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RISK OF INJURY FROM DRINKING: THE DIFFERENCE WHICH STUDY DESIGN MAKES

Cheryl J. Cherpitel, Dr.PH,
Alcohol Research Group, 6475 Christie Avenue, Suite 400, Emeryville, CA 94608; Centre for Addictions Research of BC, University of Victoria, Victoria, BC, Canada V8W 2Y2

Yu Ye, MA,
Alcohol Research Group, Emeryville, CA 94608

Jason Bond, PhD,
Alcohol Research Group, Emeryville, CA 94608

Timothy Stockwell, Ph.D.,
Centre for Addictions Research of BC, University of Victoria V8W 2Y2, Victoria, BC, Canada

Kate Vallance, MA,
Centre for Addictions Research of BC, University of Victoria V8W 2Y2, Victoria, BC, Canada

Gina Martin, MS,
Centre for Addictions Research of BC, University of Victoria V8W 2Y2, Victoria, BC, Canada

Jeffrey R. Brubacher, MD, and
Department of Emergency Medicine, University of British Columbia, Vancouver, BC, Canada V6T 1Z4

Andrew MacPherson, MD
Department of Emergency Medicine, University of British Columbia, Vancouver, BC, Canada V6T 1Z4

Abstract

Background—The magnitude of risk for injury from drinking, based on emergency department (ED) studies, has been found to vary considerably across studies, and the impact of study design on this variation is unknown.

Methods—Patients were interviewed regarding drinking within six hours prior to the injury or illness event, drinking during the same time the previous week, and usual drinking during the last 30 days. Risk estimates were derived from case-control analysis and from both pair-matched and usual frequency case-crossover analysis.

Results—The odds ratio (OR) based on case-control (2.7; 1.9 - 3.8) was larger than that based on pair-matched case-crossover analysis (1.6; 1.0 - 2.6). The control-crossover estimate suggested the case-crossover estimate was an underestimate of risk, and when this adjustment was applied to the case-crossover estimate, risk of injury increased (OR = 3.2; 1.7 - 6.0). Adjusted case-crossover estimates compared to unadjusted showed the largest proportional increase at 7 or more drinks prior to injury (OR = 7.1; 2.2 - 22.9). The case-crossover estimate based on usual frequency of drinking was substantially larger (OR=10.8; 8.0-14.3) than that based on case-control or pair-matched case-crossover analysis, but less than either when adjusted based on control-crossover usual frequency analysis (OR = 2.2; 1.5 - 3.3).

Corresponding Author: Cheryl J. Cherpitel, 510 579-3453, Fax 510 985-6459, ccherpitel@arg.org.

Discussion—The data suggest that while risk of injury based on case-control analysis may be biased, control data are important in providing adjustments derived from control-crossover analysis to case-crossover estimates, and are most important at higher levels of consumption prior to the event.

Keywords

injury risk; emergency department; case-control analysis; case-crossover analysis

INTRODUCTION

A substantial literature exists documenting risk of injury from drinking prior to the event based on emergency department (ED) studies. These studies have primarily used a case-control study design in which non-injured patients serve as controls (Cherpitel, 1993a; Cherpitel, 2007) or a case-crossover design in which patients serve as their own controls (Maclure, 1991; Mittleman et al., 1993), based on either their drinking during a pre-determined period such as the previous day or the previous week (pair-matched) (Borges et al., 2006b; Vinson et al., 2003) or on their usual frequency of drinking over a period of time (Borges et al., 2006a). Despite the fact that these ED studies have used standardized protocols and instrumentation, with strict probability sampling of patients around the clock (Cherpitel, 2009), the magnitude of relative risk (RR) estimates for injury has varied across studies (Cherpitel, in press). Since no study has compared RR of injury, based on case-control estimates and case-crossover estimates using different approaches (pair-matched and usual frequency), in the same sample of ED patients, the impact on RR estimates of variation in study design and sampling is unknown.

The usual frequency approach to case-crossover analysis has typically generated larger risk estimates for injury due to alcohol consumption than either the pair-matched approach (Borges et al., 2004; Vinson et al., 1995) or the case-control approach (Ye et al., 2010; Zeisser et al., in press), and has been attributed to recall bias, particularly among infrequent drinkers who underestimate their usual consumption (Stockwell et al., 2008; Ye et al., 2010). Additionally, recall bias in alcohol consumption using the pair-matched approach has generated mixed results.

