Lorazepam In Patients With Mixed Psychic And Somatic Symptoms

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Introduction

Lorazepam, a new compound of the benzodiazepin class, is more potent on a weight for weight basis than its analog diazepan; a potency ratio at least as high as 1 to 5 has been demonstrated in studies comparing the anxiolytic effect of lorazepam with diazepam in hospital and general practitioner populations.[1-3] Lorazepam-treated patients have reported fewer sedative side effects than patients treated with diazepam.[4,5] Such an agent is particularly desirable for use in ambulatory patients with anxiety since with it there should be less interference with the daily rountine.

Method and Materials

During an open study, 65 outpatients (28 female and 37 male) with anxiety or tension were treated with 1 to 3 mg/day of lorazepam. Their ages ranged from 15 to 77 years (average, 44 years) with over half the patients between the ages of 30 and 50. Diagnoses (Table 1) were made on the basis of a detailed history and a careful psychiatric interview. No pregnant women or patients with serious physical illnesses were admitted to the study.

At the initial and each subsequent visit, patients' symptoms were rated using the Hamilton Anxiety Scale. Each symptom was evaluated as either 5, very severe; 4, severe; 3, moderate, 2, mild; or 1, absent. Frequency and initial severity of symptoms are given in Table II. The mean severity of each symptom was compared between the initial and first week (1 to 8 days) and the initial and third week (16 to 22 days). All patients were included in these evaluations. The number of patients with relief of each symptom at the end of treatment was determined. For this purpose, relief was regarded as a reduction of at least two levels of symptom severity, i.e., moderate to absent, severe to mild or absent or very severe to at least moderate. Patients whose symptoms were mild initially were not included in this evaluation.

The overall response to treatment was also recorded for each patient. This evaluation was based on the percent reduction (actual reduction/possible reduction) of the total score on the Hamilton Anxiety Scale at the final visit as compared with the baseline total. A final score of 14 indicated the absence of all symptoms. A 70 to 100% reduction was marked improvement, 50 to 69% was moderate, 20 to 40% was slight, and 0 to 19% was nil. The latter two ratings were considered unsatisfactory.

Side effects were recorded only if volunteered by the patient.

The number of visits varied as each patient required; some patients came in several times during the first two weeks, whereas others had weekly or monthly appointments. Lorazepam was administered as 1 mg tablets in doses ranging from one-half tablet twice daily to one tablet three times daily.

According to the Hamilton Anxiety Scale ratings, the most substantial relief in the 14 symptom areas occurred within the first eight days of treatment: the mean severity of symptoms decreased by 48 to 75% (mean, 65%) during this period and decreased from 8 to 38% more (mean, 18% more) as the study continued (Table III).

Relief of symptoms (reduction by at least two levels of severity) occurred in over 75% of cases for each symptom category (Table IV). The number of patients showing improvement was statistically significant for every symptom category except "Fears," which had a sample size too small for analysis.

At the final visit, 55 patients (85%) showed marked improvement (Table V), a statistically significant number ($p<0.01$).* Thirty-six (55%) had complete remission of all symptoms.

Seven patients had an unsatisfactory overall response to treatment. Of these, two discontinued after only three days and were lost to follow-up. One woman was dropped from the study after 55 days because she was very unreliable in keeping appointments and taking medication. A 45-year-old man with anxiety neurosis improved initially on 1 mg/day lorazepam but regressed; after 26 days he was switched to diazepam and improved rapidly. Three others treated with 1 to 2 mg/day left the study between 9 and 22 days because of lack of improvement.

Duration of treatment ranged from 2 to 101 days (average, 20 days); 75% of the patients left the study by the end of the third week. All but six stopped treatment within 3 weeks because they felt well.

One woman reported giddiness on 2 mg/day. No other side effects were noted.

Discussion

During this study, depressed mood and somatic symptoms even of a severe degree were relieved rapidly and effectively-effects which also occur with other psychotropic agents of the benzodiazepine class.[7]

Although lorazepam has anxiolytic activity equivalent to that of diazepam, it has no muscle relaxant properties and produces few sedative side effects at doses that produce an anti-anxiety effect.[8] The relief of insomnia that occurred in this study probably reflects the alleviation of anxiety, tension, depression, and disturbing physical symptoms.

