

Epidemiology and Management of Alcohol Dependence in Individuals with Post-Traumatic Stress Disorder

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Abstract

Post-traumatic stress disorder (PTSD) is a chronic and disabling psychiatric disorder with an estimated lifetime prevalence of 7.8%. Co-morbid alcohol dependence is a common clinical occurrence with important clinical considerations. For example, in individuals with both PTSD and alcohol dependence, the symptoms of PTSD tend to be more severe, and there is evidence that these individuals are more prone to alcohol use relapse than non-co-morbid individuals. Co-morbidity of PTSD and alcohol dependence is also associated with a higher rate of psychosocial and medical problems and higher utilization of inpatient hospitalization than either disorder alone.

This article highlights the epidemiology of alcohol dependence in PTSD and reviews the evidence for effective treatments. Management of these individuals requires an understanding of the epidemiology and an awareness of treatment interventions, which include both psychosocial treatments (e.g. Seeking Safety, Concurrent Treatment of PTSD and Cocaine Dependence, Transcend, Trauma Recovery and Empowerment Model) and pharmacotherapy (e.g. selective serotonin reuptake inhibitors [SSRIs] and topiramate). Effective treatment of co-morbid PTSD and alcohol dependence may include a combination of these psychosocial and pharmacological interventions. The key element seems to be to ensure an adequate intervention for *each* disorder administered collaboratively.

Post-traumatic stress disorder (PTSD) is a chronic and disabling psychiatric disorder with an estimated lifetime prevalence of 7.8%.^[1] The

prevalence is much higher in populations considered at high risk, which include combat veterans, victims of rape, molestation and childhood abuse

or neglect^[1] and victims of natural disasters.^[2] The symptoms associated with PTSD fall into three clusters: re-experiencing symptoms, avoidance of trauma-related stimuli and hyperarousal symptoms.

Psychiatric co-morbidity is an important factor in the treatment of PTSD. It is estimated that 80% of individuals with PTSD also have another Axis I psychiatric disorder.^[2] In men, alcohol abuse or dependence is the most common co-morbid disorder and, in women, it is the third most common diagnosis, after depression and other anxiety disorders.^[1] The estimated prevalence of alcohol use disorders in individuals with PTSD is higher than the prevalence in the general population.^[1] In individuals with both PTSD and substance use disorders, the symptoms of PTSD tend to be more severe, particularly in the avoidance and hyperarousal clusters,^[3] and there is evidence that they are more prone to substance use relapse than non-co-morbid individuals.^[4] Co-morbidity of PTSD and substance use is associated with a higher rate of psychosocial and medical problems and higher utilization of inpatient hospitalization.^[4]

Management of alcohol dependence in individuals with PTSD is a timely and important clinical consideration. To be effective in managing patients, clinicians should understand the epidemiology, identify which individuals with PTSD are most likely to have co-morbid alcohol dependence and be aware of treatment interventions, which include both psychosocial treatments and pharmacotherapy.

1. Epidemiology

Reviews of studies have long established a high co-morbidity of PTSD and alcohol use disorders.^[5,6] Participants in the US National Co-morbidity Survey reported co-morbidity rates of lifetime PTSD for those with a lifetime alcohol dependence diagnosis as 10.3% (odds ratio 3.2) for men and 26.2% (odds ratio 3.6) for women. For participants who previously had PTSD, men were found to be at 2.67 times greater risk of developing alcohol dependence and women were at 3.37 times greater risk of developing alcohol dependence.^[7] High co-morbidity rates of PTSD

and alcohol dependence have been found across other cultures as well. A study of refugee camps in Croatia found increased rates of alcohol dependence in men with current PTSD.^[8] Also, of the individuals surveyed in the Australian National Survey, an alcohol use disorder (24.1%) was the most common substance use disorder for individuals diagnosed with PTSD.^[9]

Veterans, particularly those who have experienced combat, are one of the high-risk groups for the development of PTSD^[10] and increased alcohol use.^[11] The recent conflicts in Iraq and Afghanistan are the largest ground operations since the Vietnam War,^[10] and many of these returning veterans are presenting for treatment. There have been varying rates (4.7–24.5%) of positive PTSD screening questionnaires among returning veterans from these conflicts^[10,12–14] and alcohol misuse was found in 11.8% of returning veterans who completed the post-deployment screening questionnaires;^[12] significantly higher rates of PTSD and alcohol misuse were found post-deployment compared with pre-deployment.^[13]

1.1 Impact of Post-Traumatic Stress Disorder and Alcohol Dependence

Co-morbidity is associated with more severe symptoms of PTSD,^[4] higher rates of relapse and higher rates of psychosocial and medical problems than are found in non-co-morbid individuals.^[15] Heavy drinkers have been found to report more severe trauma symptoms than moderate drinkers or abstainers.^[16] Bremner and colleagues^[17] examined Vietnam veterans and found that the onset of alcohol abuse was associated with the onset of PTSD symptoms, and the increase in alcohol use and PTSD symptoms paralleled each other. PTSD symptoms have a positive correlation with alcohol abuse severity and poorer functional health.^[18] Additionally, Iraq and Afghanistan returnees who reported both PTSD and alcohol misuse have increased health-related problems compared with returnees with only a positive screen for PTSD.^[14]

