

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, co-existing mental health problems and fatigue, in addition to their medications. This should be assessed on an individual basis, and patients advised accordingly.

Antidepressants

- > Sedative antidepressants may impair driving ability. Patients should be advised accordingly.
- > Depression itself may also impair driving ability and successful treatment will reduce this impairment.

Antipsychotic medications

- > Sedating antipsychotics may impair driving in the first few weeks of use. Patients should be advised accordingly.
- > Psychosis also impairs driving and successful treatment will reduce this impairment.

Multiple medications

- > The combination of any sedating drugs (alcohol, opioids, benzodiazepines, sedating antidepressants, cannabis) exacerbates impairment of driving abilities and increases the risk of accidents.



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;
- > “stability” in terms of reliable attendance at appointments, dose collection, family and work commitments;
- > any reports of intoxication on presentation to medical or other reviews or pharmacy visits;
- > use of other substances and patterns of use in relation to driving;
- > collateral information from family members (taking account of confidentiality), Drugs of Dependence Unit, Pharmaceutical Benefits Scheme, Medicare Doctor Shopping Hotline.

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 the number and type of drugs found [1].

Drugs in general, other than alcohol, have been implicated in approximately 30% of Australian driver fatalities [1]. Psychoactive medicines (most notably benzodiazepines and opioids) play a role in both fatal and injurious crashes [1].

The presence of drugs other than alcohol as a factor in road crashes [2] has led to the extension of laws regarding driving under the influence of alcohol to intoxication with illicit drugs; increasing attention has also been given in recent years to prescription medicines.

Use of prescription medicines and driving is less clear-cut than the use of illicit substances or alcohol given their therapeutic role, the sometimes ambiguous information about their effects on driving and the place of motor vehicles in modern Australian society. Driving is a central activity of daily living and an essential component of quality of life for some people. Being able to drive provides a personal sense of autonomy and an independent lifestyle, and gives access to social activities and employment. However, driving performance is a complex multidimensional task requiring mental alertness; visual, auditory, and kinaesthetic information processing; hand/eye coordination; and manual dexterity [2, 3]. These dimensions of driving are potentially affected by prescription medicines with psychoactive properties. Approaches to prescription medicines and driving need to strike a balance between enabling the autonomy and independence of driving, and managing the risks of impairment due to the effects of prescription medicines.

There is now a substantial amount of research literature on the association between prescription medicines and driving. This paper seeks to provide an overview of this literature, drawing particularly on a number of recent review articles as the source of information. The primary focus of the paper is on benzodiazepines and opioids, but some information is included on other drugs with sedating properties that have also been considered in relation to driving ability.

¹ Year Book Australia, 2009-10, Australian Bureau of Statistics. Available at <http://www.abs.gov.au>, accessed 29 October 2013.

² Road deaths Australia, 2012 statistical summary, Bureau of Infrastructure, Transport and Regional Economics, 2013. Available at www.bitre.gov.au, accessed 29 October 2013.

³ Road deaths Australia, 2012 statistical summary, Bureau of Infrastructure, Transport and Regional Economics, 2013. Available at www.bitre.gov.au, accessed 29 October 2013.

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 system has the potential to adversely affect driving skills. Central nervous system depressants, for example, may reduce vigilance, increase reaction times and impair decision making in a very similar manner to alcohol. In addition drugs that affect behaviour may exaggerate adverse behavioural traits and introduce risk-taking behaviours.

Acute impairment due to alcohol or drugs (including illicit, prescription and over-the-counter drugs) is managed through specific road safety legislation that prohibits driving over a certain blood alcohol concentration (BAC) or when impaired by drugs... This is a separate consideration to long-term medical fitness to drive and licensing... Prescribing doctors and dispensing pharmacists ... need to be mindful of the potential effects of all prescribed and over-the-counter medicines and to advise patients accordingly.”

The following general advice to health professionals is provided (page 21):

“While many drugs have effects on the central nervous system most, with the exception of benzodiazepines, tend not to pose a significantly increased crash risk when the drugs are used as prescribed, and once the patient is stabilised on the treatment. This may also relate to drivers' self-regulating their driving behaviour. When advising patients and considering their general fitness to drive, whether in the short or longer term, health professionals should consider the following:

- > the balance between potential impairment due to the drug and the patient's improvement in health on safe driving ability;
- > the individual response of the patient – some individuals are more affected than others;
- > the type of licence held and the nature of the driving task i.e. commercial vehicle driver assessments should be more stringent;
- > the added risks of combining two or more drugs capable of causing impairment, including alcohol;
- > the added risks of sleep deprivation on fatigue while driving, which is particularly relevant to commercial vehicle drivers;
- > the potential impact of changing medications or changing dosage;
- > the cumulative effects of medications;
- > the presence of other medical conditions that may combine to adversely affect driving ability;
- > other factors that may exacerbate risks, such as known history of alcohol or drug misuse.”



