erythromycin, isoniazid, lithium, propoxyphene,[12] valproate. Others increase the metabolism of Carbamazepine, thereby decreasing the serum level, for example: phenobarbital, primidone, phenytoin.[13]

Discussion

When Carbamazepine under the guise of G32883 was initially reported as relieving Trigeminal Neuralgia (Blom, 1962), a new era in the treatment of this condition started. The first reports of its use in the U.K. (Taylor, 1963; Spillane,1964; Graham and Zilkha, 1966) confirmed itsefficacy and Carbamazepine was generally regarded as thedrug of choice for the treatment of Trigeminal Neuralgia.[14] Baclofen or clonazepam might be added to Carbamazepine if Carbamazepine monotherapy does not suffice. When these drugs are ineffective, monotherapy with phenytoin, pimozide and valproate would be the next choices.[15]Oxcarbazepine (10-keto analogue of Carbazepine) has been proved to be an effective treatment when the standard carbamazepine medication is not satisfactory.[16]

Conclusion

Carbamazepine is the primary drug of choice for treatment of trigeminal and glossopharyngeal neuralgias. It is also effective for lightning type ("tabetic") pain associated with bodily wasting. Most patients with neuralgia benefit initially, but only 70% obtain continuing relief. The therapeutic range of plasma concentrations for anti-seizure therapy serves as a guideline for its use in neuralgia.

References

References are available on request at editor@healtalkht.com