Curr Psychiatry Rep (2012) 14:610–618
DOI 10.1007/s11920-012-0314-7

MOOD DISORDERS (SM STRAKOWSKI, SECTION EDITOR)

Treatment of the Depressed Alcoholic Patient

Jeffrey J. DeVido · Roger D. Weiss

Published online: 21 August 2012

Abstract Alcohol use disorders (AUDs) and depressive illnesses are highly prevalent, frequently co-occur, and are associated with worse outcomes when paired. The assessment and treatment of patients with co-occurring alcohol use disorders and depressive illnesses is wrought with many significant challenges. When it comes to advocating treatment guidelines for this dually-diagnosed population, the data are limited, but, nonetheless, do suggest that an integrated approach to patients presenting with co-occurring AUD and depressive symptoms can be efficacious. In this approach, ongoing evaluation and treatment are provided under one roof according to the evolving needs of each patient. Utilizing antidepressant medications in conjunction with psychosocial therapies may augment overall treatment efficacy; data also suggest that combining and tailoring psychosocial therapies, such as motivational enhancement therapies, cognitive therapies, and twelve-step facilitation may further improve treatment outcomes for patients with co-occurring depressive and alcohol use disorders.

Keywords Depression · Mood disorders · Substance use disorder · SUD · Alcohol · Alcoholism · Alcohol use disorder · AUD · Dual diagnosis · Assessment · Treatment · Outcomes · Pharmacotherapies · Antidepressants · Psychosocial therapies · Motivational enhancement therapy · Cognitive behavioral therapy · Relapse prevention therapy · Contingency management · Twelve-step facilitation

J. J. DeVido (✉) · R. D. Weiss
Harvard Medical School, McLean Hospital,
Mailstop #109, 115 Mill Street,
Belmont, MA 02478, USA
e-mail: jdevido@partners.org

R. D. Weiss
e-mail: rdweiss@partners.org

Introduction

Substance use disorders (SUDs) and other psychiatric disorders co-occur frequently [1, 2•]; together, they are associated with worse clinical and functional outcomes than when they occur individually [3]. Furthermore, many people with these co-occurring disorders do not seek treatment [2•]; if they do, they present unique problems in assessment and management.

Of the substances used or abused, alcohol accounts for the greatest proportion [2•]. Among those who have an alcohol use disorder (AUD), mood disorders co-occur with high frequency and depressive disorders are particularly prevalent [2•, 4]. As with other SUDs, the assessment and management of people with co-occurring AUDs and depressive disorders are significantly challenging. Therefore, this article aims to review the literature on co-occurring depressive disorders and AUD, and to suggest a framework by which to conceptualize the clinical assessment and management of these disorders when they occur together.

Epidemiological Considerations

The 2010 National Survey on Drug Use and Health: Mental Health Findings estimated that 3.4 million (16.9 %) of the 20.3 million adults who met criteria for past-year SUD also reported experiencing a major depressive episode (MDE) during that same period [2•]. Notably, in the same survey, those reporting MDE in the past year were also more likely to report problems with substance abuse or dependence than were their counterparts without MDE (22 % vs 7.9 % respectively). The bulk of those with MDE and co-occurring substance abuse or dependence reported that alcohol was the most commonly used substance (17.1 % out of the total 22 %). Of all those adults surveyed with any mental illness

and co-occurring SUD (9.2 million), 55.6 % received no treatment at all for either disorder, and only 7.7 % received dual diagnosis treatment. Of note, these data are consistent with prior epidemiological studies of the co-occurrence of these disorders [5, 6].

Data suggest that the occurrence of either MDE or AUD doubles the risk of developing the other disorder [7, 8]. Additionally, co-occurrence of MDE and AUD bodes poorly for treatment outcomes; specifically, the presence of major depression has been associated with worse alcohol treatment outcomes, such as lower reported self efficacy in AUD treatment [9] and quicker time to relapse [10, 11].

