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'Potentially Driver Impairing' (PDI) Medication Use in Medically Impaired Adults Referred for Driving Evaluation

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Abstract

Background—'Potentially driver impairing' (PDI) medications, described in the literature, have been associated with poorer driving performance and increased risk of motor vehicle collision.

Objectives—The primary aim of this study was to describe frequency of medication use, as well as to determine the association between routine use of PDI medications and performance on driving and cognitive tests.

Methods—225 drivers with medical impairment (mean age 68 ± 12.8 years, 62.2% male) were referred to an occupational therapy based driving evaluation clinic and examined in this retrospective cohort study. Medication lists were provided by an informant at the time of evaluation and reviewed to identify PDI drugs, defined by a recent study examining drugs with crash risk. Outcome variables included road testing on the mWURT and cognitive scores on TMT-A, SMT®, CDT, DHI® Useful Field of View, and DHI® Motor Free Visual Perceptual Test, ESS, GDS, and FAQ.

Results—The frequency of PDI medication use was 68.9% within our sample, with the average subject taking 1.4 PDI drugs. These drivers taking routine PDI medications had a mean Epworth

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This study was approved by the Human Studies Committee at Washington University in compliance with the 1975 Declaration of Helsinki.

We disclose no relevant conflicts of interest.

Sleepiness Scale (ESS) score of 7.8, whereas subjects not taking PDI medications had a mean score of 6.0 points, indicative of a higher degree of daytime sleepiness in the PDI medication group ($p = 0.007$). Total number of routine medications, regardless of PDI designation, also correlated positively with ESS scores ($p = 0.023$).

Conclusions—Polypharmacy and the use of PDI medications were common in this sample. Use of these drugs was associated with informant ratings of daytime drowsiness on the ESS, which has been linked to motor vehicle crash risk. We recommend further investigation into the effects of individual drug classes, using larger sample sizes and a high powered study design.

Keywords

driving safety; medically impaired drivers; potentially driver impairing medications; drugs and driving; older adult drivers

Introduction

Polypharmacy is common in adults greater than 65 years of age.¹ However, more concerning than the total number of drugs being taken is the use of routine medications with central nervous system (CNS) side effects. Various classes of drugs have been implicated in sedation and driving impairment, and their corresponding adverse effects have been described in the literature.^{2,3,4} Central depressant effects of these agents have a greater impact on older adult patients as compared with their younger, healthier counterparts.⁵ This discrepancy is part of the rationale behind the Beers List, which has raised clinician awareness of the ability for ‘potentially driver impairing’ (PDI) medications to impair performance more overtly in older adult drivers.⁵ Notwithstanding, review of therapeutic regimens reveal that such drugs are commonly prescribed to older adult patients under care of the medical community.^{6,7}

Older adults are more likely to suffer from CNS effects and subsequent difficulty behind the wheel for myriad physiological reasons. Characteristics such as lipid solubility may confer more long-term deleterious effects on driving when medications are retained in the body for a longer period. Even infrequent use may pose a hazard to driving, as some agents exhibit very long half-lives and remain in the body for a longer period of time. Plausible implications of this phenomenon may include delayed or slowed reaction time; impaired selective, divided, or sustained attention; dizziness; drowsiness; hypersomnolence; tremor; ataxia; or confusion and delirium.⁸ Impairments in many of these cognitive domains have been associated with increased risk of motor vehicle crash.^{9,10}

We are not aware of any studies examining the impact of PDI drugs in driving evaluation referral patients with medical comorbidities. It is also unknown whether use in this setting is associated with impaired psychometric performance and/or driving ability. The primary objective of this study was to describe the frequency of PDI medication use within the sample, and to determine whether an association exists between use of PDI medications and hypersomnolence, depression, cognition, and driving performance, measures performed as usual care in the driving clinic. We hypothesized that use of PDI medications in medically ill drivers would be associated with poorer performance on these outcomes.

Methods

This study was approved by the Human Studies Committee at Washington University in compliance with the 1975 Declaration of Helsinki

A total of 249 patients were referred by their physicians for concerns raised regarding their ability to safely operate an automobile. Subjects were assessed at The Rehabilitation Institute of St. Louis (TRISL) Driving Connections Clinic for evaluation between January 2008 and May 2012. Recruitment occurred during this timeframe with several separately funded studies on dementia (n = 102), stroke (n = 80), glaucoma (n = 21), and general neurological disease. The studies were designed to determine whether certain off-road psychometric tests were predictive of driving performance and could be used as screens for determining driving competency.^{11,12} Recruitment was promoted through letters to Washington University clinicians, emails, newsletters, brochures, and visits to the local chapter of the Alzheimer's Association.

