Anticonvulsants used in seizures

ABSTRACT

Anticonvulsants (also commonly known as antiepileptic drugs or as antiseizure drugs) are a diverse group of pharmacological agents used in the treatment of epileptic seizures. Anticonvulsants are also increasingly being used in the treatment of bipolar disorder and borderline personality disorder, since many seem to act as mood stabilizers, and for the treatment of neuropathic pain. Anticonvulsants suppress the excessive rapid firing of neurons during seizures. Anticonvulsants also prevent the spread of the seizure within the brain.

INTRODUCTION

Conventional antiepileptic drugs may block sodium channels or enhance γ-aminobutyric acid (GABA) function. Several antiepileptic drugs have multiple or uncertain mechanisms of action. Next to the voltage-gated sodium channels and components of the GABA system, their targets include GABAA receptors, the GAT-1 GABA transporter, and GABA transaminase. Additional targets include voltage-gated calcium channels, SV2A, and α2δ. By blocking sodium or calcium channels, antiepileptic drugs reduce the release of excitatory glutamate, whose release is considered to be elevated in epilepsy, but also that of GABA. This is probably a side effect or even the actual mechanism of action for some antiepileptic drugs, since GABA can itself, directly or indirectly, act proconvulsively. Another potential target of antiepileptic drugs is the peroxisome proliferator-activated receptor alpha.

Some anticonvulsants have shown antiepileptogenic effects in animal models of epilepsy. That is, they either prevent the development of epilepsy or can halt or reverse the progression of epilepsy. However, no drug has been shown in human trials to prevent epileptogenesis (the development of epilepsy in an individual at risk, such as after a head injury).

Bromides are effective against epilepsy, and also cause impotence, which is not related to its anti-epileptic effects. Bromide also suffered from the way it affected behaviour, introducing the idea of the 'epileptic personality' which was actually a result of medication. Phenobarbital was first used in 1912 for both its sedative and antiepileptic properties. By the 1930s, the development of animal models in epilepsy research led to the development of phenytoin by Tracy, which had the distinct advantage of treating epileptic seizures with less sedation. By the 1970s, a National Institutes of Health initiative, the Anticonvulsant Screening Program, served as a mechanism for drawing the interest and abilities of pharmaceutical companies in the development of new anticonvulsant medications.

During pregnancy, the metabolism of several anticonvulsants is affected. There may be an increase in the clearance and resultant decrease in the blood concentration of lamotrigine, phenytoin, and to a lesser extent carbamazepine, and possibly decreases the level of levetiracetam and the active oxcarbazepine metabolite, the monohydroxy derivative. Therefore, these drugs should be monitored during use in pregnancy.

Many of the common used medications, such as valproate, phenytoin, carbamazepine, phenobarbitol, gabapentin have been reported to cause increased risk of birth defects. Among anticonvulsants, levetiracetam and lamotrigine seem to carry the lowest risk of causing birth defects. The risk of untreated epilepsy is believed to be greater than the risk of adverse effects caused by these medications, necessitating continuation of antiepileptic treatment.

Valproic acid, and its derivatives such as sodium valproate and divalproex sodium, causes cognitive deficit in the child, with an increased dose causing decreased intelligence quotient. On the other hand, evidence is conflicting for carbamazepine regarding any increased risk of congenital physical anomalies or neurodevelopmental disorders by intrauterine exposure. Similarly, children exposed lamotrigine or phenytoin in the womb do not seem to differ in their skills compared to those who were exposed to carbamazepine.

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