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CLOBAZAM VERSUS DIAZEPAM: A DOUBLE-BLIND STUDY IN ANXIETY NEUROSIS

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IN India, diazepam is the most frequently prescribed benzodiazepine. Clobazam (HR376), a new benzodiazepine from the joint research of the Hoechst–Roussel laboratories, is distinctly different from conventional benzodiazepines in the 1,5 positioning of the nitrogen atoms (Barzaghi *et al.*, 1973). We have therefore undertaken a clinical study to compare clobazam with diazepam in the treatment of anxiety neurosis (Doongaji *et al.*, 1978).

Out-patients diagnosed as anxious neurotics by two independent psychiatrists, with an initial score of at least 20 on the Hamilton Anxiety Scale (HAS) (Hamilton, 1959), entered the study. Following a 3-d drug-free period, patients received either diazepam 15–20 mg daily or clobazam 30–40 mg daily. Drug therapy was continued for 29 d, followed by a week of placebo therapy. Assessment on the HAS was carried out by two independent raters on days 8, 15, 22, 29 and 36. Simultaneous evaluation on the Clinical Global Impression (CGI) scale (Guy, 1976) and for side-effects was also carried out.

Motor coordination was tested using Whipple's Tracing Board and the Hand Steadiness Test at the same periods of efficacy evaluation.

On each occasion, patients were interviewed for disturbances of sleep which they had experienced in the previous week.

Data on 40 patients were available for analysis. Differences between clobazam and diazepam failed to reach statistical significance either on the total scores of the HAS or the psychic anxiety and somatic anxiety clusters of the HAS. On the CGI scale too, no significant differences were elicited during the 4-week treatment period. At the end of the post-drug placebo period, the clobazam series maintained greater anxiolytic efficacy compared with the diazepam series. This was specifically observed in the 'somatic anxiety' cluster of the HAS. The variable 'gastrointestinal and autonomic symptoms' worsened significantly in the placebo period in the clobazam series. 'Insomnia, somatic-muscular, somatic-sensory and autonomic symptoms' deteriorated significantly in the diazepam-treated group.

The 'nights of sleep disturbance' in the sleep questionnaire showed a significant increase in the diazepam-treated group, at the end of the placebo period on day 36.

Only the results in the Hand Steadiness Test were analyzed, as these showed a consistent response. Results were significantly better on day 15 in the clobazam series. Patients with an initially high error score (pre-treatment error score $\geqslant 50$) showed a significant improvement on day 15 in favour of clobazam.

All laboratory investigations were within physiological limits. Side-effects reported in both groups were giddiness, drowsiness and unsteady gait, but not of statistical significance. In two patients on clobazam and four patients on diazepam, dosage was reduced.

Our results indicate that clobazam has a delayed onset of action, with maintained anxiolytic action. This may be attributable to an active metabolite which has a long half-life. These actions of clobazam are observed in both the total scores, in the clusters of the HAS, and in the analysis of the individual variables.

Compared with the control drug, clobazam also had a significantly better action on sleep disturbances during the placebo period. This may require further laboratory evaluation.

A very significant result from our study was the improvement on the Hand Steadiness Test observed in patients with high error scores. Clobazam definitely seems to improve motor coordination.

In conclusion, clobazam seems to be a promising addition to the benzodiazepine series. Its prolonged maintenance of anxiolytic effect, its hypnotic efficacy in anxiety neurosis and improvement of motor coordination, single it out as an 'unusual' benzodiazepine.

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