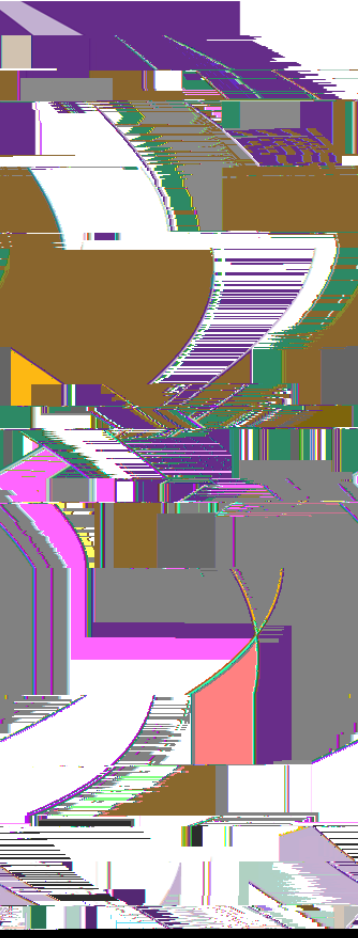

Prescription drugs and driving

Information for the prescriber

Summary

Factors affecting fitness to drive include:

The particular medications being used, their effects and duration of action, and interactions between medications used in combination.

Dose and time of administration in relation to driving.

Whether use is regular or occasional – regular use will result in some tolerance but possibly also withdrawal. The effect of tolerance depends on the type of medication.

Other medical problems such as chronic pain and sleep apnoea will increase driving risk.

History of recent driving incidents such as motor vehicle accidents or driving offences.

Benzodiazepines

Benzodiazepine anxiolytics, taken during the daytime impair driving performance independent of their half-lives. Patients with anxiety who are prescribed anxiolytic medications for day time use should be strongly advised not to drive, at least during the first four weeks of treatment.

Benzodiazepine hypnotics can have detrimental effects on psychomotor performance, attention and memory the day after bedtime use (hangover effect). Short half life medications generally do not impair morning performance, while longer half life medications may do. Advise accordingly.

The role of tolerance in mitigating these effects is unclear.

Opioids

Opioids taken in the acute setting impair driving performance. Patients should not drive in these circumstances.

Tolerance develops rapidly and driving performance may return to normal within two to three weeks.

Dose increases in patients previously stable on lower doses, may impair driving.

Patients with chronic pain may be impaired due to multiple factors such as sleep disturbance,

Notifications

Medical practitioners, physiotherapists and optometrists in South Australia are obliged to notify the Registrar of Motor Vehicles (Section 148, Motor Vehicles Act 1959) if they have reasonable cause to believe that a patient is likely to endanger the public if they were to drive a motor vehicle.

Patients using medications not in accordance with advice, or not adhering to advice not to drive are examples of situations in which notifications might be considered appropriate.

Longer term patients

When assessing fitness to drive in patients with longer term use of medications, particularly those on opioid substitution treatment or long-term use of sedatives, consider:

the extent to which the person has engaged in the treatment process;

Introduction

Context

Road fatalities in Australia peaked in 1970 at 30.4 per 100,000 people1. Multiple factors have substantially reduced the rate to 5.78 per 100,000 people in 2012, a rate that is around the median for OECD countries2. In Australia, road traffic accidents account for approximately 23% of the total injury burden and 3% of the total mortality burden across all age groups and genders [1].The economic cost of road crashes in Australia is estimated at $27 billion per annum3.

Alcohol has for many years been identified as an important factor in road crashes – around a third of drivers and riders killed in road crashes record blood alcohol concentrations above the legal limit [2]. Drivers testing positive to the presence of drugs and/or alcohol have been shown to be at increased risk of sustaining injuries, with the severity of those injuries dependent on

Role of health professionals

Health professionals have clearly defined roles and responsibilities regarding a patient's medical fitness to drive.

Specific guidelines are provided by Austroads and the National Transport Commission in the publication Assessing Fitness to Drive for commercial and private vehicle drivers: medical standards for licensing and clinical management guidelines, March 2012 (available from www.austroads.com.au). The Austroads/NTC guidelines provide general information on drugs and driving (section 4.8) and more specific guidance on substance misuse (Chapter 9) covering alcohol, illicit drugs and prescription drug misuse.

In the general information on drugs and driving (page 20) it is noted that:

> "Any drug that acts on the central nervous sy

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For further information on this requirement, contact:

Manager – Licence Services
Transport SA
Locked Bag 333, Adelaide, SA 5001
Phone: (08) 8374 5139 or (08) 8374 5130.

