A Profile of Concurrent Alcohol and Alcohol-Interactive Prescription Drug Use in the US Population

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BACKGROUND: The risk of adverse events among alcohol-interactive medication users can occur with one standard alcoholic drink. Research on the extent to which this occurs is scant.

OBJECTIVE: To examine the prevalence and correlates of concurrent alcohol and alcohol-interactive (AI) medication use across different levels of risk for an alcohol-related adverse event in a nationally representative sample of American adults.

METHODS: Cross-sectional analysis of past year, self-reported drinking history as well as past month, self-reported and visually inspected prescription drug use data from the 1999–2000 and 2001–2002 NHANES questionnaire section (n=8,246). Medications were considered AI if concurrent use of alcohol and the prescription drug could intensify the effects of alcohol, resulting in increased sedation, drowsiness, or dizziness. Weighted prevalence estimates and polytomous logistic regression accounted for the complex survey design.

RESULTS: Overall, 13.5% took prescription AI medications, of which 5.6% reported alcohol consumption of three or more drinks on each drinking occasion. Correlates of such use were being a man [adjusted odds ratio (AOR): 4.37; 95% confidence interval (CI): 1.84–10.35], between the ages of 20 and 54 (AOR=12.28; 95% CI: 3.12–48.25), and currently smoking (AOR: 2.61; 95% CI: 1.28–5.29), with alcohol-abstaining AI users as the referent group.

CONCLUSIONS: Combining alcohol and AI medications is a common phenomenon, and the risk of alcohol-related adverse drug events may be nontrivial. Screening for alcohol use before prescribing AI medications would be prudent. Better communication regarding the dangers of mixing alcohol with AI medications is warranted.

KEY WORDS: alcohol; prescription drugs; CDC; NHANES; alcohol-related adverse drug events.

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BACKGROUND

There are over 2,800 prescription medications available in the US, and many of these can interact with alcohol.¹ Physicians write over 14 billion prescriptions annually, and two-thirds of all adults use prescription drugs.^{1,2} Concurrent use of alcohol and alcohol-interactive (AI) prescription drugs can lead to increased risk of injury, illness, and death. Alcohol potentiates the sedative effects of antidepressants, muscle relaxants, antipsychotics, benzodiazepines, sleep medications, and prescription narcotics, which can increase the risk of falls, automobile accidents, and death.³ Alcohol-drug interactions are suspected as a factor in at least 25% of emergency room admissions.⁴

Approximately 60% of US adults consume alcohol at least occasionally.⁵ Over 60 prospective studies have identified an inverse association between moderate alcohol consumption and the risk of coronary heart disease.⁶ The risk-to-benefit ratio of moderate alcohol consumption may be different, however, in AI medication users. To our knowledge, research on the prevalence and correlates of concurrent use of alcohol and AI prescription medications has not been performed in a nationally representative sample. This study estimates the prevalence of concurrent alcohol and AI medication use in the US population and determines correlates of concurrent alcohol and AI medication use.

METHODS

Study Population

We used 1999–2002 data (n=21,004), the most recent survey years for which prescription drug information was available, from the National Health and Nutrition Examination Survey (NHANES). NHANES is a continuing, cross-sectional, nationally representative survey of the non-institutionalized civilian population. Details on the methods used to collect data for NHANES are available on the National Center for Health Statistics' website: <http://www.cdc.gov/nchs/nhanes.htm> (accessed 3 March 2008). There were 10,291 persons over the age of 20 who were eligible to be surveyed about alcohol consumption. We did not include pregnant women (n=603) as patterns of alcohol and prescription drug use were expected to be different. The final sample consisted of 8,246 individuals with complete information on prescription medication and alcohol use.

Alcohol-Interactive Medications

Medications were considered AI if concurrent use of alcohol and the prescription drug could intensify the effects of alcohol,

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resulting in increased sedation, drowsiness, or dizziness. AI medications were categorized into six therapeutic classes: benzodiazepines, antipsychotics, antidepressants, prescription narcotics, sleep medications, and muscle relaxants. The interviewer asked respondents to present the container of each prescription medication used within the last month and recorded the name of each medication and the length of time (in days) the medication was taken. Users were defined as those who reported taking at least one AI medication for at least 30 days.

