Challenges in Assessing if Hangovers Increase the Risk of Motor Vehicle Crash (MVC) Injuries: Is Alcohol's Influence Greater Than Expected?

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My first return of sense or recollection was upon waking in a strange, dismal-looking room, my head aching horridly, pains of a violent nature in every limb, and deadly sickness at the stomach. From the latter I was in some degree relieved by a very copious vomiting....I passed some moments in a state little short of despair.”
Introduction

• Elevation of blood alcohol concentration (BAC) is a well-recognized risk factor for motor vehicle crashes (MVCs)

• Little is known however regarding hangovers and crash risk.
Aim

• Examine evidence that hangovers could increase injury risk

• Develop a methodology to determine if hangovers represent a real injury hazard
  – Measurement of hangovers
  – Biomarkers to identify people at risk for hangovers
    • Evidence recent heavy drinking when BAC zero
  – Surrogate measures of risk
Hangovers: the neglected area of alcohol research

- After years of little research interest in hangovers, increasing interest in research on their etiology and impact
- Number recent review articles
- Etiology hangovers remains unknown
- Alcohol Hangover Research Group
  - Special issue Current Drug Abuse Reviews
    - Joris Verster
What evidence of injury risk is there?

- Experimental evidence suggests that the residual effects of alcohol impair performance in simulated tasks
  - Occupational performance
    - flying and driving simulators
  - Neurocognative performance
  - Improved methods for measurement
- No studies examine real-world crash risk
  - Objective data to document hangovers was lacking
BAC negative trauma patients have high prevalence problem drinking

- Studies screening for alcohol problems
- Trauma patients with negative BACs on admission
  - 12% met criteria for current dependence
  - 24% for lifetime dependence
  - 4-5 times higher than in the general population
- Are some injured drivers hung over?
Definitions

• “Residual alcohol effects”:  
  – any subjective, physiological, and/or behavioral effects of heavy intoxication  
  – after blood alcohol concentration (BAC) has fallen to about zero.

• “Hangover”:  
  – self-reported unpleasant residual effects:  
  – feeling lousy, thirst, headache, dizziness, faintness, fatigue, nausea, stomach ache, and feeling as though one’s heart were racing.  
  – validated Acute Hangover Scale measures hangover symptoms
Commonly observed changes over time in blood alcohol concentration (BAC) and alcohol hangover severity.

Measurement

• **Hangover Incidence:**
  “Rate your hangover now on a scale of 0 (“none”) to 7 (“incapacitating”).
  *Hangover* if answer $\geq 1$.

• **Hangover Severity:**
  Acute Hangover Scale (Rohsenow, et al. 2007)
  The sum of 9 validated items, rated from 0 (“none”) to 7 (“incapacitating”).
Hangover severity reported by men and women after consumption of 10 to 15 alcoholic drinks by time of day (Penning et al. 2010)
Hangover Resistance

About 25% of the population is resistant to hangover in survey and experimental studies (Howland et al., 2008 a,b).

No hangover reported after drinking to BACs that produce hangover for most people.
Hangover studies in real world crashes

• Major limitations in evaluating the effects of hangovers in non-experimental situations
  – Reliance on self reports of heavy drinking the night before
  – No objective marker available to detect residual effects when the BAC is zero

• Can we use biomarkers to indicate recent heavy alcohol use?
Windows of Assessment for Various Alcohol Biomarkers (i.e., the period during which the biomarker level may remain high after it originally rose assuming that no further drinking occurred)

SAMSA 2006

![Bar graph showing windows of assessment for various alcohol biomarkers.]

- **Short Term**
  - BAC: 6 hours
  - EtG (Urine): 5 days

- **Intermediate Term**
  - CDT: 3 weeks
  - PEth: 3 weeks
  - GGT: 4 weeks
  - AST: 4 weeks
  - ALT: 4 weeks
  - MCV: 8 weeks

BAC = Blood alcohol concentration
Biomarker

• Ethyl glucuronide (EtG) and ethyl sulfate (EtS) formed by alternate metabolic pathway for alcohol
  – Less than 0.5% alcohol metabolized this way

• Used in alcohol treatment programs to monitor abstinence
  – E.g., pilots or surgeons who lost license due alcoholism
  – Only formed after recent drinking
  – Identifies persons whose BAC now zero but who drank in past 20-30 hours
Median detection times of ethanol, EtG, EtS, and GTOL/5-HIAA (n = 10) in urine samples after oral ingestion of 0.5 g/kg ethanol in a fasted state. Error bars represent 95% CI.