The information in this paper is intended to provide background information to assist in determining the level of risk associated with prescription medicine use and driving.

Nature of the evidence

Research evidence on drugs and driving comes from both experimental and epidemiological studies.

Experimental studies consider the effects of drugs on driving performance and assess whether a drug has the potential to impair driving skills, and consequently to increase the risk of being involved in a crash. Experimental studies may be based on cognitive and psychomotor tests, driving simulators or (controlled) on-road driving. Experimental studies can eliminate many of the limitations of epidemiological studies, but mostly at the cost of compromising the ecological validity. Driving performance is frequently tested in a highly controlled environment where only certain components of driving behaviour are examined through specific driving tasks, for example ability to maintain the lateral position of the vehicle in the driving lane (i.e. the degree of weaving of the vehicle, termed standard deviation of lateral position or SDLP), which may have been calibrated against different blood levels of alcohol as a measure of risk for traffic accidents. While impaired performance on driving tests suggests the participant is unfit for on-road driving, unimpaired driving performance does not necessarily mean that one is able to drive safely, particularly in complex driving environments where the driver has to respond to other vehicles, pedestrians, traffic signs and other roadside objects [4].

Epidemiological studies draw data from records of traffic accidents or drivers apprehended for driving under the influence of alcohol and other drugs. While these studies provide population level evidence of risk, they can be confounded by uncertainty around the association between detection of the presence of drugs and the level of impairment, and they may not detect other factors relevant to driving ability.

The review articles on which this overview is based varied in their focus, with some considering only experimental studies, some only epidemiological studies, and some considering both. The reviews also varied in the types of drugs considered. This overview seeks to bring all this information together to provide background

duration of action is often equated to elimination half-life. However, a drug's action may be terminated by at least three mechanisms: disappearance from the receptor site by redistribution from the brain to peripheral tissue, biotransformation by the liver to inactive metabolites, and acute tolerance of the receptors. Dose is considered one of the most important determinants of a drug's duration of action. It will take longer for drug concentrations to drop below effective levels after administration of twice the recommended dose, and shorter after only half the recommended dose. The relation between half-life and duration of action is therefore not straightforward [12].

Anxiolytic use

Anxiolytics, taken in single or multiple doses during the daytime have been found to impair driving performance independent of their half-lives [4, 8, 11]. Patients with anxiety who are prescribed anxiolytic medications such as diazepam should be strongly encouraged not to drive, at least during the first four weeks of tr

maintenance therapy patients are observed to have only slight impairments of relevance to driving. The recommended approach is individual evaluation of driving performance, once a stable dose of methadone or buprenorphine has been achieved and there is no significant concomitant use of other substances, such as alcohol and benzodiazepines, that are likely to impair driving.

Antidepressants

Although antidepressants are one of the drug groups that is more commonly detected in fatally injured drivers, this tends to reflect their wide use in the community [2].

Epidemiological evidence

Studies on the effects of antidepressants on driving performance are scarce, but have indicated that elderly users of tricyclic antidepressants (TCAs) are about twice as likely to become involved in traffic accidents compared with a group of control subjects [7, 18]. However, epidemiological evidence for an association of antidepressants with accident risk in young drivers is equivocal [4, 7], and there is no clear distinction from epidemiological studies between sedative and non-sedative antidepressants in terms of their association with traffic accidents [4].

Experimental evidence

In experimental studies, sedative but not non-sedative antidepressants were found to cause short-term impairment of several measures of driving performance [4]. In a systematic review, Remaekers [18] considered 10 studies published between 1983 and 2000 that determined the effects of antidepressants on actual driving performance using a standard test. That test measured driving impairment from vehicular “weaving” (i.e. standard deviation of lateral position or SDLP) during one hour of on-the-road driving in normal traffic. Changes in SDLP after acute doses of sedating antidepressants (i.e. amitriptyline, imipramine, doxepin and mianserin) were comparable to those seen in drivers conducting the same test with a blood alcohol concentration of 0.08 g/100 mL or more. Driving performance of subjects returned to placebo levels after one week of treatment, except in the case of mianserin, for which the impairing effect lasted unabated over treatment. Nocturnal doses of sedating antidepressants (i.e. dothiepin, mianserin and mirtazapine), however, did not produce residual driving impairment when measured the next day. Non-sedating antidepressants (ie. moclobemide, fluoxetine, paroxetine, venlafaxine, and nefazodone) generally did not affect SDLP, except when used in combination with benzodiazepines.