Concurrent Alcohol Consumption in Alcohol-Interactive Medication Users

We categorized AI prescription medication users into four categories (people at zero, low, moderate, and high risk of an alcohol-related adverse event) by evaluating the responses to the following questions:

"In the past 12 months, how often did you drink any type of alcoholic beverage?"

"In the past 12 months, on those days that you drank alcoholic beverages, on average, how many drinks did you have?"

Direct ascertainment of the frequency of yearly alcohol consumption was not possible for all respondents. As an estimate, we standardized the frequency of alcohol consumption to 1 year. For example, for those respondents reporting a monthly pattern of alcohol consumption, the frequency of yearly consumption was calculated by multiplying their monthly consumption by 12.

Respondents defined as those at high risk of an alcohol-related AE were AI users consuming alcohol 90 days or more in the past year and who, on average, drank more than three alcoholic beverages when they did drink. Individuals at moderate risk of an alcohol-related AE were those drinking at least 90 days per year, but consuming three or less drinks per drinking occasion. AI users were considered at low risk of an alcohol-related AE if they reported drinking less than 90 days per year, irrespective of how many alcoholic beverages they consumed per drinking occasion. Respondents were categorized as having zero risk of an alcohol-related AE if they did not report consuming alcohol in the past year.

Analytic Approach

We considered the following as potential correlates of concurrent alcohol and AI prescription medication use as each has been recognized as a risk factor for alcohol consumption: gender, race/ethnicity, age, marital status (divorced/separated/never married/widowed, married/living with partner), education (less than high school, more than high school), total family income, employment status (working vs. not working), and smoking status (current smoker vs. non-smoker).⁷ We classified race as "White" or "Non-White," and age as 20 to 54 years old and 55 years old and older. We divided total family income into two categories: less than \$55,000 and over \$55,000 per year. As a measure of social isolation, we grouped divorced, separated, never married, or widowed and married or living with a partner. We also evaluated other factors potentially related to alcohol consumption, such as medical

contraindications (diabetes, kidney failure, liver conditions), health insurance coverage (currently insured and not insured), and the number of non-AI medications the participant was currently taking (none, one, or two or more).

Prevalence estimates and logistic regression analyses were weighted to account for the complex sampling scheme using SUDAAN version 9.0.1 software (Research Triangle Institute, Research Triangle Park, NC). The NHANES sampling weight corrects for over-sampling and non-representative sampling resulting in differential probabilities of selection based on sex, age, ethnicity/race, and other characteristics. First, we identified correlates of AI medication use using a multiple logistic regression model applied to the entire eligible population. Then, we developed a polytomous logistic regression model based on AI medication users so that the correlates of being at low, moderate, and high risk of alcohol-related AE could be identified. In the polytomous regression model, the outcome variables were being at low, moderate, and high risk of an alcohol-related AE. The referent group consisted of individuals taking at least one AI drug who had not consumed alcohol in the past year. Lastly, we used a multiple logistic regression model to identify differences between people at high risk of an alcohol-related AE and people with similar drinking habits, but not taking AI medications. We calculated crude odds ratios (OR), adjusted odds ratios (AOR), and 95% confidence intervals (CI).

RESULTS

The prevalence of AI prescription drug use for at least 30 days was 13.5%. In Fig. 1 the risks of an alcohol-related AE among

Figure 1. The risk of alcohol-related adverse events among alcohol-interactive medication users (n=22,840,389).
 Note: "Multiple AI medications" refers to persons taking more than one AI medication, and these persons are grouped in the respective drug categories for each AI medication they are taking. Zero risk of an alcohol-related adverse event (did not drink alcohol in past year); low risk of an alcohol-related adverse event (drank alcohol less than 90 days in past year); moderate risk of an alcohol-related adverse event (drank more than 90 days in past year and three or less alcoholic drinks per drinking occasion); high risk of an alcohol-related adverse event (drank more than 90 days in the past year and drank more than three alcoholic drinks per drinking occasion).

