PAPERS AND ORIGINALS

Minor tranquillisers and road accidents

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Summary and conclusions

In a prospective study of 43 117 people, prescriptions issued by general practitioners over two years were linked with records of hospital admissions and deaths. For 57 people injured or killed while driving cars, motorcycles, or bicycles the medicines that had been dispensed in the three months before were compared with those dispensed for 1425 matched controls. There was a highly significant association between use of minor tranquillisers and the risk of a serious road accident (relative risk estimate 4·9).

The increased risk of accidents to drivers given tranquillisers could be due to the known psychomotor effects of these drugs or to effects of the conditions being treated. Whatever the reason, patients taking drugs such as diazepam should be warned that they are at special risk.

Introduction

The importance of alcohol as a cause of road accidents is established beyond doubt,[1] but the role of other drugs remains uncertain. Laboratory experiments show that drugs such as diazepam and chlordiazepoxide can impair functions relevant to driving, including sensory functions and perception, cognitive skills, and motor skills.[2] In tests of low-speed vehicle-handling chlordiazepoxide, amylobarbitone, and trifluoperazine all altered performance without the subjects being aware that their behaviour had been affected.[3] Such experiments are not directly relevant to driving in traffic, however, and there is no clear evidence that drivers using psychotropic drugs have an increased risk of accidents.[4]

In a drug-monitoring study using record linkage we found that 19% of people aged 15 or over received psychotropic drugs during one year.[5] This prompted us to determine whether such patients are at increased risk of having road accidents.

Subjects and methods

We studied the population registered with 16 general practitioners: this comprised about 33 000 people at any one time, and altogether 43 117 people were included during the two years from 1 March 1974 to 29 February 1976. The following records were linked for every person in the population[6]: details of basic attributes (such as sex and date of birth); prescriptions issued by general practitioners and dispensed; and records of hospital admissions, obstetric deliveries, and deaths. During the two years 309 of the population aged 16 or over were admitted to non-psychiatric hospitals or died (in or out of hospital) with injuries due to accidents or violence (ICD (8th revision) rubrics N800-N959 and N996). If a patient had been admitted more than once during the study only the first injury was included. Using hospital or general-practice case notes and coroners' reports we ascertained the dates and causes of injury for 294 (95·1%) of the 309 patients.

Of the 294 patients, 81 were injured in road accidents during the study period. A total of 68 were driving cars, motorcycles (including mopeds), or bicycles; the numbers of pedestrians and passengers (six and seven respectively) were too small to be included in the analysis. The analysis was restricted to the 57 drivers who had been included in the study for at least three lunar months—that is, 12 weeks—before their accident. For each of these patients 25 controls were selected at random from all the people in the population who (1) belonged to the same practice, (2) were of the same sex, (3) had the same (or an adjacent) year of birth, and (4) had also been included in the study for at least three lunar months before the accident. No person was selected as a control for more than one patient.

Patients injured in road accidents and their matched controls were compared with respect to the drugs that had been prescribed for them (and dispensed) during the three months before each accident. For this comparison the constituents of medicines were classified by means of the therapeutic codes developed by the Department of Health and Social Security (DHSS).[7] The analysis took account of the matching between patients injured in road accidents and their controls. Point estimates of relative risk were calculated by the method of Mantel and Haenszel,[8] and 95% confidence limits were estimated by the method

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of Miettinen.[9] Two-tailed P values were calculated as described by Pike and Morrow.[10]

Results

A total of 21 car drivers, 22 motorcyclists (or drivers of mopeds), and 14 cyclists were included in the analysis; three-quarters were male, and about two-thirds were under 30 years of age (table I). Because of small numbers these 57 "drivers" were first analysed together. They had received a total of 29 groups of drugs during the three months before their accidents. Table II lists the numbers of drivers and matched controls who had received those groups of drugs given to at least two drivers (all types of drugs were considered in calculating the relative risk for "any drug" at the bottom of the table).