Patients with MDE and co-occurring SUD also have a heightened risk of suicide. According to a study by the Substance Abuse and Mental Health Services Administration, in 30 % of the deaths by suicide in the USA, blood alcohol levels were determined to be at, or above, the legal limit at the time of suicide, and 50 % of those who died by suicide were suffering from major depression at the time of death [12]. Compared with the general population, having an AUD puts one at a 10-fold higher risk for suicide [13], and the relationship of depression and suicidal behavior is well documented [14–17]. Therefore, patients with co-occurring AUD and depressive disorders are at a uniquely high risk for suicide, and thus warrant careful evaluation and management.

While clinical experience and epidemiologic data highlight the frequent co-occurrence of AUD and depressive disorders, there is little consensus on the etiology of this relationship. Several theoretical frameworks for understanding this relationship have been posited; these include, among others, mood disorders precipitating the AUD and vice versa (both conditions sharing a common risk factor), and/or alterations in an individual's judgment or ability to appreciate consequences of substance use because of psychopathology [18–20]. While there is no unifying consensus as to why AUD and depressive disorders co-occur so frequently, the heterogeneity of the theories themselves highlights the complex relationship between psychopathology and SUDs. The integrative approach to treatment of these co-occurring disorders that we will discuss in this article is rooted in an appreciation of these complex relationships.

Assessment Challenges

The complexity of the relationship between AUD and depressive disorders makes accurate diagnostic assessment challenging. For example, clinicians often wonder whether a patient's depressive symptoms are occurring as a result of a primary depressive disorder or are due to the effects of chronic alcohol use. Similarly, it is difficult to predict whether depressive symptoms will look the same or different if the pattern of alcohol use changes and vice versa. Finally, the patient's self-report of the relationship between drinking and depressive symptoms may not be reliable.

Some of the diagnostic confusion can be made clearer through (i) a careful diagnostic interview that focuses on the chronology of symptoms relating to *both* the AUD and psychiatric disorder, and (ii) obtaining collateral information from family members or significant others about symptoms and their temporal course. Moreover, an appropriate medical evaluation may also be prudent to ensure that mood symptoms are not the result of reversible medical issues, such as hypothyroidism. It is important to inquire about mood symptoms during periods of abstinence and to ask about a family history of mood disorders and AUDs. A treatment history can also be enlightening. For example, if a patient has had multiple relapses despite numerous encounters with AUD treatment programs but no prior treatment for depression, the clinician may be more inclined to treat the depression aggressively. Despite efforts to pursue the patient's clinical history, the diagnostic picture may remain frustratingly obscure and the clinician may have to be willing to treat despite this lack of clarity and follow the patient over time. Moreover, the clinician may need to revisit and adjust (if necessary) the patient's diagnoses as more clinical information comes to light.

Treatment Challenges

When considering the treatment approach to the depressed patient with co-occurring AUD, several different conceptual approaches have been proposed: sequential, parallel, and integrated. Historically, the sequential model has held significant sway: depressive symptoms are not addressed until a period of abstinence from alcohol has been achieved. Therefore, in the sequential model, treatment is administered for only one disorder at a time, and only after the more acute disorder is addressed will the other disorder be treated specifically. In the parallel model, however, both disorders are addressed simultaneously, but by different clinicians or treatment teams: one clinician or team aims to treat the mood disorder, while the other treats the AUD. Finally, in the integrated model, a single clinician or treatment team manages both the mood disorder and AUD simultaneously.

Each approach has its advantages and disadvantages. For example, the sequential approach can be particularly useful when a patient is hospitalized in the context of an acute exacerbation of one disorder, for example when the patient is acutely suicidal or experiencing medically complicated withdrawal. However, in the absence of a crisis warranting immediate stabilization of one disorder preferentially over another, trying to sequentially address co-occurring SUDs and other psychiatric disorders may fail to recognize a