To explore the impact of study design and sampling frame on RR of injury related to drinking prior to injury, estimates based on case-control analysis and case-crossover analysis, using both the last-week pair-matched approach and the usual frequency approach, are compared in a sample of injured and non-injured patients arriving at the ED on weekend evenings. Control-crossover analysis is also provided to determine biases in the case-crossover design, estimates from which may be used to apply adjustments to case-crossover estimates. These findings are important for informing the calculation of improved estimates of alcohol attributable fraction due to injury morbidity and ongoing work on comparative risk assessment in the Global Burden of Disease (Rehm et al., 2010). Findings are also important in establishing safe drinking guidelines (Butt et al., 2011; Chikritzhs et al., 2011) and for determining economic costs related to excessive alcohol consumption (Bouchery et al., 2011).

METHODS

Samples

Data were collected over a period of 26 months (July 2009 – September 2011) on a probability sample of 281 injured and 515 non-injured ED patients sampled on one weekend a month (Friday and Saturday evenings from 9:00 pm to 4:00 am) at one ER each in

Vancouver and Victoria, British Columbia, Canada, as part of a community surveillance project to monitor alcohol and drug use. The weekend evening sampling times were selected to capture the period which would likely reflect the highest prevalence of alcohol and drug use among those admitted to the ED. Samples at both EDs were drawn from computerized admission logs according to consecutive patient arrival to the hospital. Every patient, both injured and non-injured, were approached with informed consent to participate as soon as possible after arrival in the ED. Among those sampled 24% refused to participate.

Data Collection

A cadre of interviewers were trained by the authors and supervised by survey research staff from the Centre for Addictions Research, BC. Interviews were conducted in a private area of the waiting room or adjacent space to ensure confidentiality of responses. If time did not permit completion of the interview prior to treatment, the interview was completed after the patient's examination. Patients who were too severely injured to be interviewed at that time, but who were hospitalized, were interviewed after their condition had stabilized.

Instruments

Data were collected using a 25-minute interviewer-administered questionnaire, adapted from the WHO Collaborative Study on Alcohol and Injury (Cherpitel et al., 2003). The questionnaire obtained data, among other items, on the reason for the ED visit, drinking within six hours prior to the injury or medical problem, drinking during the same six-hour period the previous week, amount of alcohol consumed at each time, quantity and frequency of usual drinking over the last 30 days, and demographic characteristics. Quantity and frequency of drinking were obtained from a series of questions used in previous U.S. National Alcohol Surveys (Clark and Hilton, 1991), as well as ED studies conducted in the U.S., Canada and elsewhere (Cherpitel et al., 2003).

Data Analysis

Case-control analysis (controlling for age and gender) and case-crossover analyses were used to estimate the risk of injury associated with drinking within the six hours prior to the event. Case-crossover analysis was based on both drinking during the same six-hour period the previous week (the pair-matched approach), and on usual frequency of drinking over the last 30 days (the usual frequency approach) (Maclure, 1991; Mittleman et al., 1993). Using case-crossover analysis, individuals serve as their own controls in studying the effect of a transient factor (alcohol consumption) on the risk of an acute event (injury), theoretically reducing confounding of the alcohol-injury relationship from stable risk factors such as gender and age, and allows for an estimate of risk over and above that associated with usual alcohol use.

Case-control analysis—In case-control analysis, odds ratios (ORs) adjusted for age and gender are estimated from unconditional logistic regressions comparing drinking during the six hours prior to the event between injured and non-injured patients.

Pair-matched case-crossover analysis—In case-crossover analysis using the pair-matched approach, alcohol use during the six-hour period prior to the injury event was compared to use during the same six-hour period the week prior to the injury, which adjusts for day of the week. Conditional logistic regression was used to calculate the ORs for matched pairs and 95% confidence intervals (CIs) (Maclure, 1991). A dose-response relationship was also analyzed for 1-2 drinks, 3-6 drinks and 7+ drinks (categorical volume) in the six hours prior to injury, using no drinking as the reference category.

