



Alcohol use disorder and associated physical health complications and treatment amongst individuals with and without opioid dependence: A case-control study



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ABSTRACT

Background: Dependence upon one substance may increase vulnerability for dependence on other substances. This study aimed to i) examine the association between opioid dependence and alcohol use and dependence; and ii) identify demographic, mental health, substance use, and alcohol-related withdrawal, physical health complications, and treatment correlates of comorbid alcohol and opioid dependence versus the former only.

Methods: In this case-control study, 1475 participants with opioid dependence recruited from opioid substitution therapy (OST) clinics and 516 non-opioid dependent matched participants completed a structured interview covering psychiatric history, substance dependence, child maltreatment, and history of alcohol use. Analyses were mainly concentrated on cases (n = 696) and controls (n = 194) reporting lifetime alcohol dependence.

Results: Cases with opioid dependence had higher rates of lifetime alcohol dependence than controls. Binary logistic regression analyses showed comorbid cases reported greater socio-economic disadvantage, poorer psychiatric history, greater incidence of dependence on other substances, earlier onset of regular drinking and alcohol dependence, and greater severity of alcohol dependence (relative to controls with alcohol dependence only). Comorbid cases were also more likely to report endorsement of certain DSM-IV criteria (i.e., legal problems due to alcohol and desire/inability to cut down use), specific withdrawal symptoms (e.g., tachycardia, hallucinations), using other substances to relieve withdrawal symptoms, and experiencing liver disease/jaundice. Rates of lifetime treatment engagement were low overall.

Conclusions: Though strongly associated with alcohol dependence and alcohol-related harms, people with a history of opioid dependence have complex social and clinical backgrounds, which appear to be important factors associated with higher levels of alcohol dependence.

1. Introduction

Alcohol dependence is a significant health and social problem worldwide. Globally, alcohol use disorders accounted for 2.8 million deaths in 2013, most commonly as a result of injury, cancer, alcoholic liver disease and heart disease (Forouzanfar et al., 2015; Whiteford et al., 2013). In developed societies, people with alcohol use disorders

account for around half of all alcohol-related harm (Connor et al., 2016), and characteristics that predict alcohol-related treatment access remain inconsistent (Cohen et al., 2007).

Opioid dependence is a condition with a chronic, often relapsing, course which is also an important cause of disease burden globally. Indeed, in 2010 it was estimated that there were 15.5 million people worldwide living with opioid dependence (Degenhardt et al., 2014).

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Polydrug use is common amongst people with opioid dependence, and alcohol falls second only to tobacco in regards to frequency of use amongst this group (Darke et al., 2015). Moreover, alcohol dependence is 13 times as common among people with opioid dependence compared to the general population (Stinson et al., 2005).

Alcohol and opioids share similar neurobiological mechanisms in the central nervous system. Both drugs have been implicated in the endogenous opioid system (Gilpin and Koob, 2008; Kosten and George, 2002) and opioid receptors play a key role in self-administration, motivation for, and the rewarding effects of, alcohol in mice (Becker et al., 2002; Charbogne et al., 2014). Furthermore, naltrexone, an opioid antagonist, has been shown to have efficacy in the treatment of alcohol dependence (Pettinati et al., 2006). Given these shared pathways, it is possible that dependence on one drug may confer vulnerability to developing a dependence on the other.

So far, work examining comorbid alcohol and opioid dependence has focussed upon the impact of alcohol use on harms and risk behaviours associated with opioid use, such as crime (Kokkevi et al., 1993) (Kokkevi et al., 1993), overdose—both non-fatal and fatal (Coffin et al., 2003; Kerr et al., 2007)—suicide risk and mental health problems (Darke et al., 2015; Dawson et al., 2005). It has also been hypothesized that heavy alcohol use could exacerbate existing liver damage, such as that from hepatitis C virus (HCV) in opioid users (Darke, 2011).

Although it is recognized that use of cocaine by heavy drinkers increases vulnerability to developing alcohol dependence (Rubio et al., 2008), less work has examined associations between opioid use and severity of alcohol dependence and other alcohol outcomes. Using data from a large retrospective case-control study, this paper aims to identify the:

- 1 Association between opioid dependence and the likelihood of alcohol use, abuse and dependence; and
- 2 Demographic, mental health, substance use, and alcohol-related withdrawal, physical health complications, and treatment correlates of comorbid alcohol and opioid dependence versus the former only.

