Research Article

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Predictors and effects of alcohol use on liver function among young HCV-infected injection drug users in a behavioral intervention

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Background & Aims: Hepatitis C virus (HCV) screening can provide opportunities to reduce disease progression through counseling against alcohol use, but empirical data on this issue are sparse. We determined the efficacy of a behavioral intervention in reducing alcohol use among young, HCV-infected injection drug users (IDUs) (n = 355) and assessed whether changes in liver enzymes were associated with changes in alcohol consumption.

Methods: Both the intervention and attention-control groups were counseled to avoid alcohol use, but the intervention group received enhanced counseling. Logistic regression, ANOVA, and continuous time Markov models were used to identify factors associated with alcohol use, changes in mean ALT and AST levels, and change in alcohol use post-intervention.

Results: Six months post-intervention, alcohol abstinence increased 22.7% in both groups, with no difference by intervention arm. Transition from alcohol use to abstinence was associated with a decrease in liver enzymes, with a marginally greater decrease in the intervention group ($p = 0.05$ for ALT; $p = 0.06$ for AST). In multivariate Markov models, those who used marijuana transitioned from alcohol abstinence to consumption more rapidly than non-users (RR = 3.11); those who were homeless transitioned more slowly to alcohol abstinence (RR = 0.47); and those who had ever received a clinical diagnosis of liver disease transitioned more rapidly to abstinence (RR = 1.88).

Conclusions: Although, behavioral counseling to reduce alcohol consumption among HCV-infected IDUs had a modest effect, reductions in alcohol consumption were associated with marked improvements in liver function. Interventions to reduce alcohol use among HCV-infected IDUs may benefit from being integrated into clinical care and monitoring of HCV infection.

Keywords: Hepatitis C virus; Injection drug users; Alanine aminotransferase; Asparatate aminotransferase; Alcohol use; Behavior change.

Received 28 May 2010; received in revised form 6 October 2010; accepted 7 October 2010; available online 24 November 2010

Clinical trials registration number: NCT00391482

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Abbreviations: HCV, hepatitis C virus; IDUs, injection drug users; ALT, alanine aminotransferase; AST, aspartate aminotransferase; US, United States; RNA, ribonucleic acid; STRIVE, Study to Reduce Intravenous Exposures; A-CASI, audio-computer assisted self interview; AUDIT, alcohol use disorders identification test; PCR, polmerase chain reaction; ANOVA, analysis of variance.

Introduction

The most compelling reason for screening of hepatitis C virus (HCV) infection among high-risk populations is to appropriately guide interventions in order to (1) reduce the spread of infection to others; (2) increase uptake of HCV treatment; and (3) reduce additional liver damage in infected individuals through alcohol cessation. Although all three aspects are critical in preventing significant HCV-related morbidity and mortality among high-risk populations, few studies have focused on alcohol cessation as a measure of liver preservation in injection drug users (IDUs).

Among HCV-infected persons, excessive alcohol use has been proposed to result in more severe histological injury, more rapid disease progression, and a higher frequency of cirrhosis and hepatocellular carcinoma [1]. Moderate (<80 g alcohol/day) and heavy alcohol use (>=80 g/day) have been associated with increased risk of cirrhosis and hepatocellular carcinoma [2]. Lower alcohol consumption (<140 g/week [3] and >50 g/day [4]) has been associated with increased fibrosis. Since IDUs may experience more barriers to HCV treatment than other populations [5,6], abstinence from alcohol use could be extremely important in sustaining liver health.

Although alcohol use has been shown to increase alanine aminotransferase (ALT) levels in the general population [7] and among anti-HCV-positive individuals [8], few studies have

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examined liver enzymes in IDUs in relation to alcohol consumption and active HCV-infection (i.e., detectable HCV RNA). Clinical evidence suggests that HCV replication and alcohol metabolism may interact synergistically to exacerbate liver damage [9,10], and therefore could result in increased hepatic injury over a shorter period. To our knowledge, no study has compared change in serum ALT or aspartate aminotransferase (AST) levels with change in alcohol behavior among young HCV-infected IDUs. Developing a thorough understanding of the relationship between alcohol consumption, HCV infection, and liver enzymes is very important for HCV-infection management, as HCV-infected individuals may withhold disclosure of their alcohol use to a clinician for fear of disapproval, and heavy alcohol use may be common among young IDUs [11].

Different patterns of alcohol use in response to standard counseling at diagnosis have been reported among HCV-infected IDUs [12] and other patients [13], including cessation of alcohol use; modification of use without cessation; and continued high levels of alcohol consumption. High levels of alcohol use have been reported prior to HCV infection, with marked reductions in use immediately following HCV diagnosis, and rebounds in use 6 and 12 months post-diagnosis have been reported among young IDUs [14]. Brief alcohol interventions among IDUs [15] and HCV-infected IDUs in treatment [16] have also demonstrated short-term efficacy. These studies suggest that alcohol cessation interventions may be highly effective among IDUs.

We previously reported that a behavioral intervention was successful in reducing distributive needle sharing among young, HCV-infected IDUs in three US cities [17]. A secondary outcome of this intervention was to reduce alcohol consumption. Herein, we report on the efficacy of this intervention in reducing alcohol consumption among 355 young, HCV-infected IDUs. Furthermore we examine changes in ALT and AST with change in alcohol use and patterns and predictors of changes in alcohol use.

