SHOULD PATIENTS WITH CORTICAL STROKES BE TREATED PROPHYLACTICALLY FOR SEIZURES?
YES
Nese Dericioglu
Turkey

Stroke is one of the leading causes of mortality and major morbidity worldwide. Post-stroke seizures are a frequent cause of remote symptomatic epilepsy in adults, especially in older age. About 10% of stroke patients will suffer a seizure, depending on risk factors such as the type, location and severity of the stroke. Previous stroke accounts for 30-40% of all cases of epilepsy in the elderly. Unlike that in younger patients, the appearance of seizures in old age is less specific and takes time before a diagnosis can be proven. The optimal timing and type of antiepileptic drug treatment for patients with post-stroke seizures is still a controversial issue. Because of the physical and psychological influences of recurrent seizures, prophylactic treatment should be considered in an elderly person at high risk of seizure occurrence, taking into consideration the individuality of the patient and a discussion with both the patient and his/her family about the risks and benefits of both options. Recent studies related to post-stroke seizure treatment showed that newer generation drugs, such as lamotrigine, gabapentin and levetirecetam, in low doses would be reasonable because of their high rate of long-term seizure free periods, improved safety profile and fewer interactions with other drugs when compared with first generation anticonvulsants.

Antiepileptic drugs exert their action by targeting multiple neuronal mechanisms. On the basis of the similarity of the synaptic and intracellular events exhibited by epilepsy and vascular brain injuries, antiepileptic drugs have been tested as possible neuroprotective agents in animal models of stroke. Indeed some antiepileptic drugs were shown to be promising tools to counteract experimentally induced brain ischemia. Synaptic and cellular events initiated by acute energy deprivation caused by brain ischemia have been shown to be similar to those triggered by abnormal neuronal discharge induced by epilepsy. In both these pathological conditions, an acute membrane depolarization is caused by postsynaptic sodium and calcium influx via voltage and ligand-gated channels. During brain ischemia the energy supply is compromised, leading to inhibition of the Na^+-K^+ pump. Increased extracellular potassium concentration in turn further depolarizes the neuronal membrane. Consequently, excitatory amino acids are massively released into the extracellular space resulting in intracellular calcium overload which initiates a cascade of cytoplasmic and nuclear events that generate tissue damage and possibly apoptosis.

The potential antiepileptogenic effects of anticonvulsant drugs are mostly studied in various animal models of epilepsy. Among sodium channel inhibitors, phenytoin and fosphenytoin were reported to display neuroprotecive effects in a cardiac arrest-induced global ischemia model. Topiramate has been shown to significantly improve neurological deficit scores, reduce percentage of infarct volume and severity of seizures. Neuroprotective effects of lamotrigine have been reported in models of middle cerebral artery (MCA) occlusion or global ischemia. Felbamate and Remacemide, both NMDA antagonists, have been shown to possess neuroprotective efficacy in transient forebrain ischemia or permanent MCA occlusion, respectively. Also, several GABA A agonists have been shown to be neuroprotective in animal models of stroke when given after the ischemic insult. Neuroprotective effects have been reported with tiagabine and vigabatrin in animal stroke models.

There are still many anticonvulsants that have not been extensively investigated in experimental models and even more so in clinical settings. A recent study investigating the prophylactic effect of valproate in patients with intracerebral hemorrhage concluded that valproate tended to reduce early seizures and improved NIHSS scores, suggesting that this treatment may confer some neuroprotective effect. Further studies with larger numbers of patients and with other antiepileptic drugs are needed to properly clarify this issue.