Br. J. clin. Pharmac. (1991), **32**, 455–458

The effects of two anti-vertigo drugs (betahistine and prochlorperazine) on driving skills

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1 The effects of betahistine 72 mg three times daily, prochlorperazine 5 mg three times daily and placebo taken for 3 days before testing were compared on two actual driving tasks (weaving and gap estimation) and two psychomotor tasks (reaction time and kinetic visual acuity) in normal subjects in a double-blind prospectively randomised cross-over study.
2 The psychomotor effects of betahistine could not be distinguished from those of placebo.
3 Prochlorperazine impaired driving performance causing increased carelessness and slowing on the weaving test.
4 There was little subjective appreciation of impairment whilst taking prochlorperazine.

Keywords betahistine prochlorperazine driving psychomotor tests

Introduction

There is a growing awareness in the Western world that prescribed drugs taken for various conditions may have an effect on the driving performance of people who take these drugs whilst driving. Attention has largely been focused on psychotropic drugs (particularly anxiolytics, antidepressants and hypnotics) but some experimental work has also been done on antihistamines, antihypertensives and analgesic drugs.

Methods of investigation have included the use of laboratory psychomotor tasks (performance on which may extrapolate to the real driving situation), driving simulators and test track driving. Studies on the road have also been undertaken and also screening for drugs in the blood or urine of drivers involved in accidents (for full review see O'Hanlon & de Gier, 1986). A consensus view of the effect of prescribed drugs on driving behaviour has not been obtained from all these experiments, but there is a general opinion that most (but not all) psychotropic drugs do have some impairing effect on driving behaviour although this effect is likely to be a complex one and to be multifactorial.

Some drugs undoubtedly have a much greater impairing effect than others and probably should not be taken by those who drive. The condition for which the drug is being taken may, of course, also have an impairing effect on driving performance. Most studies are performed on normal volunteers, for obvious reasons, and testing is often carried out after a single dose of the drug which may not always be appropriate as there is some evidence that effects may wear off with chronic dosing.

Vertigo, either of labyrinthine origin such as in Meniere's disease, or due to other peripheral causes and often associated with nausea or vomiting is a common symptom. Drugs used to treat it include phenothiazines, various centrally active antihistamines and betahistine. Centrally active antihistamines have been shown to have an impairing effect on laboratory psychomotor tasks and on driving (Betts *et al.*, 1984; Nicholson & Stone, 1982). The effect of phenothiazine drugs on driving performance has not been well studied although chlorpromazine, even in small doses, has been shown to impair laboratory psychomotor task performance (Loomis & West, 1958) and trifluoperazine has been shown to impair test track driving performance (Betts *et al.*, 1972).

Betahistine has been shown to be an effective treatment of Meniere's disease (Frew & Menon, 1976; Wilmot, 1976). More recent evidence is also emerging that the drug is also useful in treating peripheral vertigo of varying aetiology (Canty *et al.*, 1981). High doses of betahistine are often recommended (Wilmot, 1979) and seem well tolerated (Grahne & Paavolainen, 1976).

Prochlorperazine is a piperazine side chain phenothiazine neuroleptic drug closely related to trifluoperazine which is now mainly used for symptomatic

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relief of vertigo and nausea and vomiting of vestibular origin. Drowsiness is a frequently reported side effect of prochlorperazine (Benson, 1969) and may be a particular problem in the elderly as, even with small doses, there may be Parkinsonian side effects (Stephen & Williamson, 1984). Intravenous prochlorperazine (12.5 mg) and a large oral dose (50 mg, an antipsychotic rather than an antiemetic dose) have been shown to impair reaction time and produce subjective sedation (Isah *et al.*, 1989).

Patients with vertigo associated with Meniere's disease often need long term therapy to control the condition. It is important therefore that their medication does not interfere with activities such as driving or their ability to operate machinery and that the drug in question does not have sedative side effects. It was decided to test the effects of these two drugs in normal volunteers after repeated dosing on low speed driving performance tests and compare these results with two laboratory psychomotor tasks using driving tests developed and modified in our department over the last 15 years (Betts *et al.*, 1986).

