Antiepileptic Drugs for Preventing Seizures Following Acute Traumatic Brain Injury: Appraisal of the Cochrane Commission Systematic Review

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ABSTRACT

The work was done to explore the effectiveness of prophylactic antiepileptic drugs for acute traumatic brain injury and assess risk: benefit ratios. The author asked if this intervention helped short-term survivors avoid seizures after injury and assessed the influence of such medication on death and disability which result in seizures in long term survivors of TBI. Finally, the work assessed the benefits given potential adverse reactions to these drugs. The author found that using anti-epileptic drugs in the early stages after traumatic brain injury does decrease seizures. This review found that anti-epileptic drugs were effective for decreasing seizures in the first week after a TBI. Available pooled data failed to demonstrate reductions in overall mortality, late onset seizures, or the development of persistent vegetative states. However, the conclusions are limited by the scarcity of clear data collected to investigate cognitive/behavioural, neurological, or hematopoietic adverse effects thought to result from the anti seizure medications.

Keywords: Anti-Epileptics, Evidence-Based Medicine, Head Trauma, Interactive Student Medicine, Neuroplasticity, Seizures, Traumatic Brain Injury (TBI)

INTRODUCTION

Traumatic brain injury is the most common cause of new onset epilepsy in young adults. Approximately 20-25% of severe traumatic brain injury patients will have seizures (abnormal electrical brain discharges) in the immediate period after a head injury. Factors that could tax the resources on an already damaged brain include increased metabolic demands, elevated intra-cranial pressure, and increased neurotransmitter release. Another area of concern is for the 8% of patients who present with unstable cervical injuries. The violent contractions associated with tonic/clonic seizures may aggravate existing cervical injury or cause death since there is only a small amount of space between the spinal cord and the cervical anatomy that normally protects it. In an injury of this nature, much of the space will already be compromised by swelling and inflammation.
Giving antiepileptic medication on a prophylactic basis thus seems to be a logical choice, what could be the down side? Unfortunately, these drugs are associated with adverse effects, some of them fatal. These include cognitive impairments, abnormalities in blood cells, neurologic impairment, and severe skin eruptions. Even though not every patient will experience these side effects, in those that do the results may be serious or fatal. These concerns led the Cochrane commission (http://www.cochrane.org/) to conduct a systematic review which focuses on the recommendations of using antiepileptic on a prophylactic basis.

Resources. This review was initiated by searching the Cochrane Injuries Group specialised register, as well as MEDLINE and the registers of the Cochrane Stroke Group and Cochrane Epilepsy Group. We also contacted pharmaceutical companies who manufacture anti-epileptic agents, the National Institute of Neurological Disorders and Stroke, Epilepsy Division, and the United States’ National Institute of Health.

Why was this review done? The review was done to explore the effectiveness of prophylactic antiepileptic drugs for acute traumatic brain injury and to assess risk to benefit ratios. Does this intervention help short-term? How does it affect death or disability (long term seizures) and what are the benefits given potential adverse reactions to the drugs?

What did we find? The review found that using anti-epileptic drugs in the early stages after traumatic brain injury does decrease seizures. The review found that antiepileptic drugs were effective for decreasing seizures in the first week after a TBI. Available pooled data failed to demonstrate reductions in overall mortality, later onset seizures or the development of persistent vegetative states.

There was not enough clear data within the studies collected to investigate cognitive/behavioural, neurological or hematopoietic adverse effects thought to result from the anti-seizure medications.

What do these findings mean? There is not enough evidence to conclude that prophylactic anti-epileptics used after TBI will reduce disability or death. Prophylactic anti-epileptics are shown to reduce early seizures, although this benefit is not followed by a reduction in late seizures. To put this in perspective if we treated 100 patients with acute TBI using anti-seizure agents, the probability is that ten would be seizure free in the acute phase while four out of one hundred could develop skin rashes. It may be that reducing seizure activity may result in better neurobehavioral outcomes for these ten but not enough research is available at this time to assess this with clarity.

Limitations. In reviewing some of the original studies that make up this review it were striking to note the lack of mention of EEG monitoring. Seizure risk could be more accurately assessed with routine EEG monitoring and interventions adopted according to the degree of abnormal electrical activity in the brain. Only one of these studies looked at the degree of cognition or affect damage in these TBI patients making it challenging to assess whether the drugs or the injury were the cause of secondary brain damage. For instance follow up on living patients did not include neuropsychological testing.

Results on studies of Phenytoin. Phenytoin, one of the most commonly used anti-seizure medications, demonstrated a reduction of neuronal damage in animal and in-vitro models of hypoxia by mediating a voltage dependent blockade of sodium channels according to research by Tasker (1992) and Vartanian (1996). Although these results suggest a neuroprotective effect, no research was presented on whether these neuroprotective benefits were demonstrated during human studies.
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