2. Material and methods

2.1. Participants and procedure

This study used data from the Comorbidity and Trauma Study (CATS), a retrospective case-control study examining factors associated with opioid dependence. Participants with opioid dependence ($n = 1475$; hereafter referred to as ‘cases’) and neighborhood control participants without opioid dependence ($n = 516$) were recruited to take part in a structured face-to-face 1.5–2.5 h interview between 2004 and 2008. Cases were recruited from both public and, private opioid maintenance treatment clinics from the greater Sydney region in New South Wales, Australia, with flyers and posters used to invite individuals to participate. Controls were recruited from flyer drops in social housing estates and employment centers and community centers, open street malls, and local press servicing the same geographical area as the opioid maintenance treatment clinics. Eligible cases were aged 18 years or older, English language proficient, and had received methadone or buprenorphine for the treatment of heroin dependence at some point in their lives. Control participants had fewer than 5-lifetime experiences of non-medical opioid use and were matched on gender, employment, age and area of residence (the latter as a proxy for ethnicity and social disadvantage). Written informed consent was obtained, and participants were reimbursed AUD\$50. The study received approval from the ethics committees of the University of New South Wales, Washington University, the Queensland Institute of Medical Research, and of the Area Health Services overseeing participating clinics. The complete methods of CATS have been described elsewhere (Shand et al., 2011).

2.2. Key measures

The interview covered socio-demographic parameters, substance use, mental health and family background.

The Semi-Structured Assessment of the Genetics of Alcoholism-Australia (SSAGA-OZ) (Bucholz et al., 1994; Hesselbrock et al., 1999) was used to determine Diagnostic and Statistical Manual of Mental Disorders (fourth edition; DSM-IV) lifetime diagnoses of psychiatric disorders (depression, post-traumatic stress disorder (PTSD) and panic disorder); alcohol abuse and dependence; and other substance (tobacco, cannabis, cocaine, sedative and stimulant) abuse and dependence disorders. Alcohol abuse was defined as meeting any of four DSM-IV criteria, whereas a diagnosis of dependence required meeting three or more other DSM-IV criteria; participant reported tolerance was added to the SSAGA-OZ as a criterion for tolerance. In the absence of a marker to quantify the severity of alcohol dependence, ‘number of DSM-IV criteria endorsed’ was used as a surrogate.

The SSAGA-OZ also collected detailed data on alcohol use, including the age of onset of regular drinking, lifetime experience of physiological dependence (defined as the presence of withdrawal or tolerance) and longest period of abstinence. Eight items examined lifetime experience of withdrawal (defined as symptoms lasting for 2 days or longer), including nature and number of symptoms, intensity, interference of withdrawal with daily life and coping mechanisms to deal with withdrawal from alcohol. The number of withdrawal symptoms occurring together at one time was used to index intensity of withdrawal. The questionnaire also probed for lifetime experience of physical health complications from alcohol use (i.e., liver disease, memory problems, peptic ulcer disease, and pancreatitis), continued alcohol use despite adverse health complications, as well as lifetime engagement in treatment for alcohol dependence, and age of treatment initiation.

Other questionnaire assessments included a screener for borderline personality disorder adapted from the International Personality Disorder Examination (IPDE), whereby participants were classified as screening positive if they endorsed three or more symptom criteria and indicated if symptoms interfered with their life (Loranger et al., 1994).

In addition to the questionnaire data, participants were also encouraged to provide blood samples for HCV antibody and RNA testing. For analysis, results of the antibody screen have been used as these provide an indication of lifetime HCV exposure.

2.3. Statistical analysis

Preliminary comparisons of alcohol use and disorder were made between participants with opioid dependence (cases) and without opioid dependence (controls) to identify the cohort of people with comorbid alcohol and opioid dependence versus alcohol dependence only. Subsequent analyses were restricted to those participants who met the DSM-IV criteria for alcohol dependence in their lifetime (i.e., cases with opioid and alcohol dependence, and controls with alcohol dependence only). It should be noted that 132 and 63 participants in preliminary and subsequent analyses, respectively, did not provide blood samples for HCV antibody and RNA testing.

All analyses were carried out using SPSS for Windows, version 22.0 (IBM Corp, 2013). Percentages are reported for categorical data and means and, standard deviations (SD) were calculated for continuous data were normally distributed, and medians and interquartile ranges where data were skewed. Univariate logistic regression analyses were undertaken to identify demographic, mental health, substance use, withdrawal, physical health complication and treatment correlates of comorbid alcohol and opioid dependence.

Supplementary analyses were undertaken to determine whether opioid dependence was a correlate of alcohol dependence (univariate and multivariable binary logistic regression); correlate of the severity of dependence amongst those who meet dependence criteria (univariate and multivariable Poisson regression); and of liver disease amongst

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