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Medication use and the risk of motor vehicle collisions among licensed drivers: A systematic review

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ABSTRACT

Objectives: Driving under the influence of prescription and over-the-counter medication is a growing public health concern. A systematic review of the literature was performed to investigate which specific medications were associated with increased risk of motor vehicle collision (MVC).

Methods: The a priori inclusion criteria were: (1) studies published from English-language sources on or after January 1, 1960, (2) licensed drivers 15 years of age and older, (3) peer-reviewed publications, master's theses, doctoral dissertations, and conference papers, (4) studies limited to randomized control trials, cohort studies, case-control studies, or case-control type studies (5) outcome measure reported for at least one specific medication, (6) outcome measure reported as the odds or risk of a motor vehicle collision. Fourteen databases were examined along with hand-searching. Independent, dual selection of studies and data abstraction was performed.

Results: Fifty-three medications were investigated by 27 studies included in the review. Fifteen (28.3%) were associated with an increased risk of MVC. These included Buprenorphine, Codeine, Dihydrocodeine, Methadone, Tramadol, Levocitirizine, Diazepam, Flunitrazepam, Flurazepam, Lorazepam, Temazepam, Triazolam, Carisoprodol, Zolpidem, and Zopiclone.

Conclusions: Several medications were associated with an increased risk of MVC and decreased driving ability. The associations between specific medication use and the increased risk of MVC and/or affected driving ability are complex. Future research opportunities are plentiful and worthy of such investigation.

1. Introduction

While the number of motor vehicle collisions (MVC) and subsequent fatalities has steadily declined over the past decade among many high-income countries, MVC still remains one of the leading causes of mortality not just globally, but also within the United States (U.S.) (Sise et al., 2014; Rockett et al., 2012; Oster and Strong, 2013). In 2010, this equated to approximately one death per collision every fifteen minutes in the U.S. (Oster and Strong, 2013). Besides the inherent risks to morbidity and mortality, MVCs are estimated to cost the U.S. over $300 billion dollars per year (Oster and Strong, 2013).

While driving under the influence of alcohol is a well-documented area of study, driving under the influence of drugs (DUID) is also an emerging public health and traffic safety concern (Hayman and Crandall, 2009; Morland, 2000; Movig et al., 2004; Walsh et al., 2004). Driving under the influence of drugs entails the use of illicit drugs, i.e. drugs that are obtained illegally and with no real medical benefit, such as cocaine and methamphetamine. Driving under the influence of drugs can also entail the use of licit substances, such as common prescription or over-the-counter medications, whose effects impair the driver's ability to safely operate a motor vehicle from one destination to another. However, it's important to realize that while licit drugs can be obtained illegally, abused, or misused, the intent of use by the driver is often difficult

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to determine. In 2009, approximately 28% of all fatally injured U.S. drivers that were tested for either illicit or licit drugs tested positive for one or more of these substances (National Highway Traffic Safety Administration, 2010). In addition, recent research suggests that DUID is increasing nationally (Wilson et al., 2014).

Due to the complexity of DUID, the primary focus of this paper pertains to the association between licit drug use and MVC. However, one of the fundamental challenges to studying the effects of licit drugs on driving ability is that the relationship is not always as apparent when compared to alcohol (National Highway Traffic Safety Administration, 2010). For example, some drugs may not noticeably impair the skills (cognition, psychomotor function, physical ability) necessary to operate a motor vehicle (Coopersmith et al., 1989; Carr, 2000; Carr et al., 2006; Cheung and McCartt, 2011). Drugs that are perceived to affect the central nervous system may exhibit different effects among individuals; this may be attributed to the pharmacokinetic or pharmacodynamic properties of the drug (Jusko, 2013), the drug's half-life (Brown et al., 2013), interactions with other consumed drugs (Bushardt et al., 2008), tolerance (Stein and Baerwald, 2014), drug elimination rate (Bushardt et al., 2008), dosage (Brown et al., 2013), route of administration (Bushardt et al., 2008), solubility (Augustijns et al., 2014), intestinal pH (Augustijns et al., 2014), current health status of the individual (Bushardt et al., 2008), genetics (Daly, 2014), etc. It may also be difficult to partition out the effects of the licit drug and the medical condition for which it was taken to remedy (Bushardt et al., 2008). For example, several medical conditions have been associated with an increased risk of MVC. These include, but are not necessarily limited to, sleep apnea (Ellen et al., 2006), dementia (Brown and Ott, 2004), arthritis (Cross et al., 2009), diabetes (Hansotia and Broste, 1991), epilepsy (Hansotia and Broste, 1991), anxiety (Sagberg, 2006), depression (Sagberg, 2006), and Parkinson's disease (Uc et al., 2006).

