Benzodiazepines and Driving Performance

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A comprehensive review on the subject: Benzodiazepines and driving performance is published by the authors recently in the journal: Reviews in Contemporary Pharmacatherapy (1). An overview of this review is given below.

Introduction

During the past 20 years, there has been a remarkable interest in the effects of prescription drugs on road safety. On their own and in conjunction with alcohol, psychoactive drugs and, in particular, tranquillizers have been studied in relation to driver impairment, but many of the articles and reports published do not seem to have been the subject of adequate peer reviews. Extensive knowledge of the epidemiological and experimental methodology applicable to drug-driving is indispensable for an adequate assessment of the relevant literature. An understanding of drug-driving requires the ability to relate drug effects to behavioural effects. While there seems to be no problem in defining a drug, its dosage and pharmacokinetics, and its behavioural effects are more difficult to specify. The research on drug effects in relation to car driving is a multidisciplinary task where the knowledge of psychologists, pharmacologists, statisticians, psychiatrists, and physicians specializing in traffic medicine and psychophysics, is required.

A drug's potential effect on road safety is a function of its use by the population and its action on the user. A drug used only by a few outpatients presents essentially no problem, even if it can be shown that the medication seriously impairs a number of functions which may be important for car driving. On the other hand, a widely used drug, even if it affects only a few of the functions relevant to car driving, may present a substantial hazard to road safety.
Two basic approaches to the investigation of the problem of drug effects on road safety are available: experimental research and the epidemiological method. One of the reasons why it is difficult to relate driver impairment to drugs is that there is little scientific evidence as to the kind of abilities used in car driving. Furthermore, relevant data on drug use in the population are difficult to gather.

A fact which needs to be pointed out, is that most psychoactive drugs are prescribed for conditions which, if left untreated, would tend to increase the likelihood of a traffic crash. Another extremely important question is the combined effect of drugs and alcohol. Both these issues need to be addressed in interpreting research findings.

The aim of this review of benzodiazepines and driving performance is the evaluation of the results available from several points of view:

1. application of the theoretical pharmacological knowledge of the effects of benzodiazepines on the psychological requirements of highway traffic;
2. epidemiological studies into the frequency of drug use by drivers and the frequency of accidents;
3. experimental studies;
4. possibilities of implementing the knowledge for the prevention of accidents; and
5. determination of further research requirements.

Epidemiology

In our review the pharmacology of the Benzodiazepines and the different applied Research Methods are outlined and earlier reviews and their results are described. The epidemiological approach, based on the analysis of traffic accident statistics and the presence of different drugs in the bodies of drivers and other accident victims, appears in principle to offer useful information. However, in evaluating this research it has
to be recognized that there are major problems involved in relating blood levels of drugs to driving impairment. Individual tolerance, diseases state, age and interaction with other drugs and alcohol amongst other factors make this evaluation difficult. The majority of epidemiological studies suggest that there is an overall indication that people who take benzodiazepines are overrepresented amongst crash victims, but it is quite impossible to assert from these findings whether this overrepresentation is due to the effect of the drug taken therapeutically at appropriate dose levels, to supra-therapeutic doses taken either accidentally or as a part of a drug-abuse syndrome, to synergize with alcohol, barbiturates or other agents or to the indication for which the benzodiazepines had originally been prescribed.

Experimental work

The publication (1) illustrates methods, findings and limitations of the experimental analysis of benzodiazepine effects on driving. The effect of benzodiazepines on critical flicker fusion. When diazepam was the experimental drug, three out of six reported studies showed a significant decline in performance.

24 studies are described in which a benzodiazepine was used to find effects on digit or symbol substitution tests. Chlordesmethyldiazepam, desmethyldiazepam, flurazepam all tend to impair performance, in particular in single dose studies. The studies are summarized in which an auditory stimulus was given and where reaction time or vigilance was measured. Of the ten studies in which subjects were given diazepam, four showed a significant performance impairment.

Numerous studies are outlined in which reaction time to usual stimulus was measured. In far studies performance was impaired
by diazepam, in one study it was improved and in seven no significant drug effects were reported.

The effects of benzodiazepines on tracking tasks, on letter cancellation tasks, on body sway, tapping tasks and on vehicles manoeuvres and closed-circuit driving are illustrated in our review (1) in a similar way.