Methods

Volunteers

Twelve volunteers were recruited (six male and six female) aged between 20 and 31 years. They were medically screened before taking part in the study and had to have held driving licenses for at least 2 years and to drive regularly. They were not allowed to consume alcohol for at least 24 h before drugs were administered and throughout the period of medication and for 48 h afterwards: they were not allowed to drive on the open road whilst taking medication. The study was approved by the ethics committee of the Central Birmingham Health Authority.

Protocol

It was a double-blind prospectively randomised cross-over study. In a balanced order design, with prospective randomisation to one of three treatment sequences, all subjects took betahistine 72 mg three times daily, prochlorperazine 5 mg or matched placebo (10 doses of each). Drugs were supplied as indistinguishable tablets. Subjects were given medication for 3 full days before the series of assessments, the final dose being taken on the morning of the fourth day, 2 h before the start of the tests. There was a washout period of at least 1 week between successive test drug intake. All subjects had practice on both the driving and laboratory tests before the study commenced.

Two hours after the ingestion of the last dose of the drug subjects arrived at the test centre and went first to the test track where the two driving tests were laid out. These have been fully described elsewhere (Betts *et al.*, 1986) and consist of a weaving test and a gap acceptance test performed in a standard saloon car provided by the experimenters.

Measures

The weaving test consists of a line of plastic traffic cones set apart at one and half times the length of the car. The test is performed four times and the total number of mistakes, hits on cones and the mean time taken are recorded.

On the gap acceptance test drivers proceed continually round a circular test course: at a fixed point on the course they are presented with a variable gap formed by two plastic traffic cones. 25 m in front of the gap there is a decision point at which, whilst the car is moving, they have to decide whether the gap is wide enough to drive the car through (in which case they do so) or whether the gap is too narrow (in which case they drive around the gap and avoid it). Drivers go round the course twelve times and are presented with six gaps (three wide enough to drive through and three too narrow). Each gap is presented twice in random order. Gaps are six inches, four inches and two inches wider than the car and two inches, four inches and six inches narrower than the car. Measures of performance in this test are the number of passable gaps accepted, the number of passable gaps rejected, the number of impassable gaps accepted and the number of impassable gaps rejected, the number of hits on passable gaps and the time taken to complete the task.

Having completed the driving tests subjects then repaired to the adjacent laboratory where they performed tests of kinetic visual acuity and simple reaction time.

Kinetic visual acuity is measured using the Kowa Kinetic Vision Tester which measures the para-foveal acuity of an object approaching the eyes on a horizontal plane at a constant speed and from an apparent distance of 50 m. The approaching object is a Landolt ring (a black ring on a white background with a gap in the ring). The position of the gap can be adjusted to one of eight positions on the circle corresponding to the eight major points of the compass.

The subject looks into the machine through a binocular eye piece; when the ring has got sufficiently close so that he can see where on the ring the segment is missing the subject stops the machine by pressing the foot switch. The operator measures how close to the eye the ring has reached and checks the accuracy of the subject's observation. The further from the eye that correct recognition occurs the better the subject's kinetic visual acuity. Twenty trials of this test were performed on each occasion, the position of the gap being varied over the points of the compass in randomised order. Decrements in visual acuity have been shown to occur with fatigue, accident proneness in the driver and with some psychotropic medication (Betts *et al.*, 1986).

Reaction time was measured using a portable device on which the subject has to cancel, as quickly as possible, an intermittent light signal by pressing a button in front of it (Betts *et al.*, 1986). Forty trials of this test were made on each occasion.

Subjects in the laboratory were rated on objective presentation of mood, anxiety and arousal on a five-item visual analogue scale used by an experienced observer (TB). Subjects rated themselves on a ten-item visual analogue scale before each test, 2 h after the last dose. They also rated themselves on two visual analogue rating

scales of their subjective estimate of their driving performance.

Statistical analysis

The collected data were pooled and summary statistics produced for each treatment group. Non-parametric methods of analysis were considered appropriate and medians and ranges used to summarise the data. Friedman's two way ANOVA was used to compare the three treatment groups followed by the multiple comparison test associated with this procedure (Gibbons, 1976).