potentially reciprocal connection between each disorder and, ultimately, handicap the treatment of both. The parallel approach avoids this potential pitfall of the sequential model and seeks to treat co-occurring disorders simultaneously. In settings where expertise in both depressive disorders and AUDs may not be accessible from a single clinician or treatment program, this can be a viable alternative to sequential treatment. However, it can be challenging to coordinate care in this model, as without close collaboration, patients may receive different recommendations or feedback on the relationship between their psychological symptoms and their AUD from their different treaters [21]. Therefore, the patient may become frustrated or confused, or the treatment teams could find themselves split or at cross-purposes. This phenomenon can be particularly problematic if a patient's treatment plan requires clear boundaries and firm, clear, communication of the terms of treatment. The integrated model aims to eliminate this potential for conflicting messages by consolidating treatment. Having one clinician or treatment team under one roof work with a patient simultaneously on the depressive disorder and AUD can improve communication with more consistent articulation of diagnostic impressions and treatment recommendations. Moreover, this approach could provide greater convenience for the patient (thereby improving the chances of retention in treatment) and more treatment flexibility in the face of evolving clinical impressions and management recommendations. One challenge to this model is having the resources to provide expert simultaneous AUD and depressive disorder evaluation and treatment in the form of a single clinician or treatment team. Moreover, the increased management demand placed on a single team or clinician could potentially decrease the total number of patients that that clinician or team could manage at any one time.

Although, clinicians have long recommended this integrated model of treatment for dually-diagnosed patients, the research base looking at defining specific optimal approaches and subsequent outcomes in this model remains relatively limited. Nonetheless, while the extant data on the integrated model of treatment for co-occurring AUDs and depression specifically remains scant, some positive results for combination integrated treatment approaches have emerged [22•, 23•]. Moreover, positive data have also emerged when using this model of treatment for patients with SUD and the severely persistently mentally ill [24], schizophrenia [24, 25], obsessive compulsive disorder [26], bipolar disorder [27•], and post-traumatic stress disorder (PTSD) [28]. Specifically, study results have shown improved clinical outcomes relative to treatment outside of an integrated model.

What are the components of the integrated model of treatment for the depressed patient with alcohol use disorder? A combination of psychosocial therapies along with pharmacotherapy has been shown to improve treatment outcomes and to be cost-effective [29]; the subsequent subsections will address these treatment approaches.

Pharmacotherapies

Food and Drugs Administration (FDA)-approved pharmacotherapies for the treatment of AUDs include disulfiram, naltrexone (oral or injectable), and acamprosate [30]; a myriad of FDA-approved antidepressant medications are available to help treat depressive illness, with the selective serotonin reuptake inhibitors (SSRIs) being considered a first-line pharmacologic treatment [31, 32]. Similar to the assessment challenges described above, though, the evidence base is limited when it comes to the use of pharmacotherapies in patients with co-occurring depression and AUD.

Pharmacotherapies in the Treatment of AUD and Co-occurring Depression

A recent meta-analysis of the literature by Iovieno et al. [33•] revealed some interesting themes in antidepressant treatment use in this unique population. The authors identified 11 double-blinded, randomized, placebo-controlled trials of antidepressants in patients with either major depressive disorder (MDD) or dysthymia and co-occurring AUD. In these trials, antidepressants outperformed placebo in the treatment of depression in patients with AUD, with a number needed to treat of six. The antidepressants nefazodone, desipramine, and imipramine were found to have the most robust effects on decreasing depressive symptoms.

While this meta-analysis suggested that antidepressants could be considered first-line treatment for treating depression in patients with co-occurring AUD, the data did not indicate that antidepressants had a significant impact on the pattern of alcohol use in these patients. Other studies, however, have found a positive impact on drinking patterns in patients who have been given SSRIs in doses higher than those prescribed for depressive illness. Moreover, certain subtypes of alcoholic patients appear to respond differently to SSRIs [34], which may be particularly effective in so-called Type A alcoholics, who have less severe depression and late-onset alcohol dependence [35].

In a naturalistic study that supported the importance of considering antidepressant medications in patients with depression and AUD, Greenfield et al. [36] demonstrated that among patients with MDD who were not given a prescription for an antidepressant medication at the time of discharge from inpatient AUD treatment, 100 % resumed alcohol use within the ensuing 4 months. This study brings into relief the possibility that when not treated with

medications, patients with AUD with co-occurring depression are at high risk for relapse. This also highlights the potential utility of employing antidepressant medications early in treatment in this dually-diagnosed population.