Usual frequency case-crossover analysis—In case-crossover analysis using the usual frequency approach, risk estimates were generated comparing drinking within six hours prior to the injury with the patient's usual drinking over the last 30 days. This analysis can be considered as a self-matched case-control analysis with the OR generated from the Mantel-Haenszel estimator for dichotomous exposure (any drinking versus none) (Rothman and Greenland, 1998). The expected exposed periods for those reporting drinking within the six hours prior to injury are derived from the patient's reported usual frequency of drinking in the last 30 days, with a six-hour effect period assigned to each drinking occasion in the control period, to be consistent with the six-hour effect period assigned for drinking prior to injury. The expected unexposed periods are derived by subtracting the expected number of exposed periods from the total number of possible six-hour periods in the 30-day period, defined as 30 × 3, which excludes one six-hour sleeping period each day.

Control-crossover analysis—Case-crossover analysis was performed on the control patients, a procedure called control-crossover analysis, using both the pair-matched and usual frequency approaches. Control-crossover analysis provides a factor by which an adjustment can be made to the case-crossover estimate to account for potential biases (theoretically the OR from control-crossover analysis should be 1, if no biases exist). Control-crossover analysis has been widely used in case-crossover studies for validity checks and estimate adjustments (Greenland, 1999; Hallqvist et al., 2000; Marshall et al., 2000; Suissa, 1995). To adjust case-crossover estimates based on control-crossover analysis, the OR obtained from the pair-matched case-crossover analysis is divided by the OR obtained from the pair-matched control-crossover analysis, and similarly, the OR obtained from the usual frequency case-crossover analysis is divided by the OR obtained from the usual frequency control-crossover analysis.

RESULTS

Table 1 shows the demographic and drinking characteristics of the injured and non-injured patients. Injured were significantly more likely to be male and under 30 years of age compared to non-injured ($p<0.001$). Injured patients were also more likely to be white, but less likely to be married and less likely to have a lower household income. About 38% of injured patients reported drinking during the 6-hour period prior to injury, compared to 17% of non-injured patients before their illness event ($p<0.001$). Injured patients also reported a higher volume of drinking during this time than non-injured among those who reported drinking. Injured patients were also more likely to report drinking during the same six-hour period the previous week (30%) than non-injured (23%), but no significant difference was found in volume consumed during this time. Among injured patients, 21% sustained injuries related to a fall, 14% to sports or recreation, 11% to assault, 5% to a vehicular crash, and the remainder to a mixture of other types and causes.

Table 2 shows the ORs for injury from drinking, using case-control analysis and case-crossover analysis (unadjusted and adjusted using control-crossover analysis) based on both last week's drinking and usual frequency of drinking over the last 30 days.

Case-control vs. pair-matched case-crossover determination of risk

Although both are significant, the OR estimated from case-control analysis (2.7) was greater than that estimated from case-crossover analysis based on last week's drinking (1.6). The control-crossover pair-matched estimate (OR=.5) suggests that the OR estimated from case-crossover analysis is an underestimate, since, if no biases were present, the control-crossover estimated would be expected to be 1. When the control-crossover pair-matched estimate is

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used to ‘adjust’ the case-crossover estimate, the case-crossover estimate is increased to 3.2 (1.6/.5), which is now nearer the 2.7 case-control estimate.

Both the case-control and case-crossover analysis demonstrated a dose-response relationship for drinking 1-2, 3-6 and 7 or more drinks. When the case-crossover estimates are adjusted from respective control-crossover estimates, as the volume consumed prior to injury increases, so does the proportional increase in the ORs, reaching nearly twice the risk for injury compared to case-control analysis at 7 or more drinks during the six hours prior to injury, and over twice the risk compared to unadjusted case-crossover analysis.

Usual frequency case-crossover determination of risk

The OR for injury risk base on case-crossover usual frequency of drinking (OR=10.8) was substantially greater than that from either case-control or case-crossover pair-matched analysis, but when adjusted from control-crossover usual frequency analysis (OR=2.2), was quite similar to the case-control estimate (OR= 2.7), and less than the adjusted case-crossover pair-matched estimate (OR=3.2).

DISCUSSION

Comparing risk of injury based on case-control analysis with that based on *pair-matched case-crossover analysis*, using drinking during the same time the previous week as the control period, a higher OR was found for case-control analysis (2.7 vs. 1.6). Medical patients in the ED may not be the best controls for injured patients, however, since some conditions treated in the ED, such as liver cirrhosis, are directly linked to long-term chronic heavy drinking, and would result in an underestimate of risk of injury due to drinking. Conversely, medical patients may choose not to drink due to health problems, the so-called “sick quitter” effect (Shaper, 1990), or may be less likely to recall alcohol use prior to a medical problem than an injury, both of which would result in an overestimation of risk of injury from drinking.

