

A Comparative Trial of Lorazepam and Diazepam

By IJAZ HAIDER

INTRODUCTION

Lorazepam is a psychotropic agent of the benzodiazepine class which has an action qualitatively similar to, but more potent than, chlordiazepoxide and diazepam. In animals lorazepam is about twenty times as potent as chlordiazepoxide as an anti-anxiety agent and 10-50 times as potent as an anti-convulsant. In addition it has been reported as having an effective amnesic effect in higher doses in animals.

In a previous study (Haider, *Brit. J. Psychiat.*, (1971) 119) showed the therapeutic effect of lorazepam, but that investigation was done against placebo. As lorazepam was found to be a useful anti-anxiety agent this report deals with a comparative trial of diazepam and lorazepam in a group of patients requiring a tranquillizer.

METHOD

The fifty patients included in this trial were selected from the in-patients of Whitchurch Hospital and out-patients of Cardiff Royal Infirmary. The criteria for inclusion in this trial were that the patients be suffering from anxiety or anxiety with depression and clinically it appeared that the patient required a tranquilliser. The ages of the patients ranged between 16-65 years. Any patient suffering from epilepsy, brain damage, or severe psychotic episodes was excluded.

Identical tablets containing either diazepam 5.0 mg. or lorazepam 1.0 mg. were supplied in numbered bottles. Numbers were allocated at random, thus the trial was double-blind, but no cross-over was attempted.

Both medications were given initially for one week in a three times daily dosage regime. At the end of this week the dose could be varied up or down, any increase being in the evening dose, and any decrease at the mid-day dose. All changes were recorded on the proforma.

ASSESSMENTS

Each patient was assessed at weekly intervals on the Hamilton Rating Scale (Hamilton, 1959). At the end of three weeks a global assessment was also made: this was independent of the Hamilton Rating Scale and expressed as: Greatly improved; improved; no change; worse.

RESULTS

All the fifty patients completed the trial. The groups were evenly balanced with regard to both males and females receiving treatment and also the number of out- and in-patients included.

The global rating showed no difference between the improvement shown in both groups. When the results from the Hamilton Rating Scale were assessed there was a statistically significant difference in favour of diazepam for depressed mood at the first and third weeks. In view of the multiple nature of the assessments this may have been fortuitous.

If the mean changes in the scores for all patients are taken together (Table I) there is a slight difference of 2.7 in favour of diazepam, but this is not statistically significant (Standard error 2.73, $t = 0.98$).

SIDE-EFFECTS

Side-effects were not specifically asked for but were noted when volunteered by the patient or observed by the supervising staff. The effects reported included sleepiness/drowsiness, malaise/tiredness, ataxia, light-headedness and blurring of vision. Eight of the lorazepam and eleven of the diazepam group reported one or more side-effects.

There was a statistically significant difference between the two drugs with regard to the sedative side-effects of sleepiness, drowsiness and tiredness, diazepam being the more sedative. ($p = 0.0038$, Fisher's exact probability test).

TABLE I
Mean changes in scores in each week during trial

	Lorazepam					Diazepam				
	No.	Pre-trial mean	To week one	To week two	To week three	No.	Pre-trial mean	To week one	To week two	To week three
Females ..	19	28.2	-2.2	-8.6	-17.2	18	30.2	-2.7	-11.6	-20.7
Males ..	6	28.8	-1.7	-6.8	-12.2	7	26.7	-1.7	-7.1	-13.6
All patients ..	25	28.4	-2.0	-8.2	-16.0	25	29.2	-2.4	-10.3	-18.7

Difference not significant ($t = 0.98$).

CONCLUSIONS

This double-blind controlled trial shows little difference in efficacy between the two drugs when given in a dose of 1.0 mg. and 5.0 mg., lorazepam and diazepam respectively.

On using the Hamilton Rating Scale for Anxiety, there are marginal differences in favour of diazepam, but these could have been fortuitous. There was a significantly reduced incidence of sedative side-effects with lorazepam.

SUMMARY

In a double-blind study, fifty in-patients from Whitchurch Hospital and out-patients from Cardiff Royal Infirmary were studied. Patients suffering from anxiety, either alone or associated with depression were included and received either lorazepam 1.0 mg. or diazepam 5.0 mg. three times a day: the dose being varied depending on the response.

Clinically both drugs appeared to be similarly effective, but there was a suggestion that diazepam was more active on some symptoms at this dosage level. The incidence of side-effects with lorazepam was less than with diazepam, significantly so with regard to sedation. A dose of 1.0 mg. lorazepam appears to be of the same potency as 5.0 mg. diazepam with fewer sedative side-effects. Lorazepam would therefore appear to have a definite place in the treatment of anxiety states in hospital and general practice.

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REFERENCES

- HAIDER, I. (1971). 'Evaluation of a new tranquilliser—Wy-4036—in the treatment of anxiety.' *Brit. J. Psychiat.*, 119, 000-0.
- HAMILTON, M. (1959). *Brit. J. med. Psychol.*, 32, 50-5.

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