Effect of reduction of anticonvulsants on wellbeing

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Abstract
An attempt was made over a period of a year to reduce the number of anticonvulsants used to treat epilepsy in a hospital for the mentally handicapped. At least one drug was withdrawn for each of 20 patients, without loss of seizure control. Effect on wellbeing was assessed by a behavioural scale completed before and after withdrawal, and in the 20 cases of successful withdrawal wellbeing was significantly improved.

Introduction
In 1979 Shorvon and Reynolds reported their experience in reducing the dosage and number of anticonvulsants used in treating epileptics under their care. In their conclusion they said: "Thus provided close, careful supervision is possible, with the help of blood concentration monitoring, there is a case for simplifying and rationalising treatment in even the most difficult of chronic patients. Both our own and the Milano studies suggest that if withdrawal can be achieved the benefits for some patients may be striking, in terms of both seizure control and, especially, reduction of toxicity. The evidence also suggests that in some patients polypharmacy actually exacerbates seizures."

These observations seemed logical and based on a sound therapeutic principle—that the ideal dose of drugs should be the smallest amount required to achieve the therapeutic purpose. I decided therefore to implement this policy when treating epileptics under my care in a hospital for the mentally handicapped, and to attempt to monitor the effects of the policy in terms of seizure control and "benefit to the patient"—the latter a more difficult parameter to measure. In simple terms the assessment of this approach to anticonvulsant therapy attempts to answer two questions: (1) can drug reductions and withdrawals be made without loss of seizure control? (2) if they can is the patient better off?

Method
I included all cases under my direct clinical care in 1979 except for two for whom complete records were not available and two patients who were virtually seizure free on a modest dose of a single anticonvulsant. Among the 36 cases in the study were many chronic epileptics with frequent severe seizures of various types such as simple absences (1); tonic-clonic (25); simple and complex partial (7) temporal lobe epilepsy (2) associated with tonic-clonic (5); akinetic (5); and unclassified (1).

All the patients were mentally handicapped, most in the severe and profound categories (borderline (1), mild (7), moderate (7), severe (15), and profound (6)) with major physical handicaps largely due to cerebral palsy (12).

With one exception—a day patient in a woman’s ward—all were long-term residents subject to constant supervision by nursing staff who record seizure occurrence in a nursing day-book and in a standard seizure chart. All medication was rigidly supervised, thus largely eliminating the problems of non-compliance.

Reduction of anticonvulsants was carried out in a fairly arbitrary fashion, usually starting with barbiturates. When blood level estimations showed a low figure, the relevant drug would be withdrawn as being unlikely to play a part in seizure control at such level. Sometimes evidence of harmful effects of a drug would suggest its withdrawal initially or perhaps the inappropriate use of a drug such as ethosuximide where there were no absence seizures. On occasion the choice was entirely arbitrary, there being no clear indication as to whether the drugs prescribed might be most safely omitted.

If the pattern of seizure occurrence suggested that fits were being provoked by withdrawal no change was made, but if the pattern suggested inadequate anticonvulsant levels then the drug was reinstated at therapeutic level, and when control was regained, another drug was reduced and withdrawn.

The drugs withdrawn in the 20 cases of successful reduction were: primidone (8 patients), phenytoin (3), phenobarbitone (3), sodium valproate (2), ethosuximide (2), sulthiame (2), and troxidone (1).

To assess the benefits of drug reduction in terms of the patient's wellbeing a five-point behavioural scale was devised (table I) and completed by ward staff before the withdrawal of drugs and again about 18 months later when most withdrawals had been completed. Eight aspects of behaviour were considered, arranged in such a way as to give a single score for each patient before and after drug reduction, a low figure being "better" and a high "worse." This scale was devised by a clinical psychologist working in mental handicap, and represents an attempt to assess "wellbeing" in those who are unable to give a clear account of it for themselves.

**TABLE I—Behaviour scale**

<table>
<thead>
<tr>
<th>Damaging property:</th>
<th>Never</th>
<th>Occasionally</th>
<th>Frequently</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-injury:</td>
<td>Never</td>
<td>Occasionally</td>
<td>Frequently</td>
</tr>
<tr>
<td>Attacking others:</td>
<td>Never</td>
<td>Occasionally</td>
<td>Frequently</td>
</tr>
<tr>
<td>Tantrums:</td>
<td>Never</td>
<td>Occasionally</td>
<td>Frequently</td>
</tr>
</tbody>
</table>

The patient has been generally:

<table>
<thead>
<tr>
<th>Very cheerful</th>
<th>Very sad</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very sleepy</td>
<td>Very alert</td>
</tr>
<tr>
<td>Social</td>
<td>Unsocial</td>
</tr>
<tr>
<td>Overactive</td>
<td>Underactive</td>
</tr>
</tbody>
</table>

Results
Of the 36 patients in whom anticonvulsant withdrawal was attempted, five had the original drug reinstated at the original dose, seven required replacement by an alternative drug, four had dose reductions only, and 20 had at least one drug withdrawn without replacement.

