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Clinical and Therapeutic Monitoring of Epilepsy in a Mental Handicap Unit

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Within a group of hospitals for the mentally handicapped serving the Leicestershire district, a cohort of 215 epileptic patients was identified, who were followed up for four years. The anticonvulsant medication of each patient was reviewed regularly until an optimal balance between seizure control, absence of medication side-effects, and reduction of polypharmacy was attained. After four years 172 patients remained in the study. A significant reduction in polypharmacy was attained overall. Some groups of patients showed a significant reduction in the frequency of seizures, while a small group of patients with frequent seizures remained difficult to control.

Epilepsy is a common problem of mentally handicapped patients. Corbett *et al* (1975) studied the prevalence of epilepsy in all the known severely mentally handicapped children in a London suburb with a population of about 175 000. They showed that of children with severe mental handicap (IQ under 50) a third had a history of seizures, and 19% had had at least one fit during the previous year. Similar findings were made by Tizard & Grad (1961). Additionally, Corbett (1981) showed that the prevalence of epilepsy increased in association with the severity of the mental handicap.

Mentally handicapped patients are also particularly vulnerable to the side-effects of medication, since they may be unable to conceptualise their experiences, or to communicate their experiences to their carers adequately. It is generally believed that the use of most of the anticonvulsants, possibly with the exceptions of carbamazepine and sodium valproate (Dodrill & Troupin, 1977; Thompson *et al*, 1981; Thompson & Trimble, 1982; Hirtz & Nelson, 1985) lead to cognitive impairments. While it is recognised that unwanted side-effects occur when the serum concentration of the drug lies within the toxic range, such effects in particular cognitive impairment, may also occur within the therapeutic range. Phenobarbitone has been shown to have adverse behavioural effects in children (Reynolds & Travers, 1974; Reynolds, 1975; Stores, 1975; Trimble & Reynolds, 1976; Trimble & Corbett, 1980).

Anticonvulsant polypharmacy has been considered inappropriate, as it can lead to more side-effects and the use of unnecessary medication, and behavioural difficulties and cognitive impairment are compounded (Reynolds, 1975; Shorvon *et al*, 1978; Shorvon, 1980). Moreover, it may be difficult to judge what overall effect may be obtained by adjustments to just one drug.

This paper reports the results of a systematic review of patients who were both epileptic and mentally handicapped. The primary aim was to provide optimum seizure control while reducing polypharmacy and the associated risks of side-effects.

Method

The population base for the study consisted of all in-patients of the Glenfrith Mental Handicap Unit in Leicestershire. In 1984, 738 in-patients were resident throughout 26 housing units variously scattered throughout Leicestershire, serving a population of 866 100.

At the outset of the study, data were obtained on all in-patient mentally handicapped patients who were either on medication for epilepsy, or who had sustained an epileptic convulsion within the previous two years. Such data included the patient's name, age, the types of medication received, including dose and frequency, the aetiology of the mental handicap (where known), associated medication, and the presumed seizure type. Data were obtained from a variety of sources, including staff, inspection of medical and nursing notes, epilepsy records, and drug cards. For 12 weeks we obtained from the existing recording system and in consultation with carers information about the type, frequency, and severity of seizures. These data acted as baseline information. Serum levels of phenytoin, phenobarbitone, valproic acid, and carbamazepine were analysed at the outset and throughout the study. Side-effects reported by the patients or their carers were recorded on the review sheet, after clinical assessment. Thereafter the anticonvulsant regime of all patients was reviewed jointly by a specialist in mental handicap and a specialist in clinical pharmacology. These reviews took place at regular intervals of 6, 12 or 26 weeks, until the patient had attained a 'steady state'; at this point it was considered that an optimum balance between seizure frequency, choice of medication, therapeutic dosage, and absence of medication side-effects had been achieved. The nature of the anticonvulsant drugs employed, their dose and serum concentration, and the relative frequency of seizures were compared between the

initial state and the 'steady state'. Thereafter, an attempt was made at reviewing each patient on at least an annual basis.

In reviewing medication, the initial aim was to consolidate the medication already in use so as to ensure that full therapeutic doses were available. In the case of phenobarbitone and phenytoin, once-a-day administration was introduced. A change to a 'new' drug was contemplated only when side-effects of the current medication became evident, or adequate seizure control was not achieved. The serum anticonvulsant level and the optimum range proposed by the Clinical Pharmacology Laboratory for each medication were seen as valuable guidelines, but decisions about changes to medication took into account clinical response. Important factors were adverse reactions, effectiveness, and the ability of the patient to comply.

