Topiramate prevents excitotoxic damage in the newborn rodent brain

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RESUMEN

Brain lesions induced in newborn mice by the glutamatergic agonists ibotenate (acting on NMDA and metabotropic receptors) and S-bromowillardiine (acting on AMPA-kainate receptors) mimic some aspects of white matter cysts and transcortical necrosis observed in human perinatal brain damage. Topiramate (TPM), already used in children to manage newly diagnosed and refractory epilepsy, has potential neuroprotective effects that may be useful in human perinatal brain lesions. In the excitotoxic newborn mouse model, TPM provided dose-dependent and long-lasting protection of developing white matter and cortical plate against S-bromowillardiine. TPM had no significant effect on ibotenate-induced brain lesions. TPM-induced neuroprotection potentially involved increased survival of pre-oligodendrocytes, decreased neuronal apoptosis, inhibition of microglial activation and astrogliosis, and decreased seizure activity. Diazepam, phenytoin, and carbamazepine had no neuroprotective effect in this model. The present study provides experimental support for the consideration of TPM as a candidate therapy for excitotoxic perinatal brain lesions.

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