Risk of Involvement of Medicinal Drugs in Traffic Crashes

OLAF H.DRUMMER

Victorian Institute of Forensic Medicine & Department of Forensic Medicine, Monash University, 57-83 Kavanagh Street, Southbank, Victoria, Australia 3006

Corresponding author: olaf@vifm.org

ABSTRACT

Medicinal drugs can impair, particularly those that possess depressant action of the central nervous system. These include the older generation antidepressants, many anticonvulsants, antipsychotics, the sedating antihistamines, muscle relaxants such as carisoprodol and the benzodiazepines. Most evidence for the impairment of medicinal drugs belong to the benzodiazepines which are clearly capable of causing impairment, particularly the longer acting examples, when used in the elderly, or when abused in the younger age groups. The opiate class of drugs have an uncertain effect on impairment since they are often in association with other impairing drugs. Current evidence suggests that impairment of driving skills will not be significant if doses are stabilised and the patient has neuroadapted to the drug and the patient is not taking other CNS active drugs. However, more research is required to fully understand the implications of medicinal drugs in road trauma.

Keywords: Medicinal drugs, Driving impairment, Crash risk, Benzodiazepines.

INTRODUCTORY COMMENTS

The contribution of alcohol (ethanol) to road trauma is now well established. Blood alcohol concentrations over 0.05 gram per 100 mL (0,5 promille) is associated with significant increases in crash risk. This risk rises exponentially over 0.10 gram per 100 mL [1-4]. The increased crash risks is due to its CNS depressant properties that adversely affect reaction times, vigilance, road lane control, tracking, and avoidance etc.

Illegal drugs are also associated with increasing crash risk, particularly cannabis [5, 6] and the strong stimulant drugs such as the amphetamines and cocaine. The reduced performance is due to a combination of CNS depressant effects (for cannabis) and their ability to adversely affect driving skills when consuming a strong stimulant on he one hand and the rebound fatigue issues associated with the elimination of CNS stimulant drugs.

When it comes to medicinal drugs their potential impact on crash risk is less clear, mainly due to the smaller amount of data available. The drugs most of interest are the analgesics including opiate-like drugs, anti-histamines, sedating antidepressants, benzodiazepines and related minor tranquilisers and hypnotics. All of these “medicinal” drugs are capable of adversely affecting reaction times, divided attention tasks, vigilance, tracking etc and should be associated with

increased crash risk. The net effect of drugs on persons is compounded by the presence of other CNS active drugs [5, 7].

Crash risk is dependent on many factors. These include the driver's innate driving skills, their driving experience, age, and the internal car environment including possible distractions due to passengers, use of CD players, eating and smoking. External factors include road conditions such as road surface, weather conditions and the behaviours of other drivers. Superimposed on these factors is driver fatigue and alcohol or drug use. Any one or more of these have the potential to adversely affect driver skills and reactions and lead to a crash of some type.

Therefore it is likely that any drug capable of adversely affecting driving skills should be associated with increased crash risk.

HOW ARE DRUG EFFECTS ON THE ROADS ASSESSED?

There are a number of ways drugs are assessed for their possible influence of driving skills. Initially the pharmacology of the drug must be understood in order to understand what neuronal or receptor system it may be acting on. Secondly its possible affects on driving performance is assessed using psychometric laboratory testing. This allows reaction times, vigilance, tracking etc to be assessed. Case control studies are used to provide epidemiological evidence for any over-representation of drivers using certain drugs. These studies use such techniques as culpability studies, pharmaco-epidemiological studies, linking prescriptions or drug use with a characteristic, i.e. increased accident rate. Sobriety assessments of impaired drivers through medical or police (DRE) examinations provide much useful anecdotal data on possible drug-induced effects [8]. Indeed even surveys can be used to assess driver actions.

BENZODIAZEPINES

Benzodiazepines are a large class of minor tranquilizers, marketed as hypnotics, sedatives and anxiolytics, and are also used for a variety of other medical conditions such as epilepsy, use as muscle relaxants or in panic attacks. Diazepam is used in alcohol withdrawal and as a pre-anesthetic in surgery.

Each Country has a number of legally available benzodiazepines although some may have illegal use through doctor or pharmacy shopping. It is thought that about 1-3% of the population at any given point of time is using one or more benzodiazepine. In fatally-injured drivers the incidence in Victoria is about 4-10%, while in drug-affected drivers it is about 65%. They are arguably more prevalent in some communities as a drug of abuse than the traditional hard drugs. Often they are also used (or abused) with other drugs such as alcohol or cannabis.