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. In cases where the Registrar is notified the practitioner must also notify the patient.

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 information on the relationship between prescription medicines and the risk of motor vehicle crashes or driving impairment, and appropriate advice to provide to patients.

In addition to the type and dose of medication, this overview seeks to consider factors such as tolerance (or lack thereof), stability of doses, adherence to prescribed doses and potential drug interactions, as well as individual factors such as age and gender.

Benzodiazepines

Epidemiological evidence

There is strong epidemiological evidence supporting an increased risk of a road crash associated with benzodiazepine use [5-7]. Benzodiazepines are found in about 4% of fatalities and 16% of injured drivers taken to hospital [2]. It is estimated that benzodiazepines are associated with a 60% to 80% increase in the risk of traffic accidents [4, 8, 9] and a 40% increase in 'accident responsibility', while the co-ingestion of benzodiazepines and alcohol has been estimated to result in a 7.7-fold increase in accident risk [4]. The risk of a road crash also increases with dose and the use of more than one benzodiazepine [6, 8, 9].

Although the evidence from epidemiological studies is strong, it provides limited information on the context of benzodiazepine use. In the majority of road crashes and detected cases of impaired driving where benzodiazepines or related sedative-hypnotic drugs (eg. zolpidem and zopiclone) were detected, blood levels were above the therapeutic range, or other impairing substances were also found [2, 10].

Tolerance

Evidence from epidemiological studies regarding the role of tolerance is mixed, with some studies finding increased risk in the first few weeks of use of benzodiazepines [7], while other studies found no effect of duration of use [6, 8].

Experimental evidence

Experimental studies have demonstrated diverse effects of benzodiazepines on psychomotor, cognitive, and driving performance [5]. Findings of studies using driving simulators were inconsistent, but increased deviation of lateral position was found for on-road driving tests [1].

Benzodiazepines and other sedative drugs, both in acute and repeated doses, impair the ability to perform simple repetitive tasks whether these are performed on their own or as a component of more complex tasks. The effect is related to speed of execution, participants slowing down to maintain accuracy of performance. They also impair simple tasks of attention. The size of effect is related to dose level, compound and individual sensitivity to benzodiazepines [11].

The significance of the impairment related to benzodiazepines depends on whether benzodiazepines are used as an anxiolytic (daytime use) or a sedative-hypnotic (night-time use). Experimental studies have also given consideration to the half-life of different types of benzodiazepines, and the related hypnotic medications known as "z-drugs" [1].

All hypnotics have a rapid onset of action (between 30 and 90 min), whereas the duration of their action differs considerably. Both characteristics are dose dependent. Onset of action is largely determined by the pharmaceutical formulation and the rate of absorption of the drug from the gastrointestinal tract after oral administration. On reaching the blood, all benzodiazepines quickly reach their site of action, since all are lipophilic substances that easily traverse the blood-brain barrier [12].


Benzodiazepine receptor agonist hypnotics are often divided into categories based on their elimination half-life, as very short-acting (half-life <6h⁴), short-acting (half-life 6-12 hours⁵), intermediate-acting (half-life 12-24h⁶) or long-acting (>24h⁷) drugs. As these categories imply,

⁴ Triazolam, zolpidem and zopiclone are examples of hypnotics with very short half-lives

⁵ Alprazolam, oxazepam and temazepam are examples of hypnotics with short half-lives.

⁶ Bromazepam and lorazepam are hypnotics with intermediate half-lives

⁷ Clobazam, clonazepam, diazepam, flunitrazepam and nitrazepam have long half-lives.



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 treatment. The research evidence does not readily offer safer alternatives for prescribers; all other anxiolytics, with daytime dosing, were found to impair driving, at least in healthy volunteers [4]. However, tolerance to the sedative effects of benzodiazepines used in the treatment of anxiety gradually reduces their adverse impact on driving skills [2].