The fitness-to-drive studies required the presence of an informant (typically a spouse or adult child), since the primary reasons for referral were often diseases such as dementia or stroke, which might impair decision-making capacity and the ability to accurately answer questionnaires. Consent was obtained with the participant and informant at the time of the driving assessment.

Each informant was first contacted for a 20-minute telephone screen to determine study eligibility and obtain the subject's medication history. The clinical and behind-the-wheel driving evaluation was then scheduled within 1 to 2 months. To be eligible, patients had to be at least 25 years old and have the following: 10 or more years of driving experience, an active license to drive, English-speaking ability, and a primary medical condition with physician referral for evaluation of fitness to drive. Patients with unstable illness (e.g., recent seizure), severe physical deformity, or a sensory or communication deficit were excluded out of safety concerns (n = 5). Explicit refusal to participate or follow road test instructions, as well as history of any other driving evaluation within the past 12 months, also excluded subjects from the study. Exclusion criteria also included incomplete diagnostic criteria where AD-8 (n = 2, a brief interview to identify signs of dementia) or NIHSS (n = 17, a rating scale to classify stroke severity) were not performed. Imposing these constraints brought the final sample size to 225 subjects

Retrospective analysis began with the creation of a master PDI medication list based on results of a previous study,¹³ in addition to a literature search using keywords such as: collision, driving, crash, impairment, or motor vehicle along with the name of the drug class (e.g., terms like "benzodiazepine driving"). This reference study, conducted by LeRoy and Morse¹³ in 2008, included over 33,000 drivers who had been involved in motor vehicle crashes and over 100,000 drivers without recent motor vehicle crash claims to serve as the control group. To be classified as PDI, medications had to demonstrate a statistically significant odds ratio (OR) ≥ 1.25 in the LeRoy and Morse¹³ report. To support the clinical significance of medications with a documented OR between 1.25 and 1.49, the investigators stipulated that the associated risk of driving impairment be corroborated by at least one other source.

Review and classification of each subject's medications was performed by one investigator (AH) and coded using a unique numbering system. The investigator was blinded to outcome measures during this process. Variables included total number of routine medications, total number of routine PDI medications, and use of specific classes of PDI medications, with the latter variable to stratify PDI medication use and explore additional data analyses. Both prescription and over-the-counter (OTC) medications were included regardless of dosage

form or administration site. Minerals, vitamins, herbals and dietary supplements, oxygen therapy, and diabetic testing supplies were not counted as medications. Combination medications (levodopa/carbidopa) were counted by the total number of active ingredients rather than as a single agent. Out of over 1300 total routine medications documented on 225 medication lists, only 3 were omitted for illegibility. Additionally, three medication histories did not distinguish between routine or 'as needed' use for any of the listed drugs; however, these were consistent with drugs prescribed for routine use and were included in the data set.

The 90-minute psychometric assessment portion was conducted at TRISL prior to the on-road evaluation and included tests of vision, cognition, and motor function (Table 1). Cognitive tests administered included the Short Blessed Test (SBT),¹⁴ the Clock Drawing Task (CDT),¹⁵ Trail Making Test Parts A (TMT-A) and B (TMT-B),¹⁶ Snellgrove Maze Task® (SMT),¹⁷ and two subtests from Driving Health Inventory® (DHI), which includes Useful Field of View and Motor Free Visual Perceptual Test.^{18,19} For all cognitive tests except the CDT, higher scores indicate longer times required for completion and consequent increases in impairment. Informants were present to provide responses for the Epworth Sleepiness Scale (ESS),²⁰ Geriatric Depression Scale (GDS),²¹ and Functional Assessment Questionnaire (FAQ).

The modified Washington University Road Test (mWURT)¹¹ was a secondary outcome measure in this study. Lasting approximately 60 minutes, the 12-mile course has many unprotected left hand turns, along with complex merges and intersections in the later aspects of the route. The road test involved an initial closed course in a large parking lot, allowing participants to become familiar with the car and surroundings. After demonstrating proficiency, participants were instructed to proceed out of the lot into the open course (i.e., traffic). Qualitative ratings of pass, marginal, and fail were given by an instructor in the front seat. Pass and marginal grades were merged to provide a dichotomous rating of pass or fail.