The evidence for the role of this class of drugs to cause crashes is overwhelming. In a review of 12 epidemiological studies 10 concluded that benzodiazepines increased crash risk and of the two that did not one had low study numbers. Persons using benzodiazepines and admitted to hospital following motor vehicle crashes had a 5-times higher risk [9]. This increased risk for hospitalized drivers (OR 6.5) was confirmed in a study of 78,000 patients [10], however another group found these drugs were not over-represented when their responsibility rates were assessed [11]. However, injured drivers responsible for the crash and using benzodiazepines were significantly over-represented when the drugs were present in greater than therapeutic concentrations [12].

A higher relative risk of injury in the over 65's using benzodiazepines was also reported [13]. The relative risk of accident involved elderly drivers increased 45% in first week of starting

benzodiazepines, particularly long-acting drugs [14]. These conclusions were supported by a study of 2500 injured drivers [15].

The over-representation has since confirmed a number of times on large study populations. The prevalence of benzodiazepines in fatally injured drivers was 2.5-times the rate as assessed through roadside surveys conducted at same time [Dussault, unpublished observations]. Similarly when studying injured drivers the over-representation is consistently high for the benzodiazepines [16, 17].

A review of drivers in whom only benzodiazepines were the cause of impairment the subjects had significantly higher blood concentrations of diazepam, oxazepam and flunitrazepam than those drivers not impaired [18]. The risk of being assessed as impaired rose with increasing benzodiazepine blood concentration, with an odds ratios (OR) for being assessed as impaired of 1.61, 3.65 and 4.11 for the three supra-therapeutic drug levels. A drug-concentration relationship for benzodiazepines on performance was also found.

A roadside study in Denmark found 0.7% positive for benzodiazepines and 1.4% were positive for illegal drugs (amphetamine, cannabis, cocaine or opiates) [19]. The incidence of benzodiazepines is likely to be under-represented due to sensitivity limitations of the testing method.

OPIATES

The opiates covers a large range of drugs, including heroin, morphine, codeine, dihydrocodeine, ethylmorphine, methadone, buprenorphine, fentanyl, pethidine (meperidine) and even the atypical opiate tramadol. These drugs reduce the sensation of pain but also show sedative actions by way of their narcotic activity, particularly the potent members of this class. Behavioural and epidemiological data generally show this class of drug has relatively low crash risk [20]. For example, only one of out four epidemiological studies show an increased risk [17]. Other studies show weak trends to an increased risk only [16, 21].

Patients on controlled opiates for pain relief show no observable driving impairment [22]. However, opiates do reduce vigilance due to their narcotic activity and have the potential to increase fatigue. When this occurs it is likely that opiates will impair and cause crashes

Opiates are also often used with other drugs, such as alcohol and the benzodiazepines. When this occurs it is likely that the drug combination will be a higher risk. Methadone maintenance subjects at risk particularly if starting treatment or using other drugs.

OTHER MEDICINAL DRUGS CAPABLE OF INCREASING CRASH RISK

There a re a range of other medicinal drugs that adversely affect the central nervous system and have the ability to affect a range of actions that can manifest into impairment. These include the sedating anti-histamines, barbiturates, some anti-convulsants, antidepressants belonging to tricyclic or tetracyclic class, and many anti-psychotic drugs (Table 1). Indeed all drugs that have CNS depressant activity should be regarded as impairing unless proven otherwise.

The muscle relaxant carisoprodol has been linked to impairment and increased crash risk [23, 24]. While sedating antidepressants have the potential to impair studies show the depressed patients may be impaired due to their mental state and not necessarily due to the drug [25]. Improvements in mental state will undoubtedly increase driving performance irrespective of which antidepressant they are taking.

It is true for all medicinal drugs as it is for illegal drugs that repeated use does lead to a diminution of adverse side-effects. This is caused by tolerance or neuroadaptation. For example, the sedating effects of antihistamines reduce with repeated use [26] and the road safety risks associated with drugs reduces with chronic use. However, abuse or misuse of drugs will cause significant central effects and will therefore impair the ability to drive safely.

However, there is currently little evidence to link many of these drugs to increased crash risk.

Table 1: Medicinal drugs Capable of Causing Impairment

Drug class	Examples in each drug class
Anti-convulsants (some)	Carbamazepine, phenytoin
Anti-histamines (sedating)	Chlorpheniramine, brompheniramine, pheniramine, doxylamine
Anti-psychotic drugs	Haloperidol, chlorpromazine, clozapine
Barbiturates and barbiturate-like drugs	Amylobarbital, quinalbarbital, meprobamate
Benzodiazepines and related drugs	Alprazolam, clonazepam, diazepam, flunitrazepam, temazepam, zolpidem, zopiclone
Muscle relaxant	Carisoprodol
Tri-cyclic antidepressants	Amitriptyline, dothiepin, doxepin

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