Patients and methods

Participants and study design

The data for this study were collected as part of the Study to Reduce Intravenous Exposures (STRIVE), a randomized, attention-control trial, which aimed to determine the efficacy of an intervention on reducing distributive needle sharing and increasing healthcare utilization among HCV-infected IDUs, which has been described [17,18].

Between April 2002 and May 2004, young, HCV-antibody positive IDUs were recruited from Baltimore, Maryland; New York City, New York; and Seattle, Washington. IDUs were eligible if they were 18–35 years-old; injected drugs within the previous 6 months; planned to stay in their recruitment location for 12 months; had documented HCV antibody-positive and HIV antibody-negative tests; and consented to provide a blood sample for HCV-related tests. Participants were not excluded if they were hepatitis B antibody-positive or if they had known liver disease. HCV antibody testing was conducted in other studies focusing on prevention of HCV acquisition, and HCV-infected subjects who were ineligible for those studies were referred to STRIVE. All participants enrolled in STRIVE received standard-of-care HCV counseling, including information on alcohol cessation, immediately before they were randomized.

In total, 952 IDUs were referred from other studies, 630 enrolled and completed baseline assessments, and 418 were randomized to intervention or control groups [17,18]. Among randomized subjects, 13.6% (n = 57) did not complete any follow-up interviews, 26.5% (n = 115) completed one follow-up and 59.8% (n = 250) completed both follow-up visits. Of the 365 individuals completing at least one follow-up visit, 10 lacked complete data on alcohol use, leaving 355 who were eligible for analyses. All study activities were approved by institutional review boards at participating sites and participants provided written, informed consent.

Data collection, intervention, and follow-up

Prior to randomization, STRIVE participants completed a baseline assessment interview using audio computer-assisted self-interview (A-CASI) to reduce socially desirable responding [19,20]. The assessment included injection behaviors, alcohol use, the alcohol use disorders identification test (AUDIT) [21], healthcare utilization, patient–doctor interactions, HCV treatment readiness, depression, and utilization of alcohol and drug treatment. Participants were scheduled to attend a randomization visit within 15 weeks of their baseline visit.

Participants underwent their first intervention or control session at the randomization appointment to reduce attrition [17,18]. Those in the attention-control arm watched a television docudrama about the lives of IDUs, followed by a facilitator-led discussion about family, education, self-respect, relationships, violence, parenting, and employment.

The intervention arm participated in facilitated exercises focusing on the natural history of HCV infection, HCV treatment, and how to maintain liver health, including avoiding alcohol use. Although the intervention was not specific to alcohol cessation, all intervention group sessions included HCV prevention messages targeted toward participants, encouraging dissemination to their HCV-infected peers, and stressed the dangers of alcohol use and benefits of cessation for HCV-infected individuals.

Both trial arms consisted of six 2-hour sessions held biweekly by public health professionals for three weeks. Detailed scripts were followed by facilitators in order to reduce variation in the delivery of the intervention. Participants were asked to return for follow-up 3 and 6 months after completing the intervention.

Measures Assessed

At baseline and 6-month follow-up, standard liver enzyme panels, including ALT and AST, were completed on fresh serum samples at commercial laboratories. All participants were counseled on results by physicians who were study investigators and referred for treatment if indicated. No serum samples were drawn at the 3-month follow-up visit. Presence of HCV RNA was determined at the 6-month follow-up using polymerase chain reaction (PCR). Serum samples from all sites were shipped to John's Hopkins University for assessment using a standardized protocol.

Actual homelessness was defined as an affirmative response to having slept outside, in a car, or abandoned building for seven or more days consecutively. Perceived homelessness was defined as the participant indicating that s/he thought of him/herself as homeless [22]. Participants were asked if they received any type of alcohol treatment in the preceding 3 months and if they were currently receiving drug treatment, but the type of treatment was not specified.

AUDIT scores were based on a ten item scale [21] with three questions each on alcohol consumption and dependence, and four on external problems related to alcohol consumption (problem drinking). AUDIT scores can range from 0 to 40, with a score of 8 or more indicating problem drinking [21]. Baseline AUDIT measures pertained to alcohol behaviors in the past year, however, 3- and 6-month follow-up measures pertained to the past 3 months only. For general alcohol use measures, we used a single AUDIT question pertaining to how often participants drank alcohol prior to that particular interview.

Variables that remained constant over time were measured at baseline. Time-varying factors were measured at each visit and those assessed at follow-up pertain only to the 3-month time period prior to the visit.

Statistical analysis

Analyses were restricted to the 355 individuals who completed at least one follow-up interview and had complete data on alcohol use. For analyses examining liver enzymes, 318 participants with complete data were included. Contingency tables and univariate logistic regression were used to examine differences in demographics, injection behaviors, life situations, and baseline liver enzymes between those who did and did not report alcohol use at baseline. Effects of the intervention on alcohol use, AUDIT score, and liver enzymes were examined using separate univariate and multivariate logistic regression models.

Predictors of change in alcohol use status at consecutive visits were analyzed using continuous time Markov models, which provide hazard estimates while allowing for repeated changes in outcome that are bidirectional. These models were used to estimate the transition rate between alcohol use and abstinence in terms of sociodemographic predictors, interventions and personal health status information, life situations, and substance use.

ANOVA was used to examine overall change in liver enzyme scores from baseline to 6-month follow-up according to category of change in alcohol use (i.e., (1) no change in alcohol use (whether using or abstaining), (2) change from