Owing to the criterion for inclusion in table II, for several groups the number of drivers who had received drugs exceeded the number that would have been expected from the experience of the controls. The numbers were generally very small, however, and the difference was statistically significant in the case of sedatives and tranquillisers only. Although there was a significant association between the use of any drug and the risk of a road accident, the relative risk did not differ significantly from unity when the patients who had received sedatives and tranquillisers (and their matched controls) were excluded from the analysis (point estimate of relative risk 1·5; $P > 0·3$). Of the 57 drivers, 6 (11%) had received a sedative or tranquilliser during the three months before their accident, while the corresponding number among the 1425 controls was 36 (2·5%). This difference was highly significant (analysis of matched sets: $P < 0·01$). The relative risk associated with use of sedatives and tranquillisers was estimated as 5·2 (95% confidence limits 2·2 and 12·6).

The DHSS classification includes under the heading "sedatives and tranquillisers" both minor tranquillisers (such as benzodiazepines) and major tranquillisers (such as phenothiazines). Drugs were therefore reclassified as either sedatives and minor tranquillisers (referred to here as "minor tranquillisers") or major tranquillisers. Five of the drivers had received minor tranquillisers during the three months before their accident (table III); the relative risk associated with use of these drugs was estimated as 4·9 (95% confidence limits 1·8 and 13·0). Too few people were given major tranquillisers (one driver and four controls) for any conclusions to be drawn.

Details of the five drivers who had received minor tranquillisers were as follows.

TABLE I—*Distribution by sex and age of "drivers" included in analysis*

Age (years)	Car drivers		Motorcyclists		Cyclists		All drivers	
	M	F	M	F	M	F	M	F
<20	2		15	1	2	1	19	2
20–29	8	2	3		1	1	12	3
30–39	3		1	1	1		5	1
40–49	1	1	1		1	1	3	2
⩾50	3	1			2	4	5	5
All ages	17	4	20	2	7	7	44	13

TABLE II—*Numbers of drivers in road accidents and matched controls who received drugs in three months before each accident. Only groups of drugs given to at least two drivers are shown*

Therapeutic code	Group of drugs	No (%) who received prescriptions*		Relative risk (point estimate)
		Drivers (n = 57)	Controls (n = 1425)	
013	Sedatives and tranquillisers	6 (10·5)	36 (2·5)	5·2†
017	Minor analgesics	4 (7·0)	44 (3·1)	2·5
031	Antacids	2 (3·5)	29 (2·0)	1·7
042	Diuretics	2 (3·5)	18 (1·3)	2·9
046	Other cardiovascular preparations	2 (3·5)	12 (0·8)	4·5
052	Preparations for asthma	2 (3·5)	17 (1·2)	2·9
081	Penicillins	3 (5·3)	46 (3·2)	1·7
082	Tetracyclines	2 (3·5)	25 (1·8)	2·0
093	Oral contraceptives	3 (5·3)	29 (2·0)	5·6
133	Antihistamines	3 (5·3)	43 (3·0)	1·8
146	Skin preparations	4 (7·0)	76 (5·3)	1·3
	Any drug	21 (36·8)	343 (24·1)	2·0‡

*Some people received drugs in more than one group.
†$P < 0·01$.
‡$P < 0·05$.

TABLE III—*Numbers of drivers in road accidents and matched controls who received minor and major tranquillisers in three months before each accident*

Type of tranquilliser	No (%) who received prescriptions		Relative risk (point estimate)
	Drivers (n = 57)	Controls (n = 1425)	
Minor	5 (8·8)	32 (2·2)	4·9*
Major	1 (1·8)	4 (0·3)	6·3

*$P < 0·01$.

Case 1—Man aged 52. Received three prescriptions for diazepam (Valium) over two months; 12 days after last prescription he was killed when his car collided head-on with a lorry. A blood test for alcohol was negative.