Additionally, when using medical patients as controls, while some known (e.g., demographic) characteristics which may influence the alcohol-injury relationship can be controlled, others, such as dispositional characteristics (risking taking/impulsivity and sensation seeking) for example, are more difficult to account for, and may be expected to either confound an observed association between alcohol and injury or, alternatively, modify the relationship (Cherpitel, 1993b; Cherpitel, 1999; McLeod et al., 2003).

Control-crossover analysis demonstrated that case-crossover analysis resulted in an underestimation of risk of injury, since the OR from control-crossover analysis was less than one, as expected if no bias was present. When the pair-matched control-crossover estimate was used to ‘adjust’ the case-crossover estimate, the OR increased to 3.2, and was larger than that derived from case-control analysis. Interestingly, although underestimation of risk across different levels of consumption prior to injury did not appear to vary markedly in control-crossover analysis, these adjustments, when applied to the pair-matched case-crossover dose-response analysis, resulted in substantial increases in risk of injury for each volume level, and was most marked for those consuming 7 or more drinks prior to injury, suggesting that such adjustments may be more important at higher levels of consumption.

Unlike case-control analysis, *case-crossover analysis* controls potential confounding of the alcohol-injury relationship from stable within-person risk factors (e.g., demographic and dispositional characteristics and usual substance use patterns); however, other potential biases are possible when using the pair-matched design, depending on the control period selected. For example, when using the same six-hour period the week prior as the control, bias can occur when the case and control periods differentially fall at times when the likelihood of drinking may vary (e.g., holidays or other celebrations); similarly, using the same six-hour period the previous day as the control, the likelihood of drinking may vary by day of the week (e.g., Friday evening vs. Saturday evening).

The OR for risk of injury from *case-crossover usual frequency analysis* was substantially larger (10.7) than that from either case-control (2.7) or pair-matched case-crossover (1.6) analysis, as found on separate samples in prior studies (Borges et al., 2004; Vinson et al., 1995; Zeisser et al., in press). When the case-crossover usual frequency estimate was ‘adjusted’ based on control-crossover analysis, however, the estimate was slightly less (OR=2.2) than the case-control estimate (OR=2.7) and less than the ‘adjusted’ pair-matched case-crossover estimate (OR 3.2).

A prior analysis comparing risk of injury from the case-control approach and the case-crossover usual frequency approach in 15 ER studies across seven countries, all using representative samples of patients, found the two estimates were similar after adjusting the case-crossover estimate from control-crossover analysis (OR=2.08 in case-control and 2.11 in adjusted case-crossover analysis), with both estimates similar to the respective estimates found here (Ye et al., 2010).

Since sampling in the present study occurred on weekend evenings, analysis based on the usual frequency of drinking resulted in inflated odds ratios for both case-crossover (10.7) and control-crossover (4.8) analysis, underscoring that sampling issues are important to consider in case-crossover analysis based on the usual frequency approach.

Limitations

When control-crossover estimates are used to adjust for case-crossover estimates, the assumption is made that the same magnitude of bias exists for both case and control samples, and this may be a potential issue given differences in demographic characteristics between the injured and non-injured patients observed in Table 1. For example, although the control-crossover estimates were similar between men and women (RR=0.5 and 0.6, respectively), they were different across age groups (RR=0.7, 0.2 and 1.0, for <30, 30-49 and 50+, respectively) (not shown). While age and gender were controlled in these analyses, other uncontrolled demographic differences between cases and controls may have influenced study findings, and this incomparability issue has not been fully addressed in the literature on the case-crossover method.

Another potential source of bias in this study comes from missing data on last-week drinking which was used as the control period exposure. About 11% of the injured patients and 9% of the non-injured did not answer this question, while only about 2% of both samples had missing data on drinking before the event. Among those with missing data on the last-week drinking question, 45% of the injured reported alcohol use before the event, while 25% of the non-injured reported drinking prior to their illness, and neither of these were significantly different from their respective rate of reporting drinking prior to the event reported in Table 1, suggesting results here may not be affected greatly by the missing data.