AI medication users are shown. “Multiple AI medications” refers to persons taking more than one AI medication. In this figure, multiple AI medication users are also included in the respective drug categories for each AI medication they are taking. As illustrated in Fig. 1, 60.5% of AI medication users consumed any alcohol in the past year with 5.6% of respondents at high risk of an alcohol-related AE. Figure 1 also shows that drinking behavior varies across therapeutic classes. For example, high-risk alcohol use was most common among those taking muscle relaxants (13.7%) and least common among those taking prescription narcotics (2.4%). Alcohol abstinence was highest among those taking multiple AI medications (48.5%) or benzodiazepines (47.7%) and lowest among those taking antidepressants (36.1%). Compared to those taking AI medications, people not taking AI medications were less likely to abstain from alcohol (28.0% vs. 39.6%). Conversely, they were more likely to consume alcohol at levels that put them at low (47.8% vs 43.2%), moderate (17.0% vs. 11.7%) or high (7.2% vs. 5.6%) risk of an alcohol-related AE ($p<0.001$).

Table 1 shows the correlates of AI medication use, irrespective of alcohol use. After adjusting for potential confounders, AI prescription medication use was associated with being female, aged 20 to 54, white, unemployed, and having health insurance. AI medication use was also associated with smoking or having medical contraindications to alcohol use. The strongest correlates of AI medication use were having visited a mental health professional in the past year [adjusted odds ratio (AOR)=

7.83] and taking non-AI medication (AOR=2.49 for one non-AI medication, AOR=5.60 for two or more).

Table 2 presents the correlates of concurrent alcohol use among AI medication users. Correlates of being at high risk of an alcohol-related AE included being aged 20–54, male, and a current smoker. The strongest correlate of being at risk of an alcohol-related AE was being between the age of 20 and 54 (AOR=12.28; 95% CI: 3.12–48.25). Medical contraindications to alcohol were inversely related to being at low, moderate, and high risk of having an alcohol-related AE.

Persons at high risk for an alcohol-related AE were compared to persons having similar drinking patterns, but not taking AI medications. Among those who drank at least 90 days per year and consumed more than three drinks per drinking occasion, persons using AI medications were more likely to be female (38.2% vs. 15.4%, AI vs. non-AI; $p=0.014$), aged 20 to 54 (94.0% vs. 85.4%; $p=0.001$), unemployed (53.1% vs. 19.5%; $p=0.011$), and taking non-AI medications (65.6% vs. 26.0%; $p<0.001$). Relative to those who were not taking AI medications, persons using AI medications were also more likely to have been in contact with a mental health professional in the past year (30.8% vs. 6.9%; $p=0.012$).

DISCUSSION

This study makes a unique contribution to the literature because it examines the prevalence and correlates of different

Table 1. Characteristics of Alcohol-interactive Medication Users and Non-users and the Correlates of Alcohol-interactive Prescription Medication Use Among the Non-institutionalized US Population Over 20 Years of Age*