Results

Six male and six female subjects successfully completed testing without major unwanted effects. One subject failed to take one 5 mg tablet of prochlorperazine on day 2 otherwise compliance was complete.

Weaving test (Tables 1 and 2)

There were statistically significant differences between the three treatment groups in the time taken to complete four runs of the weaving test ($P = 0.009$) and in the total number of hits on this test ($P = 0.0001$).

The multiple comparison test revealed that the time taken to complete four runs on prochlorperazine was significantly longer than on placebo ($P < 0.05$). Drivers taking prochlorperazine were significantly more likely to hit cones than when taking either betahistine or placebo ($P < 0.05$).

Other tests

There were no significant differences between the three treatment groups in any of the other variables measured.

On the subjective visual analogue scales no significant differences emerged and drivers could not detect any change in their driving skills on the two subjective visual analogue measures of driving ability. The observer also could detect no significant difference on his measures of mood, tension, irritability, sleepiness and impaired concentration.

Table 1 Weaving test—total time for four runs (s)

	Betahistine	*Prochlorperazine*	*Placebo*
Median	199.5	215.0	191.0
Range	128–301	129–279	126–267

Significant difference between groups, $P = 0.009$.

Table 2 Weaving test—total number of hits for four runs

	Betahistine	*Prochlorperazine*	*Placebo*
Median	5.5	9.0	4.0
Range	1.0–12.0	4.0–23.09	0.0–13.0

Significant difference between groups, $P = 0.0001$.

Discussion

The aim of this study was to compare the effects of betahistine, prochlorperazine and placebo on tests of driving and psychomotor performance. The high dose of betahistine could not be distinguished from placebo on any of the battery of tests performed. Prochlorperazine however caused a deterioration in driving performance. While taking prochlorperazine subjects showed an increased degree of carelessness in that they hit more cones on the weaving test despite driving more slowly (driving more slowly suggests that they were aware of some impairment). It is disquieting that despite the objective deterioration in driving performance caused by prochlorperazine subjects were unable to detect any change in their driving ability although we have found before that subjects are often unaware of actual impairment (Betts *et al.*, 1986).

It has been shown that an intravenous dose of prochlorperazine (12.5 mg) and an oral dose of 50 mg (as would be used for antipsychotic treatment) impair performance on laboratory tasks (Isah *et al.*, 1989). Prochlorperazine has a low bioavailability so it is at first surprising that a small (anti-emetic) dose should also have psychotropic effects. Since the subjects had been taking the drug for 3 days before testing it is possible that sufficient had been absorbed to have a psychomotor effect or that active metabolites of the parent compound were responsible.

Prochlorperazine, in addition to a moderately strong ability to block the dopamine (D_2) receptor—like all phenothiazines—is also a central histamine H_1-receptor blocker (Richelson, 1984) to about the same degree as chlorpromazine and thioridazine (both have strong sedative properties). Trifluoperazine, a piperazine side chain phenothiazine closely related to prochlorperazine, has less effect on the H_1-receptor (Richelson, 1984) but has also been shown to have an effect on driving performance in low dose (Betts *et al.*, 1972). The dose of prochlorperazine used in this study was one that is known to be effective as an anti-emetic (presumably from a central effect on the H_1-receptor). We conclude, therefore, that the deleterious effect we have observed on driving behaviour is probably a real one and of some importance to drivers who take small doses of it to combat travel sickness. Prochlorperazine is widely prescribed for nausea, giddiness and vertigo: in the elderly it has been shown to commonly precipitate Parkinsonian symptoms even in low dose (Stephen & Williamson, 1984). In the young we have shown a mild but definite effect on psychomotor performance, even in low dose. It should therefore be prescribed with caution.

We are grateful to our keen and cooperative subjects and to Mr J. Johnson, R. Williams, A. Hall and Miss H. Betts and Miss V. Betts for their able assistance on the test track. We are grateful to Duphar Laboratories for supplying the drugs used in the study.

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(Received 22 April 1991, accepted 20 May 1991)