Driving and Benzodiazepine Use
Evidence That They Do Not Mix

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Abstract

Although the data are sparse, epidemiological studies show that benzodiazepine use increases the relative risk of being involved in a traffic accident by a factor of from 1.5 to about 6.5, depending on dose, number of benzodiazepines used and recency of use. These risks are similar to those associated with blood alcohol concentrations of about 0.6 and 1 g/L, respectively. Experimental studies employing on-the-road driving, driving simulation and laboratory tests measuring skills related to driving have clearly established the dose-dependent performance-impairing effects of benzodiazepines.

Benzodiazepine hypnotics vary considerably in their potential to produce residual effects in the morning after nocturnal use. The main determinants of the degree and duration of action after a single dose are size of dose, rate and extent of distribution, lipophilicity and receptor affinity. With repeated administration, compounds with a long elimination half-life \( t_{1/2}\beta \) are likely to accumulate and produce increased sedation. Diazepam may have a rapid onset of action precipitating the risk of sudden intoxication, but its duration of action is relatively short after a single dose (acute tolerance). The impairing effects of diazepam on driving performance may persist at least during the first 3 weeks of daily administration. The issue of tolerance has not yet been adequately explored and patients should be warned that their performance may not return to the premedication level. Elderly patients may be more sensitive to the sedative and performance-impairing...
effects than the young, although the evidence is equivocal. Caution is warranted with concomitant use of CNS depressants, such as alcohol, and with drugs interfering with the metabolic pathways of benzodiazepines. Considerable interindividual differences in sensitivity to the behavioural effects of benzodiazepines warrant the careful monitoring of patients. Physicians should educate their patients about the risk of traffic accident during benzodiazepine use.

During the past 2 decades there has been increasing awareness of the effects of potentially performance-impairing prescription drugs on traffic safety. Attention has particularly focused on the benzodiazepines because they are the most widely used psychoactive medicines in the world, despite a declining trend in the annual number of prescriptions.\(^1,2\) Benzodiazepines are most commonly used in the treatment of anxiety and insomnia, and to a lesser extent in a variety of other clinical conditions, such as epilepsy, motor disorders and anaesthesia. To illustrate the prevalence of their use, in 1992 about 11% of the Dutch population received at least one prescription for benzodiazepines, and the percentage of daily users was estimated at 3.9%.\(^3\) In France, prevalence rates of benzodiazepine use in the general population have been reported to be 2 or 3 times higher than in most other industrialised countries. Between 25 and 30% of the population are estimated to be occasional or regular users of these agents and 5 to 7% are long term users.\(^4\) Benzodiazepine use generally increases with age and is about twice as high among women as among men.

Along with their relative safety and well-established efficacy (‘sunglasses for the soul’), there is a vast body of experimental data demonstrating the adverse effects of benzodiazepines on driving-related skills. For some years the question has been raised whether these effects would also translate into increased accident rates. Although evidence is slowly accumulating, there are already sufficient data from epidemiological studies to emphasise the need for careful prescribing of these drugs.

This article reviews both epidemiological and experimental findings. In particular, attention is given to clinically relevant differences between benzodiazepines, and factors contributing to driving impairment. From this information, prescribing guidelines have been derived which aim to minimise performance impairment in patients.

1. Mechanism of Action

All benzodiazepines have anxiolytic, sedative-hypnotic, muscle relaxant and anticonvulsant properties, and some possess antidepressant effects. While long debated, it is now generally understood that benzodiazepines enhance the activity of the inhibitory neurotransmitter \(\gamma\)-aminobutyric acid (GABA) by binding at specific sites (\(\omega\)-receptors) in the membrane of the GABA\(_A\)-benzodiazepine receptor complex. The general sedative effects of benzodiazepines are assumed to underlie their potential to impair driving skills, for example by decreasing alertness, slowing reaction times, reducing visual function and degrading motor skills and decision-making capacity.

Benzodiazepines are also known to impair memory, both secondary to and independently of their sedative actions. However, in a recent survey, experts assigned relatively low weight to memory functions as being absolutely essential for driving, with the exception of spatial working memory.\(^5\)

2. Epidemiological Studies

After alcohol, benzodiazepines are among the most frequently detected substances in blood samples obtained from drivers suspected of being under the influence of alcohol or drugs, and from drivers involved in fatal and nonfatal traffic accidents. For example, in 1993 the National Institute of Forensic Toxicology in Norway collected and analysed 394 blood samples from drivers involved in accidents. Most samples contained alcohol (62.9%), followed by benzodiazepines (13.7%), tetrahydrocannabinol...