Characteristics	AI users†	AI non-users†	Crude OR (95% CI)	Adjusted OR‡ (95% CI)
n	1,013	7,233		
Weighted n	22,840,389	145,482,331		
%	%	%		
Gender				
Male	35.4	52.0	0.50 (0.44–0.58)	0.67 (0.57–0.78)
Age				
20–54	64.3	72.0	0.70 (0.57–0.86)	1.55 (1.12–2.15)
≥55	35.7	28.0	1.00	1.00
Race				
White	81.2	70.5	1.00	1.00
Non-White	18.8	29.5	0.56 (0.45–0.69)	0.58 (0.47–0.72)
Education				
More than high school	49.5	53.5	1.00	1.00
High school or less	50.5	46.5	1.17 (0.98–1.41)	1.26 (1.00–1.59)
Family income				
<\$55,000	68.6	64.6	1.00	1.00
≥\$55,000	31.4	35.4	0.84 (0.70–1.00)	0.92 (0.70–1.21)
Marital status				
Married/living with partner	60.3	65.4	1.00	1.00
Never married/widowed/divorced/separated	39.7	34.6	1.24 (1.04–1.48)	1.06 (0.87–1.31)
Currently unemployed	49.2	32.1	2.06 (1.72–2.46)	1.57 (1.17–2.12)
Currently without health insurance	8.3	19.0	0.39 (0.30–0.50)	0.59 (0.43–0.81)
Current smoker	26.7	20.0	1.46 (1.22–1.74)	1.54 (1.23–1.94)
# Non-AI medications				
0	18.2	53.2	1.00	1.00
1	19.6	20.1	2.85 (2.14–3.80)	2.49 (1.89–3.29)
≥2	62.3	26.7	6.81 (5.21–8.92)	5.60 (4.30–7.28)
Medical contraindications§	20.4	10.6	2.17 (1.77–2.65)	1.30 (1.01–1.68)
Visited a mental health professional in past year	29.4	4.6	8.59 (6.82–10.82)	7.83 (6.22–9.87)

*Missing data were trivial except for total family income (6.38%) and marital status (5.04%);

†totals may not add up to 100% due to rounding;

‡derived from the logistic regression model including all the variables in the table as covariates.

Abbreviations: AI = alcohol-interactive

§include diabetes, kidney failure, and liver conditions

Table 2. Correlates of Being at Low, Moderate, and High Risk of an Alcohol-related Adverse Event Among Persons Using Alcohol-Interactive Medications*

Characteristics	Risk of an alcohol-related adverse event		
	Low†	Moderate§	High
n	384	115	43
Weighted n	9,878,455	2,660,968	1,267,791
	Adjusted OR (95% CI)		
Gender			
Men	0.96 (0.68–1.33)	1.60 (0.96–2.67)	4.37 (1.84–10.35)
Age			
20–54	1.75 (1.27–2.41)	0.60 (0.31–1.18)	12.28 (3.12–48.25)
≥55	1.00	1.00	1.00
Race			
White	1.00	1.00	1.00
Non-White	0.93 (0.55–1.58)	0.49 (0.22–1.12)	0.78 (0.31–1.94)
Education			
More than HS	1.00	1.00	1.00
HS diploma or less	0.85 (0.57–1.27)	0.71 (0.43–1.18)	1.59 (0.67–3.80)
Family income			
<\$55,000	1.00	1.00	1.00
≥\$55,000	2.10 (1.31–3.36)	2.15 (0.88–5.26)	1.43 (0.53–3.81)
Marital status			
Married/living with partner	1.00	1.00	1.00
Never married/widowed/divorced/separated	1.45 (0.89–2.34)	1.10 (0.63–1.93)	1.37 (0.62–3.07)
Currently unemployed	0.49 (0.30–0.78)	0.51 (0.25–1.02)	1.16 (0.63–2.15)
Currently without health insurance	1.01 (0.48–2.13)	1.22 (0.42–3.55)	0.99 (0.22–4.47)
Current smoker	1.86 (1.16–2.99)	1.80 (0.80–4.04)	2.61 (1.28–5.29)
# Non-AI medications			
0	1.0	1.0	1.0
1	1.67 (0.81–3.46)	1.25 (0.54–2.91)	1.20 (0.40–3.66)
2+	1.09 (0.67–1.75)	0.82 (0.40–1.68)	0.76 (0.32–1.82)
Medical contraindications¶	0.70 (0.40–1.21)	0.19 (0.07–0.51)	0.25 (0.08–0.76)
Visited a mental health professional in past year	1.02 (0.76–1.36)	1.86 (0.97–3.55)	0.82 (0.29–2.33)

* Missing data were trivial except for total family income (5.23%) and marital status (5.42%)

†derived from polytomous logistic regression model (with those who did not report alcohol use in the past year as the referent group). The model included all the variables in the table as covariates;

‡low risk of an alcohol-related adverse event (drank alcohol less than 90 days in past year)

§moderate risk of an alcohol-related adverse event (drank more than 90 days in past year and three or less alcoholic drinks per drinking occasion)

|| high risk of an alcohol-related adverse event (drank more than 90 days in the past year and drank more than three alcoholic drinks per drinking occasion).

