Chlormethiazole – no hangover effect but not an ideal hypnotic for the young

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Summary

The hangover effects of 768 mg chlormethiazole, an hypnotic with a half-life of approximately 4 hr, were compared with those of placebo in a double-blind cross-over study in 8 young subjects. Ten hours after dosing there were no differences between the preparations in the subjects' psychomotor performance, EEG sleep scores, or visual analogue ratings. Thus, an hypnotic which is rapidly removed from the body may confer considerable advantages. However, all 8 subjects had unpleasant nasal symptoms following chlormethiazole, and it is therefore not an ideal hypnotic for this age group.

Introduction

Most hypnotics have plasma half-lives in excess of 7 hr: thus, substantial drug concentrations persist in the body the next morning. These may produce hangover effects, especially sedation and impairment of psychomotor performance which may persist for up to 36 hr after a single dose (Castleden *et al.*, 1977). Sleep patterns on EEG tracings provide an objective evidence of such effects and these may be present at 18 hr after a single dose of some hypnotics (Malpas *et al.*, 1970). One way of avoiding such effects might be to prescribe an hypnotic with a short half-life (Breimer, 1977). To test this hypothesis, the authors compared the effects of a single dose of chlormethiazole with those of placebo in healthy young subjects.

Methods

A double-blind comparison, randomized and balanced by an independent observer was made between a single dose of chlormethiazole capsules, and matching placebos. Each treatment was separated by at least 7 days and no other medication was taken before or during the study. Eight normal young subjects with a mean age of 26 years (range 19–34

years) took part: 4 were male. Medication was taken at 10.30 p.m. and tests were carried out between 8.30 and 9.30 a.m. the following day.

A 30-min recording was made of the EEG in the morning and this was scored according to the method of Malpas *et al.* (1970). Each subject completed a psychomotor test which consisted of crossing out all the letters 'e' on a single page of prose. An identical page was used on each occasion and the time taken to complete the test and the total number of mistakes made were recorded. Subjects completed visual analogue scales which assessed sleep latency (went to sleep immediately after taking capsules – did not get to sleep at all), sleep duration (slept all night – did not get to sleep at all) and sedation (wide awake – almost asleep). The scales were 10 cm long and measurements were made from the left-hand end.

The results of the psychomotor test were subjected to an analysis of variance with 2 treatment conditions – chlormethiazole *versus* placebo and order of administration. The Wilcoxon matched pairs signed rank test was used to compare the data from the visual analogue scales, and EEG recordings.

Results

These are shown in Table 1. No difference was found between the effects of chlormethiazole and placebo on either the EEG or the psychomotor tests. However, all 8 subjects experienced a sensation of prickling and burning in the nose which was sometimes associated with increased nasolacrimal secretion after chlormethiazole.

Discussion

Chlormethiazole did not produce significant hangover effects the next day which contrasts with previous findings with other hypnotics (Malpas *et al.*, 1970; Walters and Lader, 1971; Bond and Lader, 1973; Breimer, 1977). Thus, the results of this study support the contention that an hypnotic with a half-life of only 3–4 hr might confer advantages (Moore *et al.*, 1975).

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TABLE 1. A comparison of (mean $\pm$ s.e. mean) EEG sleep scores, psychomotor performance and visual analogue ratings 10 hr after a single oral dose of 768 mg chlormethiazole and placebo in healthy young subjects

	EEG	Psychomotor test		Visual analogue scales		
	Sleep score	Mistakes	Time (sec)	Sedation	Duration	Latency
Chlormethiazole	17 $\pm$ 14	12 $\pm$ 3	194 $\pm$ 13	25 $\pm$ 6	9 $\pm$ 5	13 $\pm$ 4
Placebo	32 $\pm$ 16 *	18 $\pm$ 5 *	206 $\pm$ 20 *	45 $\pm$ 11 *	2 $\pm$ 1 *	10 $\pm$ 3 *

* $P > 0.05$

Demonstration of a significant hypnotic effect was not possible with the present experimental design, as subjects slept well even on placebo. However, this property has been adequately shown in both young and elderly subjects using similar or smaller doses of chlormethiazole (Frisch and Ortengren, 1966; Evans, Lewis and Tinker, 1972; Pathy, 1975; Harenko, 1975).

If the nasal side effects of chlormethiazole occurred as frequently in the elderly as in the young subjects in this study they would deter regular prescription. However, on present evidence, chlormethiazole is worthy of study as an hypnotic in the elderly, as are others with short half-lives

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