Overall, however, there is relatively little (and sometimes conflicting) data on the impact of antidepressant use in depressed alcoholic patients to guide specific antidepressant recommendations; there is very little evidence regarding differential efficacy to guide a clinician in choosing a specific antidepressant for this population by virtue of the patient's having a co-occurring AUD. That said, certain antidepressant medication and alcohol combinations may increase the risk for adverse events. For example, bupropion may lower a person's seizure threshold; when combined in an individual with a predisposition to have a seizure when withdrawing from alcohol, this may present unacceptable risk [37]. Similarly, the antidepressant duloxetine has been shown to have liver toxicity in those with pre-morbid liver dysfunction, including those with liver dysfunction due to chronic alcohol use [38].

Interestingly, emerging data also support the use of the anticonvulsant topiramate in the treatment of AUDs [39, 40], although topiramate is not currently FDA-approved for this purpose. Given its use in the treatment of bipolar disorder (especially the depressive phase), topiramate may present an intriguing pharmacologic agent for the treatment of co-occurring AUDs and mood disorders, such as depression [41, 42]. To date, though, little research has been conducted examining the treatment of this group of dually-diagnosed patients with topiramate [43]. Therefore, without further data, use of topiramate in patients with co-occurring depression and AUD remains off-label and speculative.

AUD Pharmacotherapies in the Treatment of AUD and Co-occurring Depression

In the spirit of integrated treatment, recent studies have sought to investigate the efficacy of co-administration of an established pharmacologic treatment for AUD with an antidepressant medication. For example, several studies have examined the impact of the opioid antagonist medication naltrexone and the SSRI medication sertraline [44–47]. These studies suggest that the combination treatment can lead to higher rates of abstinence from alcohol, longer time to drinking relapse, and improvement in mood relative to those who receive either placebo or antidepressant or AUD pharmacologic interventions alone.

The data pertaining to the combination of antidepressants and either disulfiram or acamprosate with the specific intent to treat co-occurring AUD and depressive symptoms is even more limited, with no data available to support or refute these particular treatment approaches.

Prescribing Considerations

The clinician should pay attention to several key issues when prescribing to this population. First, alcoholic patients warrant close attention to drug–drug interactions—for example, they may require higher than usual doses of tricyclic antidepressant medications to achieve therapeutic levels. Side effects, adherence, history of medication trials, presence of suicidality, and level of organization (e.g., the capacity to follow the dietary rules associated with disulfiram) should all also be considered when choosing a medication.

When considering pharmacotherapy, one should initially determine whether hospitalization for detoxification or psychiatric instability (e.g., suicidality) is warranted. Following this, for diagnostic clarification, it could be helpful, ideally, to observe the patient for at least a two-week period of abstinence from alcohol, after which a comprehensive evaluation for depressive disorder may be more accurate. However, as outlined previously, it may not always be prudent, or possible, to delay psychopharmacologic interventions. Therefore, in most cases, the clinician can consider from the outset antidepressant and AUD psychopharmacologic interventions along with psychosocial interventions (see below) [48].

In summary, medications may be helpful in the treatment of patients with co-occurring AUD and depressive disorder. Further studies are warranted, though, to examine the safety and efficacy of co-administration of antidepressant medications with medications approved for the treatment of AUD.

Psychosocial Therapies

As conceptualized by Daley et al. [49] the relationship between mood disorders and substance use in patients with co-occurring AUD is complex and dynamic; there are different phases of each patient's treatment, with the clinician and patient working collaboratively to identify problems and strategize about ways to manage these effectively. Recovery from both the SUD and mood disorder is seen as an active process that aims to help educate patients about their illness and its impact on them and those around them, stabilize them from the acute effects of either disorder, and fosters the development of skills and strategies to better manage the symptoms of both the SUD and the mood disorder [49]. Engaging the patient with this dynamic framework in mind enables the clinician to flexibly meet the patient's evolving challenges to recovery.