¶include diabetes, kidney failure, and liver conditions

Abbreviations: AI = alcohol-interactive

levels of risk associated with concurrent alcohol and AI medication use in a nationally representative sample. The findings show that 13.5% used AI medications for at least 1 month. Of those taking AI medications, 60.5% consumed some alcohol in the past year, and 5.6% did so at levels that put them at high risk of an alcohol-related AE. Given that harmful alcohol-drug interactions can occur at moderate levels of alcohol consumption,^{1,8} many people appear to be at risk of alcohol-related AEs.

Patterns of alcohol consumption vary across AI therapeutic drug classes, and the proportion of persons at-risk for alcohol-related AEs is *not* uniform across groups of AI medications. For example, persons taking muscle relaxants and sleep medications were most likely to have an alcohol intake that put them at high risk of an alcohol-related AE, whereas those taking benzodiazepines or multiple AI medications were most likely to be alcohol abstainers. This finding could reflect variability in alcohol potentiation that is dependent upon the class and the number of AI medications taken. That is, the degree of enhanced sedation, dizziness, or drowsiness that results from concurrently using a benzodiazepine and alcohol may be less tolerable than when an antidepressant is combined with alcohol.

Men, persons aged 20 to 54, and current smokers were most likely to be at high risk of an alcohol-related AE. This is

consistent with previous research that has shown that men drink more than women and that younger people are more likely to engage in hazardous alcohol consumption than their older counterparts.^{9–12} Studies have also shown that cigarette smokers are more likely to be alcohol dependent and engage in high-risk drinking than non-smokers.^{10,11} Another explanation for our findings is that, assuming that AI medication users have been warned against mixing AI medications and alcohol, males, smokers, and younger individuals may knowingly engage in high-risk activities; these results are concordant with previous research that has shown that women, non-smokers, and those advanced in age tend to engage less in potentially self-injurious or high-risk activities and behaviors.^{9,13}

AI medication users with physical health problems were more likely to abstain from concurrent alcohol use. This gives some cause for optimism, albeit guarded, that people limit their alcohol consumption in response to poor health. AI medication users with medical contraindications, such as diabetes, kidney failure, and liver problems, were the least likely to be at high risk for an alcohol-related AE. These findings are consistent with studies that found that individuals who develop potentially life-threatening medical conditions either cease drinking or substantially reduce their intake of alcohol.^{14,15}

The strength of this study is that it is an analysis of a nationally representative sample. Using statistical weights, we were able to produce estimates of the number and characteristics of people at risk of alcohol-related AEs in the US. The participation rate in this study, 81.9% for NHANES 1999–2000 and 83.9% for NHANES 2001–2002, is excellent. Given that medication containers were visually inspected by interviewers, the assessment of exposure to AI medications is expected to have been quite accurate as it did not rely on self-report. Standardized protocols also likely minimized interviewer bias.

The findings from this study must be interpreted in the context of certain limitations. The alcohol measure was based on self-reported alcohol use, which is known to be subject to underreporting.¹⁶ Previous studies have also shown that alcohol questionnaires administered as part of a larger questionnaire, like NHANES, are effective in identifying abstainers and drinkers who consume high volumes of alcohol, but are less effective in classifying drinkers whose intake of alcohol is low or moderate.¹⁷ Moreover, subjects who were aware of the dangers of mixing AI medications and alcohol might not have disclosed the full extent of their prescription drug use, drinking habits, or both. Another limitation is that simultaneous exposure to alcohol and AI medications could also not be determined with absolute certainty. Furthermore, due to the cross-sectional nature of the data, it was not possible to assess whether and how alcohol consumption changed over time in AI medication users. This investigation is also likely to underestimate the extent of concurrent alcohol and AI medication use because we focused only on select classes of AI prescription medications that potentiate the sedative effects of alcohol.