Case 2—Man aged 37. Long history of heavy consumption of alcohol. Receiving repeat prescriptions for diazepam (5 mg thrice daily). Eight days after last prescription he had head-on collision with another car in which he was knocked out and suffered fracture of upper humerus and acromion. It was noted that he was taking diazepam and had drunk a little alcohol but no blood test was done.

Case 3—Man aged 40 being treated for asthma. He had previously received diazepam but was given two prescriptions for chlordiazepoxide (Librium) before his accident. Two weeks after second prescription he drove his moped into the back of a van, sustaining a Colles fracture and other injuries.

Case 4—Woman aged 58. Given Equagesic (containing meprobamate) for back pain. Seven weeks later was knocked off her bicycle when car door opened. She suffered comminuted fracture of the femur.

Case 5—Woman aged 50. Diabetic treated with insulin. Receiving repeat prescriptions for diazepam and nitrazepam. During month before her accident she received prescriptions for diazepam and amitriptyline. She was admitted to hospital the day after falling off her bicycle and dislocating her elbow. The admitting doctor noted: "Mechanism of fall unknown!" (his exclamation mark).

There was no mention of alcohol in the case notes of the last three patients. Interestingly, all five patients were over 30. Thus 24% of the 21 drivers aged 30 or over were known to have received minor tranquillisers during the three months before their accident.

When separate analyses were carried out for each type of vehicle the numbers of drivers who received minor tranquillisers were too small for significant associations to be declared, although the association between all tranquillisers and car accidents was significant at the 5% level. There was also a significant association between use of antihistamines and motorcycle accidents (point estimate of relative risk 5·3; $P < 0·05$). The three motorcyclists concerned were male and aged 16 or 17 years; two had received chlorpheniramine and the other mebhydrolin.

Discussion

These results suggest that patients treated with minor tranquillisers have an increased risk of serious road accidents (leading to hospital admission or death). There was also a statistically significant association between antihistamines and motorcycle accidents.

We assumed that patients who received a drug during the three months before an accident were "users" of that drug and that other people were "non-users." Neither of these assumptions would always be correct: some patients would not have been taking their medicines at the time of the accident, while others regarded as non-users might have been taking drugs dispensed before the three-month period (or obtained from sources other than their general practitioner). The effect of such misclassification, however, would not be to produce spurious associations between drugs and road accidents but rather to reduce the power of the study to detect real associations.

Drivers who had road accidents were compared with controls matched for sex, age, and membership of the same practice. The controls were not matched for exposure to driving, however. We are not aware of evidence that patients taking tranquillisers are more likely to drive than other people; indeed, anxious people might be less likely to drive, so there could have been bias in the opposite direction (reducing the estimate of relative risk for use of tranquillisers). The association between tranquillisers and road accidents could not have been produced by inflation of the practice registers (from which the controls were selected). Even

if we assumed that 10% of the patients registered had actually left the practices (which is unlikely) the proportion of controls who received minor tranquillisers would still be only 2·5% (compared with 9% of the drivers in road accidents).

Such a study cannot distinguish whether the increased risk associated with use of tranquillisers is due to effects of the drugs themselves or the diseases being treated. Conceivably, for instance, the patients given tranquillisers might have been at greater risk if they had not been treated. Eelkema *et al*[11] suggested that psychotic patients were less likely to be injured on the roads after treatment in a mental hospital; but although their conclusion is often quoted it was based on accident rates among only 71 psychotic patients, with no test of statistical significance. In interpreting our findings it is also relevant that studies on healthy people had already given reason to suspect that minor tranquillisers would impair driving ability.

Apart from the underlying conditions being treated with tranquillisers other factors should be considered. One of the drivers taking diazepam was a diabetic receiving insulin, but there were no other road accidents among diabetics. Alcohol consumption is another potential confounding factor in the association between tranquillisers and road accidents; there is also the possibility of interaction, because tranquillisers may enhance the deleterious effects of alcohol on driving skills.[12] In our study only one of the five drivers who had received minor tranquillisers before their accident was known to have taken alcohol. The possible role of alcohol was excluded (by a blood test) in another case and not suspected in the remaining three accidents (all of which occurred in the daytime).