Summary

During an open study, lorazepam (1-3 mg/day) was administered to 65 outpatients presenting with anxiety, tension, depression, and somatic symptoms. Substantial symptom relief of symptoms (48-75%) was evident by the end of the first week of treatment. Fifty-five patients showed marked overall improvement by the end of treatment; 36 were symptom free. One case of giddiness occurred after 14 days of treatment with 2mg.

References

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Table I

Psychiatric Diagnoses of Patients Participating in the Study

	Number of Patients
Anxiety	31
Anxiety and depression	12
Cardiac neurosis	7
Senile depression	4
Depression	3
Reactive depression with anxiety	2
Depressive psychosis	1
Personality disorder with depression	1
Functional dyspepsia with duodenal ulcer	1
Alcoholism, paranoia	1
Total	65

Table II

Frequency and Severity of Symptoms at Baseline

Symptom	Number of patients	
	Moderate to very severe	Mild
Anxious mood	46	5
Tension	49	11
Fears	6	0
Insomnia	34	8
Intellectual (cognitive) difficulties	17	8
Depressed mood	29	11
Somatic (muscular) symptoms	37	9
Somatic (sensory) symptoms	21	8
Cardiovascular symptoms	39	7
Respiratory symptoms	29	8
Gastrointestinal symptoms	31	7
Genito-urinary symptoms	25	4
Autonomic symptoms	40	11
Behavioral symptoms	38	12

Table III

Effect of Treatment on the Fourteen Symptom Categories of the Hamilton Anxiety Scale

Symptom	No. of Patients	Severity (mean score)			Reduction (mean %)*	
		Initial	At 1–8 days	At 16–22 days	At 1–8 days	At 16–22 days
Anxious mood	51	3.6	2.1	1.5	58	81
Tension	60	3.4	1.8	1.5	67	79
Fears	6	3.8	2.0	1.0	66	100
Insommia	42	3.3	1.8	1.6	65	78
Intellectual (cognitive) difficulties	25	4.1	1.9	1.2	72	94
Depressed mood	40	4.2	1.8	1.3	75	91
Somatic (muscular) symptoms	46	3.3	2.0	1.7	56	70
Somatic (sensory) symptoms	29	3.1	2.0	1.3	48	86
Cardiovascular symptoms	46	3.7	1.9	1.4	67	85
Respiratory symptoms	37	3.2	1.6	1.2	73	91
Gastrointestinal symptoms	38	3.3	1.7	1.6	70	78
Genito-urinary symptoms	29	3.2	1.8	1.4	64	82
Autonomic symptoms	51	3.1	1.8	1.6	62	71
Behavioral symptoms	50	3.2	1.8	1.5	64	77

* Actual reduction/possible reduction. Calculations were based on the fact that severity could not be reduced to a number lower than 1.0, which is equivalent to absence of a symptom, i.e., the possible reduction for anxious mood is 2.6

Table IV

Number of Patients with Moderate to Very Severe Symptoms Initially Who Showed Symptom Relief* at the End of Treatment

	Number of patients(%)	Level of significance+
Anxious mood	37 (80.4)	0.01
Tension	44 (89.8)	0.01
Fears	5 (83.3)	N.S.**
Insomnia	30 (88.2)	0.01
Intellectual (cognitive) difficulties	14 (82.4)	0.05
Depressed mood	24 (82.8)	0.01
Somatic (muscular) symptoms	29 (78.4)	0.01
Somatic (sensory) symptoms	17 (81.0)	0.01
Cardiomascular symptoms	33 (89.7)	0.01
Gastrointestinal symptoms	24 (77.4)	0.01
Genitourinary symptoms	23 (92.0)	0.01
Autonomic symptoms	35 (87.5)	0.01
Behavioral symptoms	32 (84.2)	0.01

*Relief is defined as reduction of symptom score by at least two levels (moderate to absent, severe to mild or absent, or very severe to at least moderate).

+Sign test.

**Sample size to small.

Table V

Overall Effect of Treatment with Lorazepam

Improvement	Number of Patients
Marked	55
Moderate	3
Slight	2
None	5
Total	65