Sedative-hypnotic use

Hypnotics are intended to be taken at bedtime and rapidly induce sleepiness and sedation. Ideally, these effects should continue throughout the sleep period but should no longer be present after awakening in the morning. Hypnotics can have deteriorating effects on psychomotor performance, attention and memory the day after bedtime use (hangover effect). Important considerations for nocturnal use of sedative-hypnotics are the half-life of the medication and timing of administration. Failing to take the medication at the correct time, or not remaining in bed for sufficient time, in combination with the half-life of the medication, are factors in residual impairment following nocturnal use of sedative-hypnotic drugs [12].

Both laboratory and driving simulator studies have demonstrated the potential for residual impairment of tracking ability, visual discrimination and reaction time, up to 11 hours after night-time administration of a benzodiazepine. This effect is more prominent with long-acting benzodiazepines but has also been reported with intermediate-acting benzodiazepines [1].


Tolerance

Sedation is the most common subjective effect of the benzodiazepines. In healthy volunteers increased sedation can be detected after each dose, even after a week of treatment. Tolerance appears to develop after a few weeks [2], but some residual effects may remain, as increased alertness is reported by patients on stopping treatment with benzodiazepines [11]. Impaired performance on simple repetitive tasks has been shown to persist for up to one year and on tests of attention after several years of treatment in long-term benzodiazepine users compared to control groups [11].

Opioid drugs

Epidemiological evidence

Epidemiological studies are of two types: those assessing opioid drug use by drivers involved in road crashes, and those looking for rates of road crashes amongst people prescribed opioid drugs. Studies of drivers involved in road crashes have found the presence of opioid drugs (codeine, morphine, oxycodone, methadone) to be associated with an increased risk of



accidents [7]. However, studies of people prescribed opioid drugs have found a very low risk of accidents [3, 13]. The apparent contradiction in these findings may be due to the limited contextual information available for studies of drivers involved in road crashes. It is generally not known whether the opioids detected were prescribed, whether doses were in the therapeutic range, or the duration of opioid use. Furthermore, the use of other substances is often a confounding factor. This makes interpretation of evidence from epidemiological studies difficult.

Experimental evidence

Most of the evidence on impairment of driving ability associated with prescribed opioid drugs comes from experimental studies.

Following the administration of a single dose of an opioid, opioid-naïve healthy volunteers report central side effects such as sedation, dizziness, and impaired concentration [1, 3, 14-16]. When objectively assessed by means of psychomotor and cognitive tests, their reaction times are longer (slower), and motor coordination and short-term memory are significantly altered [3, 15]. Depending on the dose, these effects would be expected to substantially interfere with driving ability [14] and it is generally recommended that patients commencing opioid therapy refrain from driving as long as the CNS side effects are present [16].

Changing to medication with greater opioid agonist effects, or increasing the dose of opioid medication may temporarily interfere with driving ability, but once stabilised on the new medication or new dose level this effect should be less marked and driving ability may be restored [3].

However, in one systematic review of the effects of opioids on driving performance it is noted that the amount and dose of opioids used in studies was hugely variable [17]. The authors also identified multiple factors as potentially confounding findings, such as pain severity, combinations of medications, sleep disturbance and fatigue, and comorbid psychiatric and psychological disorders. The conclusion of this review was that the commonly held concept that “chronic pain patients on stable opioids are safe to drive” cannot be generalised to all such patients in everyday practice, but may be applicable to a subset who meet certain criteria, including no use of other drugs (alcohol, benzodiazepines) with significant CNS effects, not experiencing high levels of pain, and no substantial sleep disorder or daytime somnolence [17]. Another review also noticed the mixed findings of experimental and epidemiological studies, with some reporting opioids to have an impairing effect, and others finding no effects on tasks of relevance to driving [13].

Tolerance

Tolerance to the cognitive effects of opioid drugs, as well as to nausea and somnolence, develops rapidly [3]. After two to three weeks of stable opioid treatment, driving ability may not be affected [1, 15, 16].