The association between antihistamines and motorcycle accidents could also have been due to effects of the conditions being treated. Once again, however, there was already reason to suspect that the drugs would impair driving. Antihistamines often cause drowsiness, and preparations sold without prescription bear a warning about driving or operating machinery. According to Meyers *et al*,[13] however, there is no epidemiological evidence that drivers using antihistamines have an unusual number of accidents. That the risk associated with antihistamines was confined to motorcyclists could have been a chance finding, especially in view of the small number of accidents available for study. Nevertheless, Milner[14] suggested that because of the extra skills required to control a motorcycle motorcyclists would be especially vulnerable to the effects of drugs.

Other studies of the role of drugs in road accidents have been reviewed by Kibrick and Smart[15] and Milner.[14] Two particular problems hamper research. Firstly, it is difficult to obtain retrospectively accurate information about use of drugs. Interviews of patients after road accidents may be misleading, because some drivers do not admit that they have taken drugs[16 17]; studies based on blood specimens are more reliable. The second problem is in obtaining information about suitable controls, especially if blood specimens are required.

A larger record-linkage scheme would provide more information about the role of prescribed drugs in road accidents. The number of accidents included in our study was too small to permit comparisons of the effects of individual tranquillisers and antihistamines (which could be very different). The study was also too small to assess the effects of major tranquillisers and many other groups or of combinations of drugs.

Surveys comparing concentrations of drugs in blood specimens from drivers after road accidents and from adequate controls could determine the extent to which accidents are caused by consumption of excessive doses of tranquillisers or by combination of these drugs with alcohol. But even that type of study could not make a reliable distinction between the effects of drugs and the effects of the conditions being treated. Patients are, for instance, more likely to take their tranquillisers (and therefore to have measurable blood concentrations) when their symptoms are worst. A large, randomised controlled trial would be needed to disentangle the effects of drugs and underlying diseases.

From a practical point of view, however, it is important to know that drivers taking minor tranquillisers are at increased risk of having a road accident (for whichever reason); and the results of our small study suggest that the risk may be substantial. This has implications for the safety of other road users as well as the patients themselves. If our results prove to be typical patients given tranquillisers should at least be warned that they are at special risk and that, if they must drive, they should take particular care not to exceed the prescribed dose or to combine their drugs with alcohol.

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ONE HUNDRED YEARS AGO It is a satisfaction to see that the Infant Life Protection Act—in the production of which legislative measure the BRITISH MEDICAL JOURNAL played a large part—is being enforced somewhat more vigorously in the metropolis. At Hammersmith, last week, Jane Cook was summoned, at the instance of the Metropolitan Board of Works, for retaining an infant in her care contrary to the provisions of the Infant Life Protection Act of 1872. Samuel Babey, the inspector, stated that in October last the defendant was registered for the care of two infants. In March, he ascertained that the defendant had registered the death of an infant. He saw the defendant, who stated that the infant was born in the house and died, but it was never in her care. He received a note from her afterwards, stating that she was very sorry for having told him that the child was born in the house, as that statement was untrue. She received the child to nurse. The defendant, in reply to the magistrate, admitted having had three infants, but said she intended to give up one. The inspector said he visited the house once a month. He did not know of the infant being there, and he should not have known if he had not inquired of the registrar of the district. Mr Bridge said the Act must be strictly enforced. He fined her forty shillings and two shillings costs, with the alternative of fourteen days' imprisonment, and directed that her name should be struck off the register. The attention of the Home Secretary has been called to an apparent failure of the Act at Lewes, and he has promised to consider how it can be amended. (*British Medical Journal*, 1879.)