Statistical Analysis

Statistical analysis was performed by one investigator (MW) using SAS 9.3²² and involved group comparisons between subjects taking at least one PDI medication and those taking none. Since the principal objective of this study was descriptive, the TMT-A was selected as the primary cognitive outcome for power calculation. A sample of 155 subjects taking PDI medications and 70 subjects not on PDI medications provides 80% power with a 2-tailed t-test ($\alpha = 0.05$) when the true mean TMT-A difference is 13.7 seconds. Simple comparisons of PDI groups were made with Pearson Chi-square test for categorical outcomes and 2-sample t-tests for continuous outcome variables. Analysis of variance or multivariable logistic regression was used to control for dementia ($n = 102$) and stroke ($n = 80$), the most prevalent medical impairments prompting referral. Finally, the study compared outcome measures among individual PDI medication classes, in order to determine whether any classes were more strongly associated with cognitive or driving impairment. Groups were reassigned according to use versus non-use of a specific class.

Results

Demographics and clinical screens are outlined in Table 2. Each measure provides data based upon the entire sample, separate data from both the PDI and non-PDI medication group, and p-values reflecting the comparison between the latter two columns. Because several components of the FAQ were not performed or not obtained during subject interviews, data for this variable became difficult to examine and are therefore excluded from our analyses. The use of PDI medications was associated with higher scores on the ESS (absolute difference 1.8; 95% CI 0.6 to 3.1 $p = 0.007$), a difference which remained

after controlling for medical impairment. Total number of routine medications, regardless of PDI designation, also correlated positively with ESS scores ($p = 0.023$). There were no other statistically significant differences on psychometric test scores or on mWURT performance.

The average medically impaired driver was taking 5.9 ± 3.7 total routine medications, 1.4 of which were PDI drugs. Sixty-nine percent ($n = 155$) of the sample was on a least one routine PDI medication. The most prevalent subclasses included SSRIs (30.7%), PPIs (17.8%), hypoglycemic agents (16.9%), and AEDs (11.5%), while first generation antihistamines, barbiturates, and first generation antipsychotics were rarely reported (Table 3). Dementia, stroke, and glaucoma were the most frequent referral diagnoses, accounting in total for 85% of the sample. Hypertension was the most common medical comorbidity, although it was not indicated as a primary cause for referral in any subjects (Table 4).

The next set of analyses focused on the PDI subclasses of drugs to determine if there were differences in any major outcome measures. Few significant differences were noted within any of the medication classes on outcome measures. Of note, higher ESS scores were observed in patients taking NSAIDs (absolute difference 3.6; $p = 0.042$) and antiparkinsonians (absolute difference 3.8; $p < 0.001$), and patients taking second generation antidepressants exhibited worse performance on the CDT (absolute difference 0.95; $p = 0.040$). We were unable to detect any further differences within medication subclasses, owing to a small sample size further narrowed by the infrequent use of many PDI medications, including barbiturates ($n = 1$) and first generation antihistamines ($n = 2$).

Discussion

Based upon these descriptive findings, polypharmacy and PDI medication use was evident in well over half the sample. This reflects comorbidities in these drivers and, possibly, the common practice of multiple prescribing for individual diagnoses. A higher ESS mean score in patients prescribed PDI drugs is concerning, since daytime drowsiness on this scale has been associated with an increased risk of motor vehicle crash in some studies.^{20,23} The sample of medically impaired older adults often had medical conditions that could alone impact driving ability (e.g., sleep apnea). Thus, clinicians who encounter these patients should review past medical histories to appropriately consider the potential additive impact of prescribing sedating drugs.

In this sample, it is interesting to note a nonsignificant trend toward a higher fail rate in drivers using no routine PDI medications. While this could be attributed to the small sample size or perhaps severity of the medical illness outweighing PDI medication effects, it is also possible that certain drugs may have had a positive impact on driving ability, especially for those drugs that treat pain or restricted mobility (e.g., antiparkinsonians). Medications may, of course, improve cognition, attention, and mobility, which could be another important focus for further study in older adults.

Study Limitations

Some limitations to this study should be addressed. First, all medications designated as PDI were grouped into one category, recognizing that certain agents may have a less potent impact on driving than others, and some may even impart benefits on performance as discussed previously. Though a moderate association was demonstrated in the LeRoy and Morse¹³ study, classes such as SSRIs and PPIs are not typically reported to have major CNS sedating effects, creating potential to distort or dilute the results. In fact, some authors only assign sedating properties to specific drugs in these classes (e.g., paroxetine, omeprazole).²⁴ Additionally, advanced age or the primary medical impairment warranting referral may have masked any potential additive impact of PDI medications.