Methadone and buprenorphine for opioid dependence

In experimental studies, impairments of cognitive and psychomotor functions have been observed among both methadone and buprenorphine maintenance therapy patients when compared to control groups [13]. Buprenorphine patients appear to be less impaired but this difference may be unrelated to the maintenance therapy. However, the experimental studies that have been undertaken with methadone and buprenorphine patients have not involved on-road tests of driving ability [13]. Hence it is unclear how the observed impairments of cognitive and psychomotor functions relate to actual driving performance. At least some opioid

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 (i.e. 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 interact differently with depression at different stages of treatment to influence driving ability. Cognitive and psychomotor deficits of depression itself may limit driving capacity of an individual. Because the antidepressants do not bring therapeutic effects immediately after commencement of treatment, depressed patients may show driving impairment during the first one to two weeks of treatment, even if their antidepressants are non-sedative. Patients taking sedative antidepressants may be affected more than those on non-sedating antidepressants during this initial stage because of the acute sedative effects of the drugs. Continuing treatment beyond three or four weeks tends to improve depression, and patients tend to become tolerant to sedative effects. This is supported by some experimental evidence showing that young patient groups treated with sedative or non-sedative antidepressants improved their driving skills after a few weeks while untreated patients did not [4].

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 relation to age is less clear. One study reported significant increases in simple tracking errors and reaction times on a simulated driving task after acute administration of 15 mg diazepam, compared to placebo, in both young (22-24 years) and older (55-77 years) volunteers, although the effect was less prominent with the older drivers. Significant decreases in subjective arousal, skill and overall performance were also reported by only the young participants [1].

There are numerous studies on benzodiazepines indicating alterations in the distribution and elimination in old age. Benzodiazepines bind extensively to plasma albumin. Serum albumin levels may decrease by 15-20% in the elderly, leading to an increase in the pharmacologically active free drug fraction and potentiation of the effects of benzodiazepines. Reduced hepatic blood flow can modify the plasma concentrations and increase peak concentrations. In elderly patients, particularly females, there is an increased volume of distribution of the drug, which is

caused by increased proportion of total body fat to lean body mass. As a consequence, the peak plasma concentrations are lowered and the plasma half-life is prolonged. Drug metabolism decreases with age and may be reduced by 30%. Benzodiazepines are metabolised in the liver by oxidation, nitro-reduction and glucuronidation. Plasma clearance of long-acting benzodiazepines, which requires oxidative metabolism, is decreased in the elderly. Three of the intermediate-acting benzodiazepines – lorazepam, oxazepam and temazepam – require only glucuronidation and are relatively unaffected by alterations in hepatic function [19].

Chronic pain

Chronic pain is commonly associated with sleep disturbance and fatigue and depressive, anxiety, or other psychological and psychiatric comorbidities. Sleep disturbance, daytime sleepiness or fatigue, and psychological and psychiatric comorbidities are known to potentially interfere with cognitive functioning including driving ability [17].

Gender

Verster and Roth [20] investigated gender difference through a literature review of studies that conducted on-road driving tests to examine the possible effects of hypnotic drugs on driving. They found significant gender differences in driving performance the morning following bedtime administration of flurazepam (30mg) and after middle-of-the night administration of zolpidem (10mg), with the driving performance of women affected to a greater extent than men. No significant gender differences were found for ramelteon (8mg), lorazepam (1 and 2mg), zaleplon (10 and 20mg), and zopiclone (7.5mg). This suggests there is potential for gender differences, but the mechanism mediating such differences is uncertain.

Conclusions

Doctors should exercise caution when prescribing benzodiazepines and opioid medications, and should always advise patients of the potential for driving impairment when taking them, even at therapeutic doses [1]. Emphasis should be placed on drowsiness and sedation, and the implications of these effects on driving skills such as reaction time, attention and vigilance.

An extensive history should be taken of all medications being used by the patient. This includes prescribed, over-the-counter medications (such as antihistamines) and illicit drugs. Particular attention should be given where drugs have a sedating effect (as the effects may be synergistic) or may alter the pharmacokinetics of an opioid drug or benzodiazepine resulting in an increase in blood levels.

Patients should be instructed not to use other central nervous system depressants such as alcohol or cannabis in combination with benzodiazepines, opioid drugs or sedating antidepressants. They should also be advised not to use benzodiazepines and opioid drugs together except under medical supervision. Note that the benzodiazepine-alcohol combination may markedly increase the risk of accidents even if the blood alcohol levels are below the legal limit [4].

Remember that some patients may self-medicate in excess of the prescribed dosage. Patients should be informed of the increasing risk of accidents with increasing doses of medication, particularly benzodiazepines.

With the finding of increased crash risk for benzodiazepines special precautions need to be taken for the prescribing and dispensing of these drugs. If the prescriber has any concerns, or believes the patient could be mixing benzodiazepines with alcohol or other sedative medications, they have a duty of care to warn the patient of the risks, and arrange a formal

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 complete trips alone.

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