One major source of confounding in both epidemiological and experimental studies is the nature of depression [4, 7]. Antidepressants inte

Antipsychotics

If substantial psychotic-related cognitive deficits are present, the use of antipsychotic medications may actually improve driving performance [2]. However, most antipsychotics are sedating and have the potential to adversely affect driving skills through blockade of central dopaminergic and other receptors. Older drugs such as chlorpromazine are very sedating, as are some newer drugs such as clozapine, olanzapine and quetiapine, but others such as aripiprazole, risperidone and ziprasidone are less sedating. The sedating effects are most problematic early in treatment and at higher doses.

Drug interactions

The combination of any sedating drugs (alcohol, opioids, benzodiazepines, sedating antidepressants) exacerbates impairment of driving abilities and increases the risk of accidents [2, 11, 14, 15].

On-road and driving simulator studies support findings of epidemiological studies in showing exacerbation of the effects of benzodiazepines on driving impairment when combined with alcohol [1]. In two studies of road accidents where subjects had blood alcohol concentrations less than the legal limit, benzodiazepines were found in 43% and 65% of subjects [9]. The combination of opioid drugs and alcohol has also been found to increase the degree of driving impairment [1]. In a sample of driver fatalities, benzodiazepines and opioids were present in 4.1% and 4.9%, respectively. Neither drug alone showed a strong positive association with crash culpability, but when found in combination with another psychoactive drug (or drugs), there was a strong and significant association with culpability [1].

While non-sedating antidepressants do not produce serious driving impairment at therapeutic doses, caution should be taken when these are used in combination with benzodiazepines. Competitive inhibition of metabolic pathways (particularly the cytochrome P450 system) is probably the basis for the interaction [18].

Individual factors

Age

The association between sedative drugs and the likelihood of accidents is more apparent in elderly people. In this group the risk of falls and hip fractures is further increased by the combination of benzodiazepines and tricyclic antidepressants [4, 11]. Epidemiological studies have found that the risk for drivers older than 65 of being involved in reported motor vehicle collisions is higher when they take longer-acting and larger quantities of benzodiazepines.

However, the evidence from experimental studies in redr021gcm/pt1(r-al T9l Tw[(pr.3(ghie6(r-albi)s [4, 1

caused by increased proportion of total body fat to lean body mass. As a consequence, the

driving assessment, as the patient may not be aware that the drugs can cause impairment even when taken as directed.

Sedative-hypnotic drugs, and doses, that are likely to have minimal next-day residual effects are preferable. Examples of sedative-hypnotic drugs for which residual effects are unlikely include temazepam (10-20mg), triazolam (0.25mg) and zolpidem (10mg). If use of a hypnotic without clinically relevant residual effects is not possible, patients should be adequately informed about the duration and severity of the residual effects in order to be able to adjust their behaviour appropriately [12]. The course of hypnotic treatment should be continued only for the minimum required period [4].

Blanket policies regarding the activities of driving and working while using opioid drugs are inappropriate; this is best addressed on a patient-specific basis [17, 21]. Certain patients on pharmacologically stable doses of opioids are able to drive provided they

(1) are not being prescribed other sedative medications, and are not using other substances (alcohol and illicit drugs) which may exert significant central nervous system effects,

(2) do not experience high levels of pain,

(3) lack a substantial sleep disorder or daytime somnolence, and

(4) do not have significant depression or anxiety disorder or other diagnosable psychiatric condition.

The prescribing medical practitioner ultimately should retain and exercise his/her judgement as each patient should be considered individually [17]. Driving at night may be a problem due to the persistent miotic effects of opioid drugs reducing peripheral vision [2].

Patients should avoid driving for up to four weeks while stabilising on benzodiazepine or opioid dosing regimens; that is, if they are starting the medication, the dose is being altered, or they continue to take variable doses of short acting medication leading to fluctuations in blood concentrations. The immediate release formulations of all these medications (oral and/or parenteral) can cause rapid elevation in blood levels requiring additional care.

Since there is no particular medical reason why antidepressants need to be taken in divided doses during the day, prescribing physicians should consider nocturnal dosing regimens for all potentially sedating antidepressants to minimise the patients' risk for traffic injuries [18].

Patients should be aware of the effects of their medication – drowsiness or difficulties in concentrating are signs they should not drive [16].

To reduce driving risk potentially associated with medications patients should [16]:

keep trips short;

travel on familiar roads;

travel when the traffic is not too busy;

initially drive in the company of an experienced driver until confident in their ability to

For more information