Multiple psychosocial therapies have been employed in the treatment of AUDs, prominent among which are motivational enhancement therapy (MET), cognitive behavioral therapy (CBT), relapse prevention therapy (RPT), contingency management (CM), twelve-step groups such as Alcoholics Anonymous (AA), and twelve-step facilitation (TSF).

MET

Early in treatment, patients may have different levels of motivation to address their co-occurring AUD and depression. MET is an evidenced-based method of engaging patients to help evoke their own motivation to resolve this ambivalence in favor of ultimately changing problematic behaviors. It can be brief and is based on the notion that a person's level of motivation for change is malleable. MET advocates a non-coercive, collaborative way of engaging a patient.

MET's efficacy as a brief intervention for enhancing motivation to change has been well studied in both SUDs and mood disorders [50–52]. Moreover, recent literature has supported its use in the dually-diagnosed population [53, 54•]. Specifically, MET has been shown to reduce the number of hospitalizations, decrease substance use, and improve the likelihood of making the transition to outpatient treatment in several studies of heterogeneous dually-diagnosed patients [55–57], as well as specifically in those individuals with co-occurring depressive disorders and AUDs (especially when combined with cognitive-based psychosocial interventions) [58].

CBT [59]

Once a patient has been engaged in treatment through motivational enhancement, or even simultaneously with it, exploration of the dysfunctional thoughts, beliefs, and assumptions about oneself, the future, and the world (together referred to as schemas) that lead to, and perpetuate, depressed mood and/or substance use can take place [60]. One goal of CBT in SUDs is to identify the specific rewards that substances provide and to offer healthier alternative options to achieving these rewards [61].

A solid evidence base exists for the use of CBT in the treatment of the dually-diagnosed population with AUD and depression. Specifically, CBT can improve the percentage of days abstinent and reduce the number of drinks per drinking day, while also decreasing depression symptom severity [62, 63].

RPT

As its name would suggest, RPT aims to understand the nature of substance relapse and to help establish strategies for managing potential relapse situations. At its core, RPT explores and catalogs an individual's particular high-risk triggers for relapse and then applies cognitive-behavioral approaches to help the individual avoid those triggers and manage them more effectively through enhancement of self-efficacy [64].

Data regarding RPT's effectiveness in treating AUDs is robust [65]. However, studies of RPT in the treatment of patients with co-occurring AUDs and depression are lacking. Nonetheless, research on RPT in other heterogeneous dually-diagnosed populations is encouraging. For example, RPT principles have been successfully applied to an integrated group treatment approach to patients with co-occurring bipolar disorder and SUD [27•, 66, 67].

CM

CM is based on the general principle that the use of substances is associated with certain rewards and that alternative rewards are sought to supplant the rewards derived from substance use. For example, in one version, voucher-based reinforcement therapy, individuals receive vouchers for abstinence-promoting goods or services in exchange for negative drug screens. While a 2006 meta-analysis of the efficacy of this approach in individuals with SUDs demonstrated overall positive effects in terms of substance use [68], few data exist regarding the utility of CM in the AUD/depressed dually-diagnosed population. Similar to the above psychosocial therapies, though, a growing evidence base speaks positively to the applicability and efficacy of CM in a more heterogeneous dual-diagnosis population, including the severely mentally ill [69, 70].

Twelve-Step Groups

Twelve-step support groups, such as AA, have been a mainstay of SUD treatment since their inception in the 1930s. Randomized, controlled, study data on AA are scant and unlikely to be gathered because of the nature of AA, but suggest positive effects on drinking patterns [71]. Naturalistic studies have shown similarly favorable data on drinking patterns and measures of psychological well-being [72, 73]. A small literature that suggests that engagement in AA may have beneficial mood effects for depressed members; however, it is unclear if this effect is due to reductions in alcohol use [74•]. Moreover, in a heterogeneous dually-diagnosed population, data suggest a positive correlation between twelve-step group participation and rates of abstinence [75], and levels of general distress [76].