Drug compliance in this type of retrospective study could not be ensured or confirmed. Medication use was documented 1 to 2 months prior to evaluation and might have changed within that time frame; thus, it could have been helpful to document timing of the last dose before evaluation. It is also possible that patients, in anticipation of the driving evaluation, may have refrained from taking sedating medications which they suspected might negatively impact test performance.

Lastly, this convenience sample was built upon a series of driving studies that focused on recruiting specific disease categories (e.g., dementia, stroke, glaucoma), and participants were not required to pay for the driving evaluation. The small sample size precluded the use of motor vehicle crashes as an outcome and may have limited our ability to find differences, especially when performing analyses on smaller subsets of drug classes. We also acknowledge that qualitative road test scores (e.g., pass vs. fail) may not be as sensitive as a quantitative error count to detect in-traffic performance decrements.

In light of our relatively small sample size, we believe additional research is needed to confirm which specific PDI medication classes actually impact driving safety in medically impaired drivers and under what circumstances. Studies of larger samples in a variety of settings are needed to clarify the role of medications in driving performance in medically impaired drivers.

Conclusion

Polypharmacy and the use of PDI medications were common in this sample. Use of these drugs was associated with higher informant ratings of daytime drowsiness on the ESS, a tool that has been linked to motor vehicle crash risk.⁹ In lieu of multiple prescribing to medically impaired patients referred for driving evaluation, we recommend that clinicians review medication lists to aid in reducing or eliminating sedating CNS medications. This practice to lessen medication burden could have a positive impact on driving performance in older adults. However, what actually constitutes a PDI drug requires further research. In the literature on prescription drugs and driving, it is often difficult to determine whether drug or disease is to blame where driving competency is questioned. Whether a drug would enhance or impair driving performance in older adults remains an unanswered question, and which specific drugs should be labeled as 'PDI' merits additional study and clarification.

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Table 1

Purpose and administration of cognitive assessment tools

Test name	Outcome measurements	Administration	Notes
Short Blessed Test (SBT)	Mental status	Basic orientation questions regarding place, time, and ability to store and retrieve new information	Scores ≤ 9 (equivalent of 24 on MMSE ^a) indicate abnormal results
Clock Drawing Task (CDT)	Executive function, visual spatial ability	Patient to draw a clock following specific instructions	Scored 0–7 (where 7 is optimal)
Trail Making Test Part A (TMT-A)	Attention, psychomotor speed, visual scanning	Patient instructed to connect dots, alternating letters and numbers (e.g., 1-A-2-B...)	Timed test; longer completion times indicate greater impairment
Trail Making Test Part B (TMT-B)	Attention, psychomotor speed, visual scanning	Patient instructed to connect dots, alternating letters and numbers	More advanced than TMT-A; many patients have difficulty completing and time is capped at 300 seconds
DHI® Useful Field of View	Divided visual attention, visual memory, processing speed	Patient must respond quickly to flashing icons on the periphery of a computer screen	Timed test; longer completion times indicate greater impairment
DHI® Motor Free Visual Perceptual Test	Visual closure	Patients 'fill in the blanks' to logically select a stick figure that matches with the figure provided	Timed test; longer completion times indicate greater impairment
Snellgrove Maze Task® (SMT)	Attention, visual constructional ability, planning, problem solving	Basic paper maze	Timed test; longer completion times indicate greater impairment
Geriatric Depression Scale (GDS)	Depressive symptomatology	Filled out by informant via mailed questionnaire	
Epworth Sleepiness Scale (ESS)	Hypersomnolence (daytime sleepiness)	Filled out by informant via mailed questionnaire	
Functional Assessment Questionnaire (FAQ)	Functional capability	Filled out by informant via mailed questionnaire	

