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A double-blind comparison of the anxiolytic activity of two benzodiazepines, metaclazepam and bromazepam, in anxiety neurosis

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Summary

A double-blind controlled trial was carried out in 50 patients with anxiety neuroses to compare the effectiveness of metaclazepam, a recently developed benzodiazepine with anxiolytic activity, and bromazepam. Patients were allocated at random to receive treatment for 13 days with either 15 mg metaclazepam or 4 mg bromazepam per day, in 2 divided doses. The patients' anxiety status was assessed on entry and after 7 and 13 days of treatment by the physician, using the Hamilton multi-factorial rating scale, and by the patients, using a self-assessment rating scale. Both drugs produced a highly significant reduction in mean total scores, improvement being evident by the Day 7 assessment. Correlation between scores on the two scales was significant at all time points. Metaclazepam, however, was rated as producing a significantly greater improvement from baseline than with bromazepam on the self-rating scale.

Key words: Metaclazepam – bromazepam – neuroses, anxiety

Introduction

Metaclazepam, 7 bromo-5-(2'elozophenyl)2,3-dihydro-2-(methoxy methyl) 1 methyl-1H-1,4 benzodiazepine), is a new benzodiazepine recently described from both a chemical[1] and pharmacodynamic standpoint.[3] Pre-clinical studies[8,9] show that its anxiolytic effect is an extremely selective one. Moreover, metaclazepam seems to interfere to a lesser extent, as compared to diazepam and bromazepam, with cardiovascular and respiratory functions, resulting in a lesser potential for side-effects with respect to these latter benzodiazepines. The clinical studies performed so far[6,7,11] confirm the anxiolytic effects of metaclazepam.

The present study was aimed at evaluating the effectiveness of metaclazepam compared with that of bromazepam in the treatment of patients with anxiety disorders. Bromazepam is a widely prescribed benzodiazepine with well-documented anxiolytic activity.[4]

Patients and methods

Fifty patients of either sex suffering from anxiety symptoms of neurotic origin, based on DSM III criteria,[2] were included in the trial provided they had a minimum

score of 18 on the Hamilton anxiety rating scale.[5] Patients excluded were those with known hypersensitivity to the benzodiazepines, with closed-angle glaucoma or a serious organic pathology, those who had been treated with antidepressant and/or neuroleptic drugs during the 2 weeks preceding the trial, and women with confirmed pregnancy.

After a run-in period of 5 days during which patients only received placebo, patients were divided, on a randomized basis, into two balanced groups, each of 25 patients. Patients in the first group (Group A) were treated with 15 mg metaclazepam† per day in 2 divided doses, with an interval of 12 hours between doses; those in Group B were treated with 4 mg bromazepam‡ per day, also in 2 divided doses. To ensure the double-blind nature of the study, both drugs were prepared in identical oral solution form and an equal number of drops of each drug was administered to patients per day. The duration of treatment was 13 days.

Assessments of the patients' condition were made on entry and after 7 and 13 days of treatment by the physician using the Hamilton anxiety rating scale[5] and by the patients using a self-rating scale developed by Snaith *et al.*[10]

Statistical analysis of the results was processed using an IBM XAPC computer with SPSS-PC programme.

Results

All 50 patients completed the trial period. There were 18 males and 32 females with a mean age of 35.9±11.65 years (range 20 to 65 years). The two groups were homogeneous with regard to age, sex and initial scores on the two rating scales.

Table I. Assessments of patients' anxiety status on entry (Day 0) and after treatment using the Hamilton multi-factorial scale and the Snaith *et al.*[10] self-rating scale: mean (±S.D.) and range of scores for 25 patients in each group

Assessment	Metaclazepam		Bromazepam	
	Mean	Range	Mean	Range
Hamilton scale				
Day 0	45.53±6.09	34 to 54	44.53±6.39	32 to 54
Day 7	35.47±7.08*	22 to 43	34.87±7.25*	20 to 40
Day 13	25.27±5.18*	12 to 30	26.67±5.65*	17 to 34
Snaith et al. scale				
Day 0	27.47±5.38	16 to 36	25.60±5.72	15 to 35
Day 7	19.60±4.05*[a]	12 to 26	19.33±4.94*	11 to 26
Day 13	12.00±2.85*[b]	7 to 18	13.53±3.18	7 to 20

*$p<0.001$, within-group difference with repect to Day 0. Between-group difference with respect to Day 0, [a]$p=0.05$, [b]$p<0.05$

Table I gives details of the mean total scores on the two rating scales on entry and after 7 and 13 days of treatment. There was a statistically significant ($p<0.01$) correlation between the total scores of the two methods of assessment.

†'Talis', trade mark Farmades. ‡'Lexotan', trade mark Roche

Discussion

The results clearly indicate that, at the dosage used, metaclazepam is an effective anxiolytic agent in patients with anxiety neurosis. There was a highly significant reduction in mean total scores on the Hamilton rating scale and this improvement was evident as early as Day 7 of treatment. The results were at least equal to those with bromazepam, a benzodiazepine widely accepted clinically as an effective anxiolytic agent. Similar improvement was evident from the self-assessment scores of the patients, and using this scale metaclazepam produced a significantly greater response than did bromazepam.

It is particularly interesting that there was a statistically significant correlation between the scores on the multi-factorial Hamilton scale and on the self-rating scale of Snaith *et al.*,[10] at baseline, during and at the end of the treatment period. This confirmation of the appropriateness and sensitivity of the latter scale in such trials on out-patients is of practical importance because, among other things, it is less time consuming and easy to use, and is favourably accepted by patients.

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