Results

The initial cohort consisted of 215 epileptics (58% male), who comprised 29% of the in-patient population of a group of hospitals for the mentally handicapped. The mean age of this population was 38 (s.d. 14) years. After the four-year study period, 43 patients had left the study (19 patients died, and 24 had been discharged as part of the policy of de-institutionalisation). The final cohort of 172 patients represented 80% of the initial cohort. The 43 patients lost to follow-up showed no statistical differences with respect to age, sex, degree of handicap, initial seizure frequency, or polypharmacy compared with the final cohort.

The total number of reviews undertaken on the whole cohort of 215 patients was 1058. The mean number of reviews undertaken per patient was 5.9 (s.d. 2.5), with a maximum of 11 reviews per patient.

The seizure frequencies at both the initial and final reviews are given in Table I. The number of patients who were free of fits had increased significantly by the end of the study ($\chi^2 = 27.62$, d.f. = 6, $P < 0.005$). This is accounted for by the improved seizure control of patients who initially sustained seizures infrequently. Patients who had frequent seizures remained difficult to control. Overall, seizure frequency was reduced in 48% of patients, increased in 33% of patients, and remained unchanged in 19%.

TABLE I
Seizure frequency

	Initial review		*Final review*	
	No. of patients	*%*	*No. of patients*	*%*
Seizure-free	37	22	71	41
Less than one seizure per year	52	30	24	14
Up to 4 seizures per year	36	21	27	16
Up to 1 seizure per month	18	10	15	9
Up to 1 seizure every fortnight	14	8	15	9
Up to 1 seizure per week	13	8	16	9
1 or more seizures per week	2	1	4	2

TABLE II
Number of anticonvulsants per patient

No. per patient	*Initially (%)*	*Finally (%)*
0	17 (9.9)	31 (18.0)
1	90 (52.3)	107 (62.2)
2	48 (27.9)	31 (18.0)
3	12 (7.0)	3 (1.7)
4	5 (2.9)	0 (0.0)
Mean	1.41	1.05

The number of different anticonvulsants used with each patient both initially and at the final review is given in Table II. The mean number of anticonvulsants given to each patient initially was 1.41. At the final review, the mean number of anticonvulsants given to each patient had decreased to 1.05. This is a statistically significant reduction of polypharmacy ($\chi^2 = 56.86$, d.f. = 16, $P < 0.005$). Eighty per cent of patients were maintained on either no anticonvulsant, or by the use of a single drug. Less than 2% of patients were maintained on combinations of more than two anticonvulsants.

Table III shows the changes in the prescriptions issued. There were significant reductions in the use of phenobarbitone, phenytoin, and sulthiame, but a significant increase in the use of carbamezepine and sodium valproate. Ethosuximide and primidone were withdrawn completely. When the patients were finally reviewed, over 90% of the anticonvulsant prescriptions issued were for just three drugs, namely carbamazepine (48.3%), phenobarbitone (23.9%) and sodium valproate (18.8%).

Among drugs taken in combination, there were significant reductions in phenobarbitone + phenytoin ($\chi^2 = 152.90$, d.f. = 1, $P < 0.005$), phenobarbitone + sodium valproate ($\chi^2 = 8.74$, d.f. = 1, $P < 0.005$), phenobarbitone + sulthiame ($\chi^2 = 48.55$, d.f. = 1, $P < 0.005$), and phenytoin + sodium valproate ($\chi^2 = 15.77$, d.f. = 1, $P < 0.005$).

Associated with the reduction in polypharmacy were increases in the doses of drugs employed, particularly of carbamazepine, phenobarbitone and sodium valproate (but not phenytoin) (Table IV).

TABLE III
Anticonvulsants employed

Anticonvulsant	*No. of prescriptions*	
	Initially	*Finally*
Beclamide	1	1
Carbamazepine	60	85*
Clonazepam	3	3
Ethosuximide	6	0*
Phenobarbitone	62	42*
Phenytoin	33	9*
Primidone	8	0*
Sulthiame	20	3*
Sodium valproate	50	33*

*$P < 0.005$.

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TABLE IV
Initial and final mean daily doses of anticonvulsants

Drug	*Mean (s.d.) initial daily dose: mg*	*Mean (s.d.) final daily dose: mg*
Carbamazepine	735.44 (317.00)	940.96* (309.70)
Phenobarbitone	147.65 (81.45)	182.98** (64.78)
Phenytoin	313.33 (143.79)	313.89 (61.36)
Sodium valproate	1171.40 (504.67)	1516.70* (632.20)

*$P<0.005$, **$P<0.05$.

TABLE V
Mean serum anticonvulsant concentrations (mg/l)

Anticonvulsant	*Initial concentration (s.d.)*	*Final concentration (s.d.)*
Carbamazepine	7.35 (2.49)	9.71* (2.63)
Phenobarbitone	24.54 (9.85)	28.80** (10.28)
Phenytoin	11.2 (5.74)	12.91 (4.34)
Sodium valproate	63.82 (23.74)	70.95 (18.28)

*$P<0.001$, **$P<0.05$.

For those patients who continued on the same anticonvulsant throughout the study, the increased doses of anticonvulsants prescribed were associated with increases in the mean serum concentrations of those drugs for which assay was available. The increases in serum concentrations of carbamazepine and phenobarbitone were statistically significant ($P<0.001$ and $P<0.05$ respectively). The mean increases in the serum concentrations of phenytoin and sodium valproate were not significant. These changes are shown in Table V.

Discussion

The systematic review of institutionalised patients with both mental handicap and epilepsy involved over a thousand separate reviews which took place within the patients' residential units. Visits to the wards for this purpose were generally welcomed and interest in the management of epilepsy increased.

The identification of seizure type presented difficulties. Nearly 80% of patients were considered to have generalised tonic-clonic seizures. The remaining 20% were considered to have petit mal, focal fits, myoclonic jerks, or a combination of seizure types. The identification of seizure type, other than tonic-clonic seizures, was difficult; it is likely also that tonic-clonic fits are over-represented by focal fits that became generalised. Our facilities for special observation and investigation of seizure type were minimal.

Our study has shown that it is possible to achieve a significant reduction in anticonvulsant polypharmacy in institutionalised mentally handicapped patients and effect a significant decrease in the frequency of seizures in some groups. Eighty per cent of patients were maintained either without anticonvulsant therapy or by the use of just one drug. Fewer than 2% of patients were maintained on more than two anticonvulsants. Carbamazepine, phenobarbitone and sodium valproate were found to be the most effective drugs clinically, while the use of beclamide, clonazepam, ethosuximide, phenytoin, primidone, and sulthiame was uncommon.

At the beginning of the study, a number of patients were found with serum anticonvulsant levels within the toxic range, while others had drug levels well below the accepted therapeutic range. These extreme positions were seen as cues for early action in order to achieve the rational use of medication.

At each review, careful inquiry was made to the carer for the emergence of side-effects; results were recorded on the review sheet. Side-effects included sedation, fluid retention associated with sodium valproate, rash and nausea with carbamazepine, ataxia and nystagmus with phenytoin, etc. They were all found to be reversible with either a reduction in drug dose or by a change in anticonvulsant.

Some patients would not take tablets, others refused syrup. The form and frequency of administration of the medication was a matter of negotiation between prescriber, patient, and carer. Two of the more able patients would not co-operate with any proposed changes of medication.

There have been few studies of the systematic management of epilepsy in patients with a mental handicap. This is perhaps surprising, in view of the known effects of anticonvulsant drugs on cognition, and the major difficulty of communication in this group. Fishbacher (1982) showed in a series of 36 mentally handicapped patients that it was possible to achieve a reduction in polypharmacy while at the same time reducing the frequency of epileptic seizures. He demonstrated that the reduction in number of drugs was associated with improvement in behaviour.

Sheppard *et al* (1987) studied the changes in anticonvulsant medication prescribed to an institutionalised mentally handicapped population over ten years. Polypharmacy reduction was not a major aim of their work, however. Their initial cohort of 179 patients in 1972 had fallen to 130 in 1982, of whom 52% were controlled on monotherapy.

While we have demonstrated a reduction in polypharmacy and an increase in the number of patients who were free from fits, there remained a small group who, in spite of everything, continued to take several drugs and whose seizures were exceedingly difficult to control. This group merits further study.

The association between psychiatric disorder and epilepsy, and especially between severe mental retardation and epilepsy, is noted in a document from the Department of Health and Social Security (1986) on services for people with epilepsy. The work described in this paper is in accord with one of the recommendations from that report: "People with both epilepsy and psychiatric disorder or mental handicap should receive proper assessment for their epilepsy, and this should not be overlooked where patients with a dual handicap are being managed within an institution". Careful review of anticonvulsant therapy is mandatory.

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