Last, both the case-crossover and case-control approach are subject to potential bias due to contextual factors that may be critical in determining risk of injury, and such factors were not taken into account in these analyses. Such environmental factors or activities may be independently correlated with both alcohol use and injury risk, and bias may occur if context is not represented equally in the case and control period comparisons (Watt et al., 2006), an issue that has been virtually ignored in empirical research (Stockwell et al., 2002).

Conclusions

Risk of injury based on case-control analysis in the ED may result in either underestimates or overestimates, and while case-control estimates cannot be relied on as the 'gold standard,' data from non-injured controls are important for applying adjustments derived from control-crossover analysis to case-crossover estimates, particularly important at higher levels of consumption. When using the pair-matched case-crossover approach, an average OR based on multiple matching of control periods, using both the previous day and the previous week, would appear optimal to circumvent biases related to the differential likelihood of drinking during pre-determined time periods.

Future research on risk of injury from drinking should include representative samples of patients in comparing different approaches to risk estimation at various volumes of consumption prior to injury, controlling for context where possible. Such research is important for improved estimates of alcohol attributable fraction for injury morbidity to inform comparative risk assessment for determining the global burden of disease, establishing safe drinking guidelines, and determining economic costs related to excessive alcohol consumption.

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Table 1

Demographic and drinking characteristics between injury and non-injury ER patents (%)

	Injury (n=281)	Non-injury (n=515)
Gender male	63.0	44.9***
Age		
<30	54.6	38.3***
30-49	32.1	35.4
50 and up	13.2	26.3
Race		
White	76.9	66.8**
Non-white	23.1	33.2
Marital status		
Married/living together	27.5	33.8**
Widowed/separate/divorced	10.6	15.6
Single	61.9	50.6
Education		
High school graduate or less	25.3	30.9
Some college	40.3	38.4
College graduate or higher	34.4	30.7
Household income		
<$40,000	31.0	37.1*
$40,000-$80,000	21.7	21.7
>$80,000	27.4	18.6
Missing	19.9	22.5
Any drinking before injury/illness	38.2	17.4***
Volume before event, if drinking		
1-2 drinks	25.7	44.7*
3-6 drinks	33.3	31.8
7 drinks or more	41.0	23.5
Any drinking same time last week	30.0	22.9*
Volume, if drinking		
1-2 drinks	37.8	41.7
3-6 drinks	29.7	33.0
7 drinks or more	32.4	25.2

Chi-square test between injury and non-injury groups.

* $p<0.05$

** $p<0.01$

*** $p<0.001$

Table 2

Odds Ratios of Injury Associated with Acute Drinking Estimated from Case-control and Case-crossover methods

Case-control [1]	
Adjusted ORs	2.7 (1.9, 3.8)***
Model 1: any versus none	
Model 2:	
1-2 drinks versus none	1.9 (1.1, 3.3)*
3-6 drinks versus none	3.0 (1.7, 5.1)***
7 or more versus none	3.9 (2.2, 7.0)***
Case-crossover Pair-matched	
Last Week	
Case-crossover ORs	
Model 1: any versus none	1.6 (1.0, 2.6)*
Model 2:	
1-2 drinks versus none	1.0 (0.5, 1.9)
3-6 drinks versus none	1.9 (1.0, 3.6)†
7 or more versus none	2.7 (1.2, 5.8)*
Control-crossover ORs	
Model 1: any versus none	0.5 (0.3, 0.8)**
Model 2:	
1-2 drinks versus none	0.6 (0.4, 1.1)
3-6 drinks versus none	0.4 (0.2, 0.8)*
7 or more versus none	0.4 (0.2, 0.9)*
Adjusted case-crossover ORs	
Model 1: any versus none	3.2 (1.7, 6.0)***
Model 2:	
1-2 drinks versus none	1.6 (0.7, 3.7)
3-6 drinks versus none	4.6 (1.7, 12.3)**
7 or more versus none	7.1 (2.2, 22.9)**
Case-crossover 30-day	
Usual Frequency	
Case-crossover ORs	
Model 1: any versus none	10.7 (8.0, 14.3)***
Control-crossover ORs	
Model 1: any versus none	4.8 (3.7, 6.3)***
Adjusted Case-crossover ORs	
Model 1: any versus none	2.2 (1.5, 3.3)***

[1]Controlling for gender and age

†$p<0.10$

*$p<0.05$

**$p<0.01$

***$p<0.001$