**SEIZURES**

Figure 1(a) shows the seizure frequency recorded as a total monthly figure for all 36 patients over the two years 1979 to 1980 inclusive,
the drug withdrawal policy starting in summer 1979 and being largely completed by mid-1980. It shows a slight rise in numbers of seizures in the first half of 1980, the period during which the main withdrawal was being carried out. Three of these higher monthly peaks were associated with a large number of seizures occurring in single patients as the result of withdrawal of anticonvulsants, and once this operation was completed the seizure level fell in the latter half of 1980.

Figure 1(b) shows how many seizures occurred in the group of 20 patients in which at least one anticonvulsant drug was completely withdrawn and not replaced. The same pattern is evident with a rise in the first half of 1980. Allowing for the effects of withdrawal seizures, however, the overall trend is not upwards.

Withdrawal occasionally led to a series of fits, all such incidents were controllable with the usual emergency measures such as parenteral diazepam or paraldehyde, and in this group of 36 patients no case of uncontrolled status epilepticus occurred. No persistent postictal neurological deterioration was seen in any patient.

**BEHAVIOUR SCORES**

Table II shows in composite form the changes in behaviour scores before and after withdrawals. Overall there was a significant improvement (p<0.001) in behaviour and presumed wellbeing, and in the 20 successful withdrawals a highly significant improvement (p<0.002). The remaining 16 who required reinstatement or replacement of anticonvulsants showed no significant change in behavioural scores.

In the individual parameters it can be seen that some were little influenced by the medication change, others strikingly altered. In particular, "self-injury" was not significantly affected, presumably as this is an ingrained feature of some severely mentally handicapped patients.

### Discussion

This paper describes an attempt to put into clinical practice a fresh approach to anticonvulsant treatment suggested by colleagues. It has been shown that patients with epilepsy can benefit from reducing the number and dosage of their anticonvulsants, and the results of this study seem to confirm that view. Despite reduction in total drug intake seizures have not increased in the long term, and behaviour score improvements suggest that these patients are more comfortable.

There are hazards associated with this approach to treatment. Withdrawal of anticonvulsants will often provoke "withdrawal seizures," and these could be harmful if not closely monitored and controlled. Patients who have had no seizures for a long period may have to relive the experience, and relatives may not take kindly to this disturbance of the peace. Staff may be concerned about the reduction in medication and the temporary increase in seizure frequency, and full discussion is imperative with staff and relatives, as well as the patients themselves where possible, before starting action that may cause temporary discomfort in the interest of long-term benefit.

Withdrawal of certain drugs was found to be more hazardous than others. Reduction of phenobarbitone and primidone was most likely to result in an increased number of seizures and very few. Such reduction of dosage was necessary—for instance, removal of 15 mg of phenobarbitone every six weeks became the routine. Drug levels of other drugs being given concurrently, especially phenytoin, required careful monitoring, since metabolism of drugs is often interdependent and serious toxicity could be inadvertently precipitated.

Other questions have to be asked. While a patient may show no increase or even a reduction in the number of seizures on the lower dosage, is he adequately protected in the event of provocation in the form of a respiratory infection? One of our patients who had been seizure free for years remained free after withdrawal of one of two drugs but during a chest infection had a series of severe fits. Several adjustments in the regimen were required before adequate protection was assured.

When are fits withdrawal fits, and when are they simply due to inadequate anticonvulsant levels? If the former we may expect them to pass but if the latter the medication must be restored or an alternative offered, thus losing the possible benefit of reduction. Only close observation and use of short-term medication such as parenteral diazepam can help to clarify this point. It is essential when a patient is taking more than one drug that blood concentrations of the remaining drugs are maintained in the therapeutic range.

Further study of these patients over the next year or two will be required to estimate the stability of the new regimen, with allowance for natural fluctuations in seizure frequency and the influence of other factors on their epilepsy.

There is still work to be done in the smooth streamlining of anticonvulsant treatment, but provided serious hazard can be avoided there is clearly much to be gained in the long term by reducing medication in a condition that requires continuous treatment over many years.

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### References


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