Abstract

Introduction

In recent years, there has been increasing evidence pointing to a relationship between medicinal drug use and crash culpability. In particular, benzodiazepines and opioid analgesics are implicated in a considerable proportion of road crashes in Australia. There is also mounting concern about the potentially devastating effects of medicinal drug use in combination with an otherwise low-risk level of alcohol consumption.

Methods

13 healthy volunteers were recruited to this randomised double-blind placebo-controlled crossover study. Participants attended 8 sessions each in which they were administered three study drugs in unique combinations: (1) intravenous alcohol (target BAC=0.05g/100ml); (2) oral oxazepam 30mg; and (3) oral codeine 60mg. Driving ability was measured on a STISIM driving simulator before and after drug administration.

Results

Mixed-model analysis with repeated effects revealed significant impairment of driving on parameters such as standard deviation of the mean lateral lane position (SDLP, car-weaving tendency) and time-to-collision (TTC, speed/distance perception) after drug administration compared to placebo (no drug). Moreover, the deleterious effects were more pronounced in the poly-drug conditions.

Discussion

Acute therapeutic doses of oxazepam, alone and in combination with a social dose of alcohol, significantly impaired performance on a number of salient driving tasks and driving-related skills. As such, poly-medicinal drug use, even in the absence of alcohol, has the potential to cause deleterious effects on driver performance. These findings highlight the need for strategic educational campaigns regarding the risks of driving whilst taking prescribed medicines.

Introduction

Alcohol and drugs are implicated in approximately 20% of Australian driver fatalities (Drummer et al., 2004). The role of prescription medications, most notably benzodiazepines and opioid analgesics, in both fatal (11.2% and 9.3% respectively) and injurious (14% and 3.4% respectively) crashes is becoming increasingly apparent (Drummer et al., 2003; Griggs et al., 2007). An investigation into driver fatalities in Victoria, NSW and Western Australia
between 1991 and 1999 revealed that in 9.3% of cases, the driver tested positive to both drugs and alcohol (Drummer et al., 2003). Although opioids and benzodiazepines were present in approximately 4% of all drivers that tested positive for drugs other than alcohol (Drummer et al., 2003), neither drug alone showed a strong positive association with crash culpability (Drummer et al., 2004). However, when detected in combination with other psychotropic drugs and/or alcohol, a strong and significant association with culpability was apparent. The abundance of epidemiological data linking the presence of drugs, other than alcohol, with increased crash risk has led to new policy initiatives that provide for random roadside drug testing across most Australian states, and Standard Impairment Assessments with the potential to convict for driving under the influence of prescription drugs. However, despite evidence relating the use of opioids and benzodiazepines to driving offences, very limited experimental research exists to confirm the nature of any impairment (Drugs and Crime Prevention Committee, 2007).

**Aim**

This double-blind randomised placebo-controlled crossover trial was conducted to examine the effects of therapeutic doses of oxazepam and codeine, alone and in combination with a moderate dose of alcohol delivered by intravenous (IV) infusion (target blood alcohol concentration = 0.05%), on simulated driving performances using a high fidelity driving simulator.

**Methods**

13 healthy volunteers were recruited to this study. Each participant attended 8 experimental sessions of approximately 6 hours duration (1 hour preparation and 5 hours monitoring) in which they were required to complete a driving task on the STISIM Driving Simulator and associated questionnaires, and also provide blood samples both before and after drug administration. At each session, participants were blinded to the study condition: (i) intravenous ethanol or 5% dextrose, (ii) 30mg oral oxazepam or a matched placebo; and (iii) 60mg oral codeine or a matched placebo. Target blood alcohol concentrations were achieved and maintained via the oral/IV clamp method.

**Table 1: Example schedule of drug administration.**

<table>
<thead>
<tr>
<th></th>
<th>Alcohol (IV infusion)</th>
<th>Codeine</th>
<th>Oxazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Session 1</td>
<td>Placebo</td>
<td>Placebo</td>
<td>Placebo</td>
</tr>
<tr>
<td>Session 2</td>
<td>Placebo</td>
<td>60mg</td>
<td>Placebo</td>
</tr>
<tr>
<td>Session 3</td>
<td>Placebo</td>
<td>Placebo</td>
<td>30mg</td>
</tr>
<tr>
<td>Session 4</td>
<td>Ethanol (0.34g/kg)</td>
<td>Placebo</td>
<td>Placebo</td>
</tr>
<tr>
<td>Session 5</td>
<td>Ethanol (0.34g/kg)</td>
<td>60mg</td>
<td>Placebo</td>
</tr>
<tr>
<td>Session 6</td>
<td>Ethanol (0.34g/kg)</td>
<td>Placebo</td>
<td>30mg</td>
</tr>
<tr>
<td>Session 7</td>
<td>Placebo</td>
<td>60mg</td>
<td>30mg</td>
</tr>
<tr>
<td>Session 8</td>
<td>Ethanol (0.34g/kg)</td>
<td>60mg</td>
<td>30mg</td>
</tr>
</tbody>
</table>

Participants were familiarised with the driving simulator upon arriving at their first experimental session with an initial 5 min practice drive incorporating variations in road curvature, changes to speed limits and a road environment similar to that in the test condition. Following that, participants practiced on a second simulation drive, which include exposure to the relevant test tasks. The duration of the second practice drive was dependent upon the
participants achieving a plateau effect in their responses (approximately 10 mins). Workload in the test drives was manipulated through the use of a conventional human factors method (a secondary task) built into the simulator and the inclusion of near-miss scenarios. The time-to-collision (TTC) task required participants to judge the time, distance and speed of oncoming traffic. Vehicular control was measured as the standard deviation from the participant’s mean roadway position (SDLP).

Data were analysed using a mixed model design (full factorial) with repeated effects (experimental sessions 1-8; testing times 0, 2, 3 and 4 hours) and autoregressive covariance structure. A type 1 error rate of 0.05 was adopted.

**Results**

Data analysis revealed that TTC estimates were not sensitive to alcohol and codeine alone, but were sensitive to oxazepam. It was apparent that the presence of oxazepam, in any drug condition, resulted in a significant increase in accuracy of TTC estimates (less underestimation of time), translating to a decreased margin of safety and thus increased risk (Figure 1).

![Figure 1: Mean TTC estimates from baseline (pre-drug administration) to putative peak testing time (3 h post drug administration) for all oxazepam conditions.](image)

A similar relationship was observed with SDLP measurements. That is, SDLP was significantly (p<0.005) greater (i.e. greater swerving tendency) in all oxazepam conditions compared to the no-drug condition. No such impairment was observed in the alcohol alone, codeine alone or alcohol and codeine combined conditions (Figure 2).
Figure 2: Mean SDLP at each testing time (i.e. before drug administration; and 2, 3 and 4 hours post drug administration) for all conditions.

Discussion

The results of this study demonstrate that oxazepam, in particular, significantly impairs a driver’s ability to safely perceive gaps in traffic and also maintain vehicular control. This was observed even in the absence of any other drug. In contrast, a therapeutic dose of codeine and a moderate dose of alcohol (BAC = 0.05g/100ml) did not appear to influence driver performance, alone or in combination. Given these findings, and poor community understanding of the impact of medications upon driving performance (Mallick, Johnston, Goren, & Kennedy, 2007), there is a need for further research into the effects of therapeutic doses of common medicines on driver behaviour.

References