Coffey and colleagues^[19] have found that the re-experiencing symptoms of PTSD, which often results in significant distress to the individual experiencing the symptoms, may increase alcohol

craving. Based on a laboratory study in individuals with PTSD and co-morbid alcohol dependence, individuals reported increased craving for alcohol following presentation of trauma stimuli compared with neutral stimuli.^[20] Not surprisingly, a greater severity of PTSD symptoms is associated with greater risk of relapse of alcohol abuse,^[20,21] particularly when the individual is in difficult interpersonal situations and negative physiological contexts.^[22] Another laboratory-based study conducted by Coffey and colleagues^[23] examined participants with PTSD and alcohol dependence who received trauma-focused imaginal exposure or imagery-based relaxation. Participants receiving the trauma-focused imaginal exposure were found to have decreased alcohol craving and distress resulting from trauma images compared with the participants who received the imagery-based relaxation. Individuals with PTSD and co-morbid substance use disorders, including alcohol dependence, attribute relapse to negative emotions rather than cue-based urges compared with individuals without co-morbidity.^[24] In addition, these individuals benefit less from substance use treatment. For example, co-morbid PTSD and alcohol dependence place individuals at greater risk of early withdrawal from treatment and poorer outcomes following treatment.^[25]

2. Treatment

There are established treatments for PTSD and alcohol dependence, but their efficacy in individuals with co-morbidity is not well established. These include psychosocial treatments and pharmacological treatments. Studies evaluating pharmacological interventions include studies testing the medications approved to treat one disorder in a co-morbid population. More recently, the development of medications specifically targeting individuals with co-morbidity is being undertaken.

2.1 Psychosocial Treatments

Several behavioural therapies have been developed to treat individuals with PTSD and co-morbid alcohol dependence (see table I). These include: (i) therapies developed specifically for

co-morbid individuals such as Seeking Safety, Concurrent Treatment of PTSD and Cocaine Dependence (CTPCD) [modified to treat alcohol dependence], Transcend, Trauma Recovery and Empowerment Model (TREM) and collaborative care; (ii) modified or enhanced behavioural therapies of existing interventions such as cognitive-behavioural therapy and cognitive-processing therapy; and (iii) treatments developed to treat non-co-morbid PTSD that have been evaluated in individuals with co-morbid alcohol dependence such as Acceptance and Commitment Therapy and prolonged exposure therapy.^[40-45] The latter treatments were used *in combination* with an intervention designed to target the substance use disorder.

Perhaps the most commonly used and well researched treatment designed specifically for individuals with PTSD and co-morbid substance abuse is Seeking Safety.^[46,47] Seeking Safety^[26] is a present-focused, cognitive-behavioural therapy for PTSD and substance use disorders. The goal of therapy is abstinence and a reduction in symptoms of PTSD.^[48] It is a group intervention initially developed for women, but has since been modified for men and can also be delivered in an individual format.^[49] Uncontrolled studies support its efficacy in improving substance use and PTSD outcomes, primarily in women.^[27,28] However, there are negative studies as well, when compared with an active control group.^[29,30] Najavits and colleagues^[31] conducted a pilot study examining the use of Seeking Safety and a revised version of prolonged exposure, which found improvements in multiple areas of functioning.

The other well researched treatment (CTPCD^[32]) was originally developed and found to be effective for the treatment of PTSD and co-morbid cocaine dependence,^[33] but has since been modified for individuals with any substance dependence including alcohol dependence.^[19] CTPCD involves a combination of empirically supported cognitive-behavioural treatments^[50,51] and prolonged exposure.^[40,52] Of note, these studies provide support for the use of exposure treatment for individuals diagnosed with co-morbid PTSD and substance dependence without increasing substance use relapse.^[20]

Table 1. Psychosocial treatments for post-traumatic stress disorder (PTSD) and co-morbid alcohol dependence

Psychosocial treatment	Treatment format	Key components	Study design	No. of participants, sample population	Treatment outcomes
Seeking Safety ^{[28]a}	Individual or group 25 topics covered in 60- to 90-minute sessions 1-2 sessions per week	Present focused Psychoeducation Cognitive-behavioural therapy Coping skills Interpersonal case management	Pilot ^[27]	27 women, community	Decreased substance use and trauma symptoms Improved suicide risk, social adjustment and depression symptoms Improved PTSD symptoms and decreased substance use severity after release Potential benefits for the use of Seeking Safety for incarcerated women
			Pilot ^[28]	17 women, incarcerated	Seeking Safety and comparison group (Women's Health Education) