Where to start anticonvulsant treatment in childhood epilepsy: the case for avoiding or delaying treatment

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Lastly we may observe, to the great comfort and satisfaction of the parents of those children subject to convulsions, or the epilepsy infantilis, that they need not be apprehensive of its changing into the true epilepsy, for it generally disappears by degrees, as they grow older and acquire more strength.

As a young doctor I held the fairly simplistic and conventional view that patients with epilepsy need to start long term treatment with anticonvulsant drugs as soon as the diagnosis is clear. I accepted that epilepsy could not be diagnosed after a single seizure but believed that treatment was necessary if a recurrence happened within a year. These views were first challenged for me by a middle class couple in whose six year old daughter idiopathic grand mal epilepsy had been diagnosed after she had had three short seizures over four months. After getting me to agree that anticonvulsant drugs did not always work and were not without potential side effects they asked me to spell out the benefits from preventing further seizures. My four answers seemed a little lame to them and to me that (a) a seizure without warning may cause physical injury—for example, a fall into a fire or in front of a motor vehicle—(b) there is a slight risk of status epilepticus, which if prolonged may cause brain damage, (c) seizures are socially embarrassing, and (d) there is a widely held belief that early treatment of epilepsy improves the chances of “growing out of it.”

For a risk-benefit analysis of early long term anticonvulsant treatment my last answer seemed the most important but the evidence was poor. Are things any clearer now? What is the evidence that early treatment of epilepsy with anticonvulsant drugs prevents some children from developing chronic intractable epilepsy?

Does early treatment improve prognosis?

Studies of groups of patients with epilepsy in referral clinics based in hospitals show that rates of remission are better in patients referred early for treatment than in those referred late. The conclusion from these data that early treatment improves the rate of remission should be resisted. Proportionately more patients with longstanding intractable epilepsy may be referred to such clinics than patients with a short history of a few seizures and a good prognosis. Even in community based studies of the prognosis of epilepsy patients with severe epilepsy are more likely to be enrolled than those with two or three seizures, especially if the seizures occur at long intervals. Only by randomising entrants prospectively to early or delayed anticonvulsant treatment will reliable answers to this important question be found. Such a study has yet to be done.

Most patients with epilepsy go into remission after a period of active epilepsy. Annegers et al identified all newly diagnosed epileptic patients in Rochester, Minnesota, from 1935 to 1974. Of those followed up for 20 years, as many as 65% were in a remission that had lasted at least five years. Roughly half of them had successfully stopped treatment.

Although prolonged seizures, especially febrile ones, may cause brain damage and secondary intractable epilepsy, most children with recurrent short seizures are not at great risk of developing status epilepticus. General acknowledgement of the importance of controlling prolonged seizures and the advent of intravenous diazepam for use in hospitals and rectal diazepam for administration by parents have made this risk extremely small.

Is kindling a relevant model?

An experimental animal model of epilepsy known as kindling has been held by some to be an important mechanism in the development of human epilepsy. Repeated subconvulsive electrical stimuli are given to an animal’s brain and after a variable period of time seizures occur with each stimulus. After this stage seizures occur spontaneously and become intractable. Kindling, however, has never been shown in humans. Indeed, the more “encephalised” the brain the more difficult it is to kindle—for example, a rat’s brain can be kindled more easily than a monkey’s.

Studies of the prognosis of childhood epilepsy do not give support for this theoretical model. All paediatricians have known children with severe epilepsy who have gone on to complete remission. Thurston et al reported a 15-23 year follow up study of 148 children with epilepsy whose anticonvulsant treatment was withdrawn after prolonged control. Only 41 (28%) had a recurrence of seizures. Moreover, when the severity of epilepsy was categorised according to the total number of seizures before control was achieved by anticonvulsant drugs no significant relation was found with the rate of relapse (table).

Analysis of patients with temporal lobe epilepsy treated by temporal lobectomy has shown that the
longer the interval between the first seizure and surgery, the less favourable the clinical result.1

Relapse rate after withdrawal of anticonvulsants related to total number of seizures before control by anticonvulsant treatment

<table>
<thead>
<tr>
<th>Total No of seizures before control by anticonvulsants</th>
<th>Relapse after withdrawal of anticonvulsants (%)</th>
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<tbody>
<tr>
<td>3-5</td>
<td>27</td>
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<tr>
<td>6-12</td>
<td>32</td>
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<td>&gt;12</td>
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Kindling of the hippocampus and amygdala by the irritative temporal lobe focus has been a suggested explanation for this observation. There is, however, an equally tenable but more mundane interpretation; cases of short duration temporal lobe epilepsy have a better prognosis than those of long duration whether or not they come to operation.

Treatment considerations

Long term treatment with anticonvulsant drugs carries well known risks of idiopathic and dose related side effects, some of which may be life threatening such as Stevens-Johnson syndrome, blood dyscrasias, and liver failure. Little is known of the permanent effects of these drugs on the developing nervous system, but many are recognised as being able to produce subtle cognitive and behavioural changes in some children even when blood concentrations are maintained within the so called therapeutic range. No completely safe anticonvulsant drug is known or is likely to be developed. Children should not be given long term anticonvulsant treatment unless the benefits clearly outweigh the risks.

Parents of children who have had febrile convulsions should be instructed in managing fever and giving rectal diazepam if required. The overall prognosis for febrile convulsions is excellent. Only 2% develop epilepsy with non-febrile seizures, although recurrence with one or more febrile convulsions occurs in 35%. Even in children with prolonged, recurrent, or other complicated febrile convulsions the risk of subsequent epilepsy is only 4%.

There is no indication for starting long term anticonvulsant treatment after a single afebrile convulsive seizure. Hauser et al found that the cumulative risk of recurrence was only 18% at one year, 21% at two years, and 27% at three years.1 If the seizure is prolonged, however, the parents should be taught how to give rectal diazepam. In the case of recurrent afebrile seizures many factors come into the decision, including the type of epileptic seizure and parental attitudes. In general, however, long term anticonvulsant treatment should be delayed until it becomes clear that there are no signs of spontaneous resolution and that the continuing seizures are adversely affecting the child’s life. In so doing some children will avoid ever having to start long term treatment.

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