Some studies in which real on-the-road performance was observed after experimental medication with long, short and ultrashort acting benzodiazepines. In many of the studies the effect of diazepam was tested and all report some impairment on one or more parameters.

Results of some experiments with the driving simulator are also presented. It is shown that diazepam, after both short- and longterm treatment impaired steering control and reduced driving performance.

Conclusion

An examination of the investigations indicated that some studies have shown that performance is impaired after experimental medication with benzodiazepines. A lesser number of studies has shown that performance improved after drug administration, but the vast majority of studies yielded inconclusive results. As expected, when impairment occurred it happened more frequently after a single dose or at the onset of chemotherapy when multiple doses were given. There was also some evidence that when impairment was found it was either dose related or occurred at a time when drug plasma concentrations were rising, rather than when steady-state levels were reached.
The present review also indicated that the newer benzodiazepines seem to have fewer behavioural side effects than the older ones. The analysis of the published data shows that improvement and impairment of performance were reported for nearly all types of tests used and it would be difficult to assert that sensory-perceptual (e.g., critical flicker fusion frequency), cognitive-motor (e.g., letter cancellation), cognitive (e.g., symbol substitution), perceptual-motor (e.g., tracking and reaction time) or motor tests (e.g., bodysway and tapping) were better tests to measure impairment.

The experiments in which subjects drove in traffic whilst under medication indicated that therapeutic doses of diazepam impair performance, at least on the onset of chemotherapy. Vehicle manoeuvres also tended to show impairment after medication with benzodiazepines hypnotics. When antianxiety agents were tested, diazepam and clobazam yielded inconclusive results, but subchronic administration of lorazepam impaired performance.

In general, there seems to be some evidence that people who take benzodiazepines are overrepresented in crashes. However, it is quite impossible to assert from the available data whether this overrepresentation is due to the effect of benzodiazepines or to the indication for which the benzodiazepines had been prescribed.

It must always be remembered that there are many things which interfere with car driving ability. Alcohol is the most frequently cited example.

The general prohibition of driving whilst under medication with benzodiazepines will not reduce the number of crashes. Some drivers who take benzodiazepines are safer because of their medication. It is believed that the correct therapeutic use of benzodiazepines under medical supervision presents less of a hazard to road safety than that posed by the presence of anxious, depressed and aggressive drivers. A person whose judgement, reaction, psychomotor responses and general behaviour pattern are affected by anxiety, aggression, stress
or depression should not drive until his mental condition has been ameliorated.

In conclusion:

1. Benzodiazepines used as hypnotics should have a short or very short half-life and any active metabolites should have a similar elimination rate to the parent drug. Probably half-lives of less than three hours are desirable. Obviously, the drug should have no other unwanted side effect.

2. Benzodiazepines used as anxiolytic should have minimal sedative effects.

3. Patients to whom benzodiazepine anxiolytics are prescribed should be advised to exercise particular caution when driving during the early stages of medication whilst their body is adjusting to the presence of the new drug.

4. The drug dose should be titrated to maximize therapeutic and minimize unwanted sedative effects.

Similarly, it is possible, on the basis of the foregoing review, to establish a number of guidelines for future research into the effects of benzodiazepines on driving performance.

1. Experimental research should examine both the objective and subjective effects of benzodiazepines. In behavioural tests, wherever possible unobtrusive and objective measures should be used to assess performance.

2. Epidemiological data should be collected from accident victims and help should be offered to medical examiners, coroners and associated laboratories to ensure that proper drug screening of the body fluids of car crash victims takes place and, in positive cases, to distinguish between proper therapeutic doses and possible cases of drug abuse.
3. Comparative data should be collected from an adequate control group of non-crash involved drivers. Alternatively, the proportion of positive benzodiazepine screening amongst accident-involved drivers should be related to the number of filled prescriptions and minor psychiatric morbidity.

4. Attempts should also be made to find a control group amongst anxious drivers, who, for reasons of religion or conscience, refuse to take any medication. From these data one may be able to estimate whether patients who take therapeutic doses of benzodiazepines are overrepresented amongst crash victims. These data should exclude cases when non-therapeutic doses of benzodiazepines were taken and where drug abuse is suspected, as well as those cases where a blood alcohol concentration in excess of 50 mg/100 ml may have been an additive causative factor of the crash.

Reference

(1) B. Friedel
M. Staak : Benzodiazepines and Driving Performance
Rev. Contemporary Pharmacotherapy 1992, 3: Number 9, 415 - 474