^aMMSE: Mini Mental State Examination

Table 2

Demographics, screens, psychomotor test scores, and on-road performance^a

Characteristic	Total sample (n = 225)	1 or more routine PDI medications (n = 155)	No PDI medications (n = 70)	P-value Simple ^b	P-value Controlled for dementia and stroke ^c
Age (years)	68.1 ± 12.8	68.4 ± 11.8	67.4 ± 14.8	0.51	0.34
Gender (% male)	62 %	63 %	61 %	0.87	0.85
Education (years)	14.7 ± 3.0	14.6 ± 3.0	14.8 ± 3.1	0.74	0.75
Short Blessed Test (SBT)	5.8 ± 6.2	5.7 ± 6.4	6.0 ± 6.0	0.79	0.98
Clock Drawing Task (CDT)	5.5 ± 1.9	5.9 ± 1.9	5.4 ± 1.9	0.51	0.62
Trail Making Test Part A (TMT-A)	61.7 ± 33.7	60.0 ± 31.6	65.4 ± 37.8	0.26	0.32
Trail Making Test Part B (TMT-B)	167.5 ± 82.6	166.0 ± 82.3	170.6 ± 83.9	0.70	0.82
Useful Field of View	270.4 ± 145.6	261.3 ± 141.5	293.5 ± 154.8	0.19	0.20
Motor Free Visual Perceptual Test	3.4 ± 2.8	3.4 ± 2.9	3.2 ± 2.6	0.51	0.48
Epworth Sleepiness Scale (ESS)	7.3 ± 4.6	7.8 ± 4.7	6.0 ± 4.0	0.007*	0.005*
Geriatric Depression Scale (GDS)	1.4 ± 1.6	1.4 ± 1.7	1.2 ± 1.5	0.40	0.41
Modified Washington University Road Test (mWURT, % fail)	47%	44%	54%	0.15	0.20

^aData, unless indicated otherwise in column 1, are reported as mean ± standard deviation.^bPearson Chi-square test or Student's t-test^cAnalysis of variance or multiple logistic regression

Table 3

PDI medications selected for the study, in descending order of use

Medication class	N (%)	Primary attributable PDI effects
Selective serotonin reuptake inhibitors (SSRIs)	69 (30.7)	Impaired concentration / judgment
Proton pump inhibitors (PPIs)	40 (17.8)	Dizziness; drowsiness
Hypoglycemic agents	38 (16.9)	Symptoms of hypoglycemia (e.g., shakiness, impaired concentration, lightheadedness)
Antiepileptic drugs (AEDs)	26 (11.5)	Sedation; reduced excitatory neurologic activity
Antiparkinsonian agents	22 (9.8)	Drowsiness; blurred vision; 'sleep attacks' without prodrome
Second generation antidepressants	18 (8.0)	Reduced seizure threshold (bupropion)
Benzodiazepines (BZDs)	15 (6.6)	Sedation
Opioid analgesics	10 (4.5)	Sedation
Non-benzodiazepine hypnotics	9 (4.0)	Drowsiness; impaired vision
Tricyclic antidepressants (TCAs)	9 (4.0)	Hypotension; risk of falls; sedation; reduced seizure threshold
Antiplatelet agents	7 (3.1)	Orthostatic hypotension in elderly
NSAID analgesics	7 (3.1)	Drowsiness; blurred vision
Skeletal muscle relaxants	6 (2.6)	Sedation; drowsiness; blurred vision
Second generation antipsychotics (SGAs)	4 (1.8)	Sedation
Intestinal agents	4 (1.8)	Drowsiness; blurred vision
Second generation antihistamines	3 (1.3)	Sedation (cetirizine)
First generation antihistamines	2 (0.9)	Sedation
First generation antipsychotics (FGAs)	1 (0.4)	Sedation
Barbiturates	1 (0.4)	Sedation
Antitussives	0	Sedation; dizziness
Histamine-2 receptor antagonists (H ₂ RAs)	0	Sedation
Sympatholytic / cardiac agents	0	Hypotension; risk of falls; lightheadedness

^a Medication classes have been renamed and/or recategorized according to ASHP classification and conventional nomenclature, and may not match exactly with that published by LeRoy and Morse.¹³

Table 4

Common medical conditions represented in the study, in descending frequency

Medical condition	N (%)
Hypertension	121 (53.8)
Dementia	102 (45.3)
Depression	89 (39.6)
Stroke	80 (35.6)
Coronary artery disease	55 (24.4)
Diabetes mellitus	52 (23.1)
Cataracts	46 (20.4)
Glaucoma	35 (15.6)
Sleep apnea	27 (12.0)
Chronic obstructive pulmonary disease	23 (10.2)
Parkinson's disease	22 (9.8)
Syncope	20 (8.9)
Seizure	8 (3.6)
Age-related macular degeneration	8 (3.6)
Alcohol abuse	4 (1.8)
Bipolar disorder	1 (0.4)