

CLONAZEPAM IN THE TREATMENT OF EPILEPSY IN HANDICAPPED PATIENTS

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Clonazepam (Rivotril) is a benzodiazepine derivative which has been available in Ireland since 1974. Other benzodiazepines include diazepam, widely used as a tranquilliser, which has anti-convulsant properties and, used intravenously, has been the drug of choice in status epilepticus for nearly ten years (Parsonage, 1975). Nitrazepam is widely used as a sleep inducer, but it also has a place in the treatment of akinetic seizures. Clonazepam was developed because of its anti-convulsant properties. It has been particularly recommended for myoclonic and akinetic seizures (Eadie and Tyrer, 1974; O'Donohoe, 1974). This paper describes its use in a limited number of patients with a variety of seizures.

Patients and Methods

Twenty female patients from two centres for the mentally handicapped, aged 6 to 41 years and suffering from epileptic seizures, entered the trial. Of the 20 patients, 10 had some spasticity or paralysis and 10 had behaviour problems. Fifteen suffered from a combination of grand mal with either myoclonic, akinetic, petit mal or partial seizures, two had grand mal seizures only, two myoclonic only and one patient partial seizures.

In most cases clonazepam was given because the seizures were particularly frequent, prolonged or liable to cause injury. However, the frequency varied from almost continuous in the case of a patient having partial seizures with twitching of the face and limbs, to one to six grand mal per year in a girl with a provisional diagnosis of Huntington's chorea who was given clonazepam primarily to control her choreiform movements.

All but one of the patients were being treated with a variety of anti-convulsants with inadequate seizure control. The seizures were carefully observed and recorded by the nursing staff.

Dosage

Of the 20 patients who entered the study, 19 had clonazepam added to their usual anti-convulsant, starting with 0.5mg. twice daily and increasing the dose gradually once or twice a week to a maximum of 2mg. four times a day. If severe side-effects occurred the dose was reduced, and if they persisted clonazepam was withdrawn. Patients were observed on clonazepam for 2 to 12 months with an average of 6 months.

Results

The results could only be assessed in 19 patients as clonazepam had to be discontinued after three weeks treatment in one patient due to unwanted side-effects. Of the 19 remaining patients seizures ceased or were reduced by 50% in 9, there was no significant change in seizure frequency in 7 and the seizure frequency increased in three (Table 1). In two of these the increase in grand mal seizures appeared to be more closely related to the incidental administration of thioridazine than to clonazepam. The effect of clonazepam on different types of seizures is shown in Table 2. It was most effective in myoclonic seizures and these ceased or were reduced in frequency by more than 50% in 7 out of the 9 patients with this type of

seizure. Similar improvement was noted in 4 of the 6 patients with akinetic seizures but the effect on grand mal was less, in only 5 of the 15 patients was the frequency of this type of seizure reduced by more than 50%. Improvement in mood and behaviour was spontaneously reported in 6 patients, in one of whom the seizure frequency doubled. There was a dramatic reduction in choreiform movements in the patient with presumed Huntington's chorea. This patient was given clonazepam following a report of its use in the treatment of drug-induced dyskinesia (O'Flanagan, 1975).

The effective dose of clonazepam was between 1mg. and 6mg. daily, and was smaller in those in whom it was most effective.

Side-effects

Side-effects (Table 3) were frequent, and though not a danger to life they required the withdrawal of clonazepam in 5 cases. In a further 7 the side-effects cleared up spontaneously after about one month. Drowsiness was the most frequent, occurring in 10 patients, hypersalivation causing dribbling in 4, hypotonia with weakness and unsteadiness in 2 and anorexia and vomiting one, loss of hair in one and irritability in one. The hair loss stopped without withdrawing clonazepam, but the anorexia and vomiting persisted intermittently for 5 months until clonazepam was withdrawn. The drowsiness cleared up in 2 patients when diazepam and chlorpromazine respectively were withdrawn. Two patients became over-active and aggressive. They had had many similar episodes previously, so this could not be ascribed to clonazepam.

