Substance Use Disorders and Major Depressive Disorder

Budip S. Khosa, MD, and Shaohua Lu, MD
Presented at the University of British Columbia’s 6th Annual Pacific Psychopharmacology Conference in Vancouver, British Columbia, on September 21, 2012.

Alex’s Case
Alex is a 50-year-old man who drank socially until five years ago. He now drinks up to 12 drinks a night; he has not had more than three days of sobriety over this time. He has developed persistent depressive symptoms (characterized predominantly by low mood and passive suicidal ideation) over the past year. He has not had any treatment for addiction. He is requesting an antidepressant so he can stop drinking. He has a family history of bipolar affective disorder. He is still working.

Epidemiology
Major depressive disorder (MDD) is the most common psychiatric disorder in those seeking treatment for a substance use disorder (SUD), and it affects up to 50% of such patients. Among those with a mental health disorder, such as depression, the odds ratio of having an addictive disorder is 2.7.¹ There is significant comorbidity of alcohol use disorders and major depression throughout the general population, with odds ratios greater than 1.0 when considering sex, ethnicity, and age.² Patients with affective disorders have a higher lifetime risk of developing an alcohol use disorder (AUD). Comorbidity of these disorders is important because of worsening symptoms and outcomes. Compared to nonsubstance-dependant subjects, the depressive episodes of those with AUDs have more severe symptoms, longer duration, and are linked to a higher rate of suicide.³ Comorbidity of these two conditions increases the lifetime risk of suicide.⁴

Alcohol and other substances are effective in the short-term alleviation of the dysphoric affects of major depression. The common belief is that patients use alcohol as a form of “self-medication” for depressive symptoms, suggesting that, if underlying depression is treated pharmacologically, the substance use could stop. However, there is little evidence to indicate long-term pharmacological success if patients continue to abuse alcohol.⁵ Antidepressants have little or no effect on alcohol consumption if alcohol use disorders are not simultaneously treated. There is ample evidence to suggest that chronic substance use can induce a range of psychiatric illnesses. During active use, substance-induced psychiatric disorders can be indistinguishable from primary psychiatric illness. For clinicians in addictions medicine, it is more appropriate to use the term “self-obligation” to describe the continuing use of substances in the face of psychiatric symptoms.
**Treatment**

When considering pharmacological therapy, physicians should be aware of potential pitfalls. It is difficult to predict which patients will continue to have enduring depressive disorders after abstinence. Symptoms of depression change dramatically during the course of the intoxication, withdrawal, and dependence cycle. A more accurate assessment of an underlying psychiatric disorder is possible at 6 to 12 weeks post-detoxification. Physicians should be wary of over-diagnosing “depression” in patients recovering from AUDs. Such patients may use distortions and externalization to deal with interpersonal losses. Significant deterioration in neurovegetative functions (including sleep, appetite, and energy) and suicidal ideation are helpful indicators of “true” major depression. Family history and past history of depression with neurovegetative symptoms while abstinent are clinical indicators as well.

It is important to be aware of the limits of pharmacotherapy. Finding the “right” medication or the “right combination” should not become the sole focus of therapy; rather, a hard look at social and interpersonal conflicts may be more fruitful. Psychopharmacological treatment should be accompanied by simultaneous addiction counselling, self-help groups, or psychotherapy. Most studies looking at pharmacologic treatment of comorbid AUD have incorporated some aspect of psychosocial treatment. Most patients’ target symptoms (e.g., depression, anxiety, insomnia, and anhedonia) will improve with abstinence without medical interventions. There is little indication for antidepressants or anxiolytics prior to detoxification.

Early trials of such agents may be indicated for those with severe depression and suicidal ideation. Antidepressants are modestly better than placebo in reducing depressive symptoms but not

---

**Table 1**

**Questions & Answers**

1. **What are the factors that can help delineate an independent mood disorder in a patient who is actively abusing substances such as alcohol?**

   A history of depressive episodes (predating the substance abuse), a family history of depression, neurovegetative symptoms, and prominent mood symptoms during periods of abstinence can indicate the presence of an independent mood disorder.

2. **Which mental health disorder has the highest rate of co-occurrence with substance use disorders?**

   Depressive disorders are the most common psychiatric disorders in patients with substance use disorders, occurring in up to 50% of such patients.

3. **When should I initiate antidepressant treatment in the comorbid patient?**

   Ideally, antidepressants should not be initiated until after 6 to 12 weeks of complete abstinence. However, in patients with prominent neurovegetative symptoms or suicidal ideation, it may be prudent to initiate treatment for the mood symptoms concurrently with addiction treatment.

---

**Back to Alex**

With encouragement from his GP, Alex was able to engage in a comprehensive approach to address his alcohol misuse. This included referral to a professional counselling service and a mutual self-help group. He was able to abstain from further use. After six weeks of abstinence, he noted that his depressive symptoms were no longer present and elected to not initiate antidepressant therapy.
In terms of depressive symptoms, meta-analysis showed an effect size of 0.38 (95% CI = 0.18–0.58) for antidepressant treatment in depressed patients with comorbid substance dependence. When combined with addiction treatment, the improvements in mood can decrease SUD, and, conversely, abstinence can improve depressive symptoms. Addiction treatment in this case comprises manually guided psychosocial interventions, including cognitive behaviour therapy, motivational interviewing, and 12-step facilitation.

When considering antidepressants in this population, there are important clinical differences. There are some reports of an association with SSRIs and worse drinking outcomes in women and patients with an early onset or a heavy binge pattern of alcohol use. Tricyclic antidepressants (TCAs) can be dangerous due to their cardiovascular effects, particularly with overdose. However, TCAs and more noradrenergic agents (venlafaxine, duloxetine) may be more effective overall in the comorbid population. Monoamine oxidase inhibitors should also be used with great caution due to drug interactions. Except for early withdrawal treatment, benzodiazepine use should be limited, and it should only be used under close monitoring. There have not been large clinical trials, and clinical experience is variable in terms of which antidepressant is better in this population. A recent Canadian Network for Mood and Anxiety Treatments study recommended mirtazapine as a potential first line option.8

Psychoeducation is the key to the success of pharmacologic treatment. No medication can replicate the instantaneous and temporary relief of pain and suffering seen with drugs and alcohol. Antidepressant effects are intended to increase mental strength to cope, but they will not take away all suffering. Finding new meaning and joy in life is the long-term goal for patients recovering from addiction. Practitioners should take heart that even brief interventions with their patients can result in reductions in substance use and emergency visits.10

### Take-home Messages

- Substance use disorders are highly comorbid with major depressive disorder and present with worse symptoms and poorer outcomes
- Adequate treatment of alcohol use disorders should be initiated first in most cases of comorbidity
- With the presence of severe depressive symptoms, concomitant antidepressant therapy may be warranted

### References


Dr. Buldip S. Khosa is a PGY4 Resident in Psychiatry at the University of British Columbia in Vancouver, British Columbia.

Dr. Shaohua Lu is a Clinical Associate Professor in the Department of Psychiatry at the University of British Columbia in Vancouver, British Columbia.