Numerous reviews and meta-analyses have investigated the association between licit drug use and MVC and/or driving ability. These reviews have focused predominately on opioids (Borgeat, 2010; Fishbain et al., 2002; Fishbain et al., 2003; Jones et al., 2012; Kress and Kraft, 2005; Leung, 2011; Mailis-Gagnon et al., 2012; Soyka, 2014; Strand et al., 2013), benzodiazepines (Jones et al., 2012; Leung, 2011; van Laar and Volkerts, 1998; Dassanayake et al., 2011; Rapoport et al., 2009; Smink et al., 2010), antihistamines (Popescu, 2008; Roberts, 2005), psychoactive drugs (Cooper et al., 2011; Joris and Monique Anna Johanna, 2009; Krueger, 2010; Rapoport and Baniña, 2007; Verster and Mets, 2009), antidepressants (Dassanayake et al., 2011; Brunnauer and Laux, 2013; Ramaekers, 2003; Ravera et al., 2012; Verster and Ramaekers, 2009), hypnotics (Krueger, 2010; Verster et al., 2006), anxiolytics (Vermeeren et al., 2009; Verster et al., 2005), and sleep medications (Gunja, 2013; Leufkens and Vermeeren, 2014; Verster et al., 2007a,b). Some reviews have also examined multiple drug categories (Hetland and Carr, 2014; Elvik, 2013; Kelly et al., 2004; Orriols et al., 2009). However, the majority of these studies have reviewed or analyzed licit drugs in broad groups (Fishbain et al., 2002; Jones et al., 2012; Kress and Kraft, 2005; Leung, 2011; Dassanayake et al., 2011; Rapoport et al., 2009; Joris and Monique Anna Johanna, 2009; Ravera et al., 2012). There is the potential that if the drugs within these groups were reviewed individually, the outcome measures of interest may be varied as some drugs may be more or less driver-impairing than others. Therefore, the purpose of this study was to perform a systematic review of the literature to investigate which specific medications, including typical prescription or over-the-counter drugs, may be associated with an increased risk or odds of MVC and/or driving ability among licensed drivers 15 years of age and older.

2. Materials and methods

2.1. Study eligibility

The inclusion criteria for studies, which was defined a priori, were as follows: (1) English-language studies published on or after January 1, 1960, (2) licensed drivers 15 years of age and older, (3) studies published in a peer-reviewed journal or non-published (i.e. "grey literature"), which included master's theses, doctoral dissertations, and conference papers, (4) studies limited to randomized control trials, cohort studies, case-control studies, or case-control types of studies, i.e. case cross-over, case-time series, etc. (5) outcome measure reported for at least one specific medication, 6) outcome measure reported as the odds or risk of a motor vehicle collision or some affected aspect of driving ability during an on-road assessment or driving simulation (e.g. brake reaction time, weaving, standard deviation of lateral position, etc.). If the study reported outcome measures for both specific medications and illicit drugs or specific medications combined with alcohol, only outcome measures for specific medications alone were reported. A 'medication' was defined as a substance either available by prescription or over-the-counter to remedy a medical condition. Therefore, caffeine, nicotine, vitamins, and nutraceuticals were excluded. If the medication usage was combined with a medical procedure, then the study was excluded to avoid bias. While marijuana has been legalized for medicinal purposes in several states, it was not considered a medication in this analysis as it is still defined as an illegal substance by federal law. Because of the vast difference in the fidelity of driving simulators, a driving simulator must have consisted of a screen, pedals, and steering wheel. If the study did not specify the components of the simulator, an attempt was made to search the make and model of the simulator noted in the study to see if it was comprised of these constituents. The search date of January 1, 1960 was arbitrarily chosen as no DUID studies existed or were published prior to this time. Because of the complexity of the initial study question, it was decided post-hoc to only present the studies whose outcomes reported the association between a specific medication and the odds or risk of a motor vehicle collision.

2.2. Data sources

Studies were acquired from the following fourteen databases: (1) Medline (within EBSCO host), (2) PubMed, (3) Scopus, (4) International Pharmaceutical Abstracts (IPA), (5) Cochrane Central Register of Controlled Trials (CENTRAL), (6) CINAHL (within EBSCO host), (7) AgeLine, (8) Web of Science (WOS), (9) PsychInfo, (10) Transportation Research Information Services (TRID), (11) Academic Search Complete, (12) EconLit (13) SafetyLit, and (14) ProQuest Dissertations and Theses (ProQuest). All searches were performed by TMR with the assistance of a Health Sciences Librarian from West Virginia University. The last search was performed in June 2014. All searches were conducted using Medical Subject Headings (MESH) terminology. Each search contained the phrases, "drug", "medication", "traffic collision", and "motor vehicle". An example search strategy (ProQuest) is included in Appendix A. In addition to the fourteen databases, studies from TMR's personal library were also reviewed for eligibility. Hand searches from the reference lists of included studies were also examined. Government websites, such as the National Highway Traffic Safety Administration, were also searched for relevant government-performed studies.

2.3. Selection of studies

All included studies were independently selected by TMR and BR. Any discrepancies regarding the inclusion of studies were