Engaging a patient in a self-help program may create unexpected challenges for alcoholic patients with co-occurring psychiatric illness. For example, despite official AA literature speaking to the contrary, in some groups there may still be a bias against the use of medications. Clinicians should be aware of this potential complication of engagement in self-help groups and discuss this with their patients. Moreover, clinicians can help guide patients to self-help groups that best fit their particular demographic profile (young persons, women, self-management and recovery training (SMART), gay/lesbian/transgender), which may also enhance their engagement in these groups.

TSF

Recognizing the potentially positive effects of engagement in self-help groups, TSF aims to enhance engagement in self-help groups. Unlike AA, which is a mutual-help group, TSF is a professionally-led treatment designed to foster engagement in AA and other twelve-step groups. In TSF, the clinician works with the patient to assess substance use, educate the patient about the self-help principles of accepting the need for abstinence and encourage active participation in self-group activities. Studies have validated the efficacy of TSF in engaging patients in self-help groups and increasing the percentage of days abstinent from alcohol relative to patients receiving MET or CBT [77, 78]. Moreover, other studies have examined and validated the efficacy of TSF in patients with co-occurring SUD and depressive disorders [79–83].

Combining Treatment Approaches: What Does the Evidence Say?

In the previous sections we outlined several pharmacotherapies and psychosocial therapies available for patients with co-occurring AUD and depressive disorder. Some studies have examined these approaches either head-to-head or in combination. In a study of adolescents with AUD who were also receiving fluoxetine for depression, for example, those who received a combination of CBT/motivational enhancement fared significantly better over the two-year study in terms of objective measures of depression and AUD symptoms than those who did not receive this combination [54•]. Other studies have looked at the combination of psychosocial therapies in the absence of a specific pharmacologic intervention and have likewise demonstrated better outcomes than when employed alone. For instance, in one study, depressed participants with co-occurring AUD received an integrated brief intervention for both disorders, followed by either no more intervention or 10-session programs for AUD, depression, or both. Participants who received the integrated treatment that focused on both alcohol use and depression reported an overall decrease in mean drinks per week, drinking days per week, and maximum drinks on one occasion [84].

While the data presented here suggest that an integrated approach to the depressed alcoholic patient may be efficacious, the data are not prescriptive; there is not a clear treatment algorithm for this population. Individual differences in response to treatment based on demographic or diagnostic differences are not well-defined in these studies, for example. However, given the body of positive evidence suggesting the efficacy of integrated treatment in a heterogeneous dually-diagnosed population (severely mentally ill) [25], it is, nonetheless, encouraging that data will someday likewise support an integrated treatment approach specifically for the patient with co-occurring AUD and depression.

Conclusions

AUDs and depressive illnesses are highly prevalent, frequently co-occur, and are associated with worse outcomes when paired. Assessment of AUDs and depressive symptoms can be challenging when they co-occur and clinical impressions may shift as more information comes to light. When it comes to advocating treatment guidelines for this dually-diagnosed population, the data are limited. Nonetheless, the risks of non-treatment or of taking a watch-and-wait approach are high. The data suggest that an integrated approach to patients presenting with co-occurring AUD and depressive symptoms can be efficacious. In this approach, ongoing evaluation and treatment are provided under one roof according to the evolving needs of each patient. Utilizing antidepressant medications *in conjunction* with psychosocial therapies may augment overall treatment efficacy; data also suggest that combining and tailoring psychosocial therapies, such as motivational enhancement therapies, to establish rapport and build motivation to remain in treatment, cognitive therapies to address maladaptive patterns of thinking and behaving, along with other behaviorally-activating interventions, such as TSF, may further improve treatment outcomes for patients with co-occurring depressive and alcohol use disorders.

Acknowledgment Work on this article was supported, in part, by Grant K24 DA022288 from the National Institute on Drug Abuse (R. D. Weiss).

Disclosure No potential conflicts of interest relevant to this article were reported.

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