Br. J. clin. Pharmac. (1979), **7**, 107S–108S

MODE OF ACTION OF MODERN TRANQUILLIZERS FROM THE BENZODIAZEPINE GROUP: A CLINICAL VIEW

HANS H. WIECK

Universitäts-Nervenklinik mit Poliklinik, Schwabachanlage 6 u 10, 8520 Erlangen, West Germany

THERE is a large heterogeneous group of emotional disturbances in which the clinical picture is often dominated by anxious mood. The interaction of various psychic and somatic influences in the pathogenesis and continuation of these disorders is complex, and therapeutic intervention with drugs could itself become inextricably linked in a pathological cycle which may either intensify the initial symptoms or result in some other clinical syndrome. Purely psychic distrubances invariably become associated with somatic manifestations, and this has important implications for patient management, as it is not sufficient merely to institute psychological treatment; the somatic symptoms also must receive specific attention.

The complexity of these clinical syndromes makes their assessment and measurement extremely difficult. A number of established psychometric methods are available but there are as yet no really satisfactory psychopathometric tests or assessment scales. The Erlangen group have been particularly involved in the development of scales and tests which would be appropriate to assess these disorders and to measure the effects of the drugs used to treat them. A number of brief assessment scales have been developed for specific disorders. A new scale, the Erlangen Anxiety Scale, is currently undergoing validation trials. The advantage of this scale is that it measures both trait and state anxiety. The lack of sensitive and specific psychopathometric scales means that the assessment of drug effects, with specific regard to tranquillizers, still depends to a large extent on the clinical experience and evaluation of experienced physicians.

The search for 'ataraxia' (a state of 'restfulness of the soul') dates from antiquity, and this term encompasses a much wider concept than merely the absence of conflict and stress. It may be useful to assess how near the various benzodiazepines have come to achieving this ideal state. These drugs possess a typical pharmacological profile of activity but their mode of action as far as anxiety reduction is concerned is still not understood. We suggest that this anxiety-reducing effect is an indirect one, secondary to their antinociceptive activity.

We believe that the ideal tranquillizer should not produce impairment of patients' faculties, and the classical profile of activity of this group of drugs (namely sedation, hypnosis, anxiolysis and anti-aggression, muscle-relaxant and anticonvulsant effects) does not fulfil this ideal. The more recent benzodiazepines, however, tend to lack some of the adverse peripheral effects of diazepam and chlordiazepoxide. Prazepam, clorazepate and lorazepam, for example, may be considered as daytime tranquillizers because they produce less depressant and sedative effects than other members of this group.

How does clobazam fit into this classification? Our clinical experience has been that clobazam certainly has a tranquillizing effect. Inner tension states, where present, are alleviated or eliminated. Discomfort and organ-associated distress were removed in most cases. Because of the brief time available we have not yet been able to investigate the combined effect with analgesics. The relaxing and balancing effect of clobazam means that it elevates mildly depressed mood and relieves anxiety.

These statements still apply when daily doses of clobazam up to 60 mg are administered. Clobazam may therefore justifiably be referred to as a daytime tranquillizer.

Our experience indicates that clobazam is particularly suitable for combination therapy with other psychotropics, especially antidepressants. No interactions have been encountered to date.

With one exception, no undesirable side-effects have been observed by us. The one exception concerned a 40-yr-old clergyman suffering from endogenous depression; he was treated on an outpatient basis with antidepressants and clobazam 10 mg three times daily. For the first 2 d the patient complained of slight fatigue during the day, but this disappeared completely despite retention of the same dosage regimen.

One noteworthy feature is the positive effect of clobazam on sleeping/waking behaviour: therapeutic doses do not produce troublesome sedative effects.

A 56-yr old male teacher, suffering from idiopathic insomnia for 6 yr and referred to us as a result of poisoning with barbiturates and other non-benzodiazepine hypnotics, was able to sleep undisturbed through the second night after receiving clobazam 20 mg three times daily. This success persisted over a 3-week period and no relapse has yet been reported by the patient.

It is therefore possible that, in addition to its broad-spectrum activity as a daytime tranquillizer, clobazam has a particular effect in protecting sleep.

This is an abstract of a paper translated from the German by David Beattie.