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Review

Depression in patients with alcohol use disorders: Systematic review and meta-analysis of outcomes for independent and substance-induced disorders

James A. Foulds [a,*], Simon J. Adamson [a], Joseph M. Boden [b], Jonathan A. Williman [c], Roger T. Mulder [a]

[a] Department of Psychological Medicine, University of Otago, Christchurch, New Zealand
[b] Christchurch Health and Development Study, University of Otago, Christchurch, New Zealand
[c] Biostatistics and Computational Biology, Department of Public Health and General Practise, University of Otago, Christchurch, New Zealand

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ABSTRACT

Background: In patients with an alcohol use disorder, depression is commonly categorised as independent (ID) or substance-induced (SID). It is not established whether these conditions respond differently to treatment.

Methods: MEDLINE, Embase and Cochrane databases from 1980 to 2014 were searched for studies on alcohol use disorders with coexisting depressive symptoms. Meta-analyses were conducted using random effects models, to derive pooled effect estimates of the change in depression during treatment and the effect of antidepressant therapy.

Results: Twenty-two studies met inclusion criteria for the review, of which 11/22 were included in the meta-analysis. All studies reported a large improvement in depression symptom score, most of which occurred within the first 3–6 weeks of treatment. The amount of improvement during follow up was similar in studies on ID in comparison to those in undifferentiated depression. Evidence on the outcome for SID was limited.

The effect size of antidepressant therapy compared to placebo was 0.25 (0.06, 0.44) for ID and 0.08 (−0.31, 0.47) for SID or undifferentiated depression.

Limitations: Few studies examined the natural history and treatment response of SID. There was heterogeneity between studies, which was partly explained by baseline depression severity.

Conclusions: Treatment for depression co-occurring with an alcohol use disorder is associated with a large early improvement in depression, even if depression is believed to be independent of drinking. The effect of antidepressant therapy on depression in patients with alcohol use disorders is modest, with stronger evidence in ID.

Contents

* Corresponding author. Tel.: +64 3 3720 400; fax: +64 3 3720 407.
E-mail address: james.foulds@otago.ac.nz (J.A. Foulds).

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1. Introduction

Patients entering treatment for an alcohol use disorder often have high levels of depressive symptoms (Davidson, 1995; Schuckit, 1995). These symptoms typically improve rapidly with treatment (Baker et al., 2013; Brown, 1988; Davidson, 1995; Kiefer and Barocka, 1999; Schuckit, 1985, 1995) but in spite of this, comorbid depression predicts worse outcomes in alcohol treatment (Lejoyeux and Lehert, 2011; Pettinati, 2013) and heavy drinkers have an increased risk of future depression even if they cut down (Hasin and Grant, 2002). Knowing which groups of patients are more or less likely to improve during treatment would allow scarce treatment resources to be allocated more effectively, but to date the ability to predict patient outcomes accurately has been limited.

1.1. Subtyping depression in patients with alcohol use disorders

An early approach to guide treatment and predict depression outcome in patients with an alcohol disorder was to classify depression as primary or secondary according to whether it developed before or after the onset of heavy drinking (Schuckit, 1985). In the 1990's, the typology evolved to also incorporate information about a past history of depression during abstinence (Schuckit et al., 1997). The term independent was used for depression that began before the onset of alcohol dependence or during sustained abstinence while depressive syndromes occurring only during a period of active alcohol dependence were labelled substance-induced (Schuckit et al., 1997). Structured clinical assessment tools such as the Structured Clinical Interview for DSM (SCID) (Spitzer et al., 1992) and the Psychiatric Research Interview for Substance and Mental Disorders (PRISM) (Hasin et al., 1996) have helped to operationalise these definitions and introduce greater diagnostic reliability.

1.2. Implications of subtypes

It has been argued that the distinction between independent depression (ID) and substance-induced depression (SID) has important implications for treatment and prognosis: SID is considered a self-limiting condition that remits with abstinence while ID requires specific depression treatment (Pettinati, 2013; Schuckit, 1985; Schuckit et al., 1997). In particular the view has been put forward that ID, but not SID, responds to antidepressant medication (Schuckit, 2006) but the evidence for this has not been systematically evaluated.

1.3. Aims of the review and meta-analysis

This review aimed to answer the following questions:

i. In depressed patients with an alcohol use disorder, how much do depressive symptoms improve during treatment for depression?
ii. Do patients with ID and SID have different patterns of treatment response?
iii. Does antidepressant efficacy differ between patients with ID and SID?

2. Methods

2.1. Selection criteria

Studies were chosen according to the following criteria:

1. Studies reported longitudinal data on alcohol use and depression in adults over at least 8 weeks.
2. Change in mean score on a validated depression scale was reported.
3. Subjects had an active alcohol use disorder (alcohol dependence or alcohol abuse) diagnosed according to DSM or ICD criteria.
4. Mean baseline score $\geq$ 10 on the 17-item Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960), or equivalent severity on another depression rating scale. Given the uncertain nosology of depression in alcohol use disorders, subjects were not required to have a diagnosis of a depressive disorder. The low severity threshold was chosen to avoid excluding studies in which baseline measures were taken after a short period of abstinence. A published score comparison table available at