Hangover study

Hangovers and Traffic Injuries: Is Alcohol's Influence Greater Than Expected?

• Quantify potential for residual effects ethanol in injured drivers

• Use, ethyl glucuronide (EtG) and ethyl sulfate (EtS) to indicate recent heavy drinking even when blood alcohol is zero.

• Assess biomarkers EtG & EtS in urine
Initial grant review

- Lack of information about the time course of the metabolite in at-risk subject samples
  - no information on how our proposed biomarkers EtG and EtS, performed among chronic drinkers and those with very high BACs.
  - Prior studies restricted to controlled dosing studies
    - only BAC levels up to 100 mg/dl evaluated due ethical concerns.

- Saved by 2 studies of biomarker among those admitted to alcohol withdrawal unit
  - High BACs
  - Elimination EtG in heavy drinkers not differ from health volunteers
Figure 3. Urinary excretion time profiles for EtG concentrations in relation to the estimated time for a zero ethanol concentration after normalizing the results to urinary creatinine (B) in 32 alcohol-dependent patients during detoxification. Solid red lines represent our proposed residual effects cut-off of 45 mg/L. Inset: Box-and-whisker plots for the times from estimated zero ethanol concentration until urinary EtG/creatinine had returned to below their cut-off limits (<0.5 mg/g)^3

Methods

- Admissions drivers to Shock/Trauma UM – Baltimore
- Admissions from all over state of MD
- Only trauma patients
  - Blood alcohol testing all admissions
  - Urine drug screen
- Use urine for EtG and EtS testing
- Deaths for whole state also to be studied- medical examiner
Hangovers and Traffic Injuries: Is Alcohol's Influence Greater Than Expected?

Overview of Study Plan:

**Phase I**
- **Interviewed Drivers**
- **Testing Biomarkers & BAC**
  - **Aim 1**: Evaluations biomarkers & Clinical data
  - **Aim 2**: Risk factor study
    - **Case-crossover**
  - **Aim 3**: Risk factor study crash responsibility & injury circumstances
  - **Aim 4**: Prevalence biomarkers
    - **Drivers only**
    - **Non-drivers**
  - **Aim 5**: Alcohol injury surveillance
    - **Alcohol attributable fraction for hangovers**

**Phase II**
- **Testing Biomarkers & BAC**
  - **All Cases**
  - **BAC = 0**
  - **Drivers only**
    - **Police report**
    - **Non-drivers**
Individual concentrations of EtG in urine after ingestion of 0.5 g ethanol/kg body weight. Each line represents one subject (n = 10).

Risk estimation

- Case-crossover analyses will provide one estimate of risk
- Compare self-reported drinking 12 hours prior to injury with:
  - Comparable period week before
  - Usual drinking patterns
Risk estimation

• Culpability studies will be used as another estimate of risk
• Determine the extent to which injured zero BAC drivers with biomarker evidence of hangover are responsible for causing their crash, compared with drivers without hangover biomarkers
  – Can include fatalities
Conclusion

• This study is an innovative use of biomarkers in injury research and may indicate that hangovers are an important but unrecognized risk factor in many injuries.
Questions and advice
Questions???

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Hangover Helpers From Around the World


Hangover Helpers

Around the world, suggestions abound for how to cope with the effects of one too many.

Roll over images to see how different cultures cope with a hangover.

When hungover in China, do what the Chinese do: Drink tea—strong green tea, to be specific. Water with lemon or vinegar is also thought to do the trick.

U.S.A.
Tomato juice, eggs

Netherlands
Beer

Japan
Pickled plums

Poland
Sour pickle juice

Romania
Tripe soup

Italy
Coffee

Mexico
Shrimp

Russia
Leafy birch branches
Cures
"You may already be a Nobel Prize winner!"