The study findings point to the importance of recognizing and attending to concurrent exposure to alcohol and AI medication because it is a common practice. Concurrent use of alcohol and AI medications, especially hazardous misuse of alcohol, can lead to health outcomes such as a dangerous rise in blood pressure, severe drowsiness, an increased risk of automobile or household accidents, increased sedation resulting in impaired coordination, depressed heart functions, potentially fatal breathing difficulties, and an increased risk of death from overdose.¹ Although persons taking AI medications tended to drink less than their counterparts not on AI therapy, there may be opportunities for clinicians to routinely screen and counsel AI users who consume alcohol. Unfortunately, research has shown that physicians often fail to provide patients with important information on medication use, including AEs.¹⁸ Moreover, not all pharmacies consistently provide patients with information leaflets, and when these leaflets are made available, the information on contraindications, precautions, and how to avoid AEs is often lacking or inadequate.¹⁹ Nearly one third of patients do not read leaflets provided with new medications.²⁰ Furthermore, verbal prescription counseling by pharmacists, although meeting minimum federal and state requirements, is considered neither excellent nor good²¹, and this may have important ramifications for patients with low health literacy. Thus, patients may concurrently use alcohol and AI medications because they are unaware that doing so places them at high risk for harmful interactions.

From a public health standpoint, it is essential for physicians, particularly primary care physicians, to screen for alcohol use and encourage patients to avoid alcohol consumption while taking AI medications. Brief counseling by physicians and nurses in primary care settings has been shown to

be effective in reducing alcohol consumption in high-risk and “problem” drinkers.^{22–24} Moreover, a recently published guide for physicians treating patients with alcohol problems offers new strategies to help patients reduce or quit drinking and can be found at: <http://www.niaaa.nih.gov/guide> (accessed 3 March 2008). Both pharmacists and physicians also need to inform patients about the risks of concurrent alcohol and AI pharmacotherapy. The reinforcement of warnings by physicians and pharmacists concerning the dangers of concurrent alcohol and AI medication use will underscore the importance of alcohol abstinence during treatment and could alter the drinking practices of non-alcohol dependent patients.

Alternatively, physicians may be advising their patients to avoid consuming alcohol while taking AI medications, but patients may not heed this warning. It was not possible in this study to assess if physicians warned against concurrent alcohol and AI medication use and, if so, whether it had an impact on the drinking habits of their patients. An encouraging finding of this study was that persons taking AI medications were more likely to abstain from consuming alcohol than their counterparts not taking AI medications. If this is an indication that physicians are warning against concurrent alcohol and AI medication use, the fact that nearly one in five (17.3%) AI users remain at moderate or high risk of an alcohol related AE means that there is room for improvement. As previously mentioned, studies have shown that brief interventions for alcohol use by health professionals are effective in reducing alcohol intake in high-risk and in “problem” drinkers. To date, the effect of alcohol counseling in people taking AI medications has not been studied. The findings from this study suggest that people who are on AI pharmacotherapy and at high risk for an alcohol-related AE constitute a different population than those patients who have similar drinking patterns but are not taking AI medications. Future studies should address if counseling by physicians, nurses, or pharmacists reduces alcohol consumption among patients taking AI medications.

A substantial proportion of the American population is currently at risk of alcohol-related AEs. A recent study has shown that 77% of the elderly are taking at least one AI medication²⁵ and, as the population ages, the absolute number of AI prescription drug users may increase. The prevalence of alcohol consumption among elderly persons is expected to increase because baby-boomers are more likely to drink and are also heavier drinkers compared to previous elderly cohorts.²⁶ The elderly population is especially at risk for alcohol-drug AEs because their sensitivity to alcohol and medications is heightened due to physiological changes accompanying advanced age.^{27,28} Clinicians are best positioned to influence alcohol consumption and prevent alcohol-drug interactions as prescribing and dispensing AI medications provides the opportunity to screen for and advise against alcohol use. Routine screening and prescription counseling of AI medication users is critical for patient safety and well-being.

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