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A Controlled Comparison of Diazepam and Amylobarbitone in Anxiety States

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Amylobarbitone has been shown to be effective in the symptomatic treatment of neurotic anxiety in a number of controlled trials (Raymond *et al.*, 1957; Scott, 1955; Robin, 1959), and can therefore be used as a standard of comparison in the treatment of anxiety states. It is here compared with diazepam (7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one).

Method

Twenty-eight consecutive out-patients suffering from anxiety states were treated in a double blind cross-over trial with diazepam and amylobarbitone; each drug was prescribed for a period of a fortnight, the order of prescription being randomized. Amylobarbitone was used in doses of 60 mg. t.i.d. and diazepam in doses of 5 mg. t.i.d. The patients were interviewed and rated on an anxiety scale (Robin *et al.*, 1961) before commencing treatment, after the first period of treatment at two weeks, and after the second period of treatment at one month. Each of the 23 items on the scale was assessed on a three point rating. For scoring purposes symptoms were counted as "2" if severe, "1" if moderate or mild, and "0" if absent. The anxiety score is the sum of ratings achieved by a patient. Standardized actuarial data were collected on all patients admitted to the trial. The symptomatic picture of the patients treated resembled that of the patients with anxiety reactions studied in three previous trials (Robin, 1959; Robin *et al.*, 1961; Robin *et al.*, 1964)—(see Table I)—but patients in this trial produced fewer symptoms. Non-parametric tests were used to analyse the data statistically.

Results

Of the initial 28 patients, 5 discontinued treatment: 3 because of possible side-effects, one through admission to hospital, and the fifth because of an administrative error.

The 23 who completed the trial showed significant improvement ($N = 22$: $T = 25$: $p = < \cdot 01$) in their total anxiety score after two weeks of treatment (using the Wilcoxon Matched Pairs Signed Ranks Test, Siegel, 1956), regardless of the drugs used. The average anxiety score dropped from 19·7 to 14·1. At the end of a month these patients remained significantly better than at the start of the trial, but the second fortnight of treatment was not contributory, and indeed there was a slight overall deterioration—average scores rising from 14·1 to 15·4.

Eleven patients were treated with diazepam in the first fortnight of the trial and 12 with amylobarbitone, the order being reversed in the second fortnight. Diazepam resulted in significantly greater improvement in anxiety scores than amylobarbitone ($N = 23$: $T = 43$: $p = < \cdot 01$) without regard to the period during which the drugs were administered.

Twenty-nine symptoms were analyzed individually. Tension or anxiety ($p = \cdot 004$), irritability ($p = \cdot 006$), weepiness ($p = \cdot 016$), fidgeting ($p = \cdot 029$), claustrophobia ($p = \cdot 031$), broken sleep ($p = \cdot 031$), and increase in dreaming ($p = \cdot 031$) were significantly improved on diazepam in comparison to amylobarbitone, using the Sign Test (Siegel, 1956).

Twenty-nine complaints were noted for the first time during the period in which diazepam was prescribed, and 36 during the period of amylobarbitone. These were possible side-effects. Fatigue, headache, loss of pleasure and irritability were the commonest to be reported, and were mentioned, roughly, equally with both drugs. Two patients discontinued diazepam —one saying that the drug made him feel ill

TABLE I

Distribution of Symptoms in Anxiety States

	Trial 1 (Robin, 1959)	Trial 2 (Robin *et al.*, 1961)	Trial 3 (Robin *et al.*, 1964)	Trial 4
Total patients	21	20	50	28
	Percentage of Patients Affected			
Tremor	62	40	50	57
Fidgety	96	65	78	64
Muscle twitching	38	35	30	25
Headache	67	65	62	46
Muzziness or pressure	72	60	64	39
Tension, strung up, anxious, unrelaxed	100	100	100	100
Could scream or smash	77	70	56	43
Could cry	96	80	74	64
Can't get off to sleep	62	55	40	46
Sleep broken or restless	72	45	44	39
Dreaming more	53	20	34	21
Poor concentration	77	85	72	54
Loss of interest	67	65	62	64
Loss of pleasure	77	65	68	64
Fatigue: lassitude	77	80	72	61
Irritable or excitable	82	85	88	71
Worrying about trivialities	86	75	84	82
Ideas of reference	67	35	30	32
Phobias: insanity	53	40	30	29
Dry mouth	67	70	50	39
Loss of libido	57	80	60	50
Dyspepsia	53	35	64	50
Sweating	62	55	64	36

and the other that it was depressing. One patient discontinued amylobarbitone complaining of exhaustion and palpitations.

Patients were ranked according to their response to diazepam, and the 10 patients who showed most improvement compared with the 10 who showed least. No differences were noted in diagnostic sub-group, number of previous attacks, sex, age, civil state, prognosis rating, personality type or intelligence. Patients who fared best had significantly higher initial anxiety scores than those who showed least response.

DISCUSSION

Diazepam has been shown in controlled studies to impair psychomotor performance in volunteer subjects (Lawton *et al.*, 1963), and improve sleep and appetite (Payne *et al.*, 1964) in non-psychiatric patients with musculoskeletal disorders. The drug did not influence chronic schizophrenic patients treated for a month with doses of 30 mg. daily (Merlis *et al.*, 1962), but was beneficial as far as anxiety symptoms were concerned in general medical cases (Cromwell, 1963), and mixed groups of psychiatric patients with mainly psychoneuroses and depressive reactions (Hare, 1963; Daneman, 1964; Beerman, 1964). In similar patients diazepam has been reported as superior to chlordiazepoxide (Kerry *et al.*, 1962; Aivazian, 1964), trifluoperazine and a combination of meprobamate and benactyzine (Vilkin, 1964). This study is in line with the pattern reported above and shows diazepam to be an effective sedative as far as neurotic anxiety symptoms are concerned. In doses of 15 mg. daily it produced few side effects and certainly no more than were observed with therapeutic doses of amylobarbitone.

Summary

A double blind cross-over study comparing the effect of 15 mg. diazepam with 180 mg. amylobarbitone daily in outpatients with anxiety states showed diazepam to be superior in alleviating symptoms measured on an anxiety rating scale.

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