Discussion

It may be argued that the expectations of improvement due to a new drug lessened the frequency of seizures. Whilst this could be so, it must be stated that several patients had been tried on different "new" drugs in previous years without effect. Individual seizure charts have been in use in both centres for over ten years and their importance has always been stressed, so staff are accustomed to keeping accurate records. However, minor seizures may often be overlooked or be so frequent that individual recording is impossible, but with the renewed exhortation during this study it is more likely than not that most were recorded. The patients carried on their normal activities including going home for weekends and holidays and being treated for illness or behaviour disorder.

These could have affected seizure frequency and may have done so in 2 patients given thioridazine.

Several studies have suggested that the success rate of clonazepam decreases with time (Kruse and Blankenhorn, 1973; Beaussart, 1973; Rett, 1973; Dumermuth and Kovacs, 1974). The follow-up period in the present study was not long enough to comment on this point.

The effectiveness of clonazepam in myoclonic, akinetic and partial seizures, as reported in the literature (Dumermuth and Kovacs, 1974) is broadly similar to that found in this study, although Carson and Gilden (1975) findings are much better than most. However, even 50% success rate is important in these types of seizures which respond little to the traditional anti-convulsants. Clonazepam has been shown in several studies (Martin and Hirt, 1973; Rebollo, 1971) to be more effective against grand mal and absence seizures than against myoclonic, akinetic or partial seizures. Other drugs, notably phenobarbitone, phenytoin and carbamazepine, are extremely effective in grand mal seizures, but when these fail the evidence suggests that clonazepam might be considerably more successful than in this study (Carson and Gilden, 1975; Mundler, 1973; Munthe-Kaas and Standjord, 1973). There are reports which record a few cases in whom fit frequency increases as found in this present

study. Furthermore, there are reports of "activation" of grand mal seizures in those with myoclonic seizures who have not previously had this type of seizure (Kurse and Blankenhorn, 1973).

Several authors report lack of correlation between dose and effectiveness (Eeg-Olofsson, 1973; Rett, 1973; Beaussart, 1973) and this was noted in this study.

Side-effects reported in the literature are generally of similar type and frequency to those in this study (Dumermuth and Kovacs, 1974; Vassella, 1973). Ataxia, however, is reported more frequently in several studies (Carson and Gilden, 1975; Beaussart, 1973; Kruse and Blankenhorn, 1973; Eeg-Olofsson, 1973).

TABLE 1. Results of seizure control by clonazepam

	Seizures ceased or reduced by more than 50%	No change in frequency	Increased frequency
Number of patients	9	7	3

TABLE 2. Effect of clonazepam according to type of seizure

Types of seizure	Seizures ceased	Frequency reduced by more than 50%	No effect or less than 50%	Increased frequency
Grand mal	3	2	8	2
Myoclonic	5	2	2	0
Akinetic	0	4	1	1
Partial	2	0	2	1
Absence	0	0	1	0

TABLE 3. Side-effects reported

Side-effect	Transient	Persistent-drug withdrawn	Total
Drowsiness	7	3	10
Hypersalivation	4	0	4
Hypotonia	0	2	2
Anorexia	0	1	1
Irritability	1	0	1
Loss of hair	1	0	1

Conclusions

The ideal anti-convulsant would prevent all seizures and have no side-effects. Clonazepam does not reach this ideal. However, this report shows that it does have a beneficial effect on most types of seizures. Other drugs are more effective in absence and grand mal seizures but not in myoclonic and akinetic seizures, and it is therefore in the treatment of these that clonazepam is most useful. Side-effects are common and, although not serious, may necessitate withdrawing the drug. Drowsiness and hypersalivation causing dribbling are the most frequent but can be lessened by increasing the dose very gradually.

Summary

Twenty patients with mainly myoclonic and akinetic seizures, treated with clonazepam, are reported. In nine the seizures ceased or were reduced by more than 50%. Adverse side-effects (mainly drowsiness and hypersalivation) occurred in twelve, and in five caused the drug to be stopped. The results are discussed and compared with other reports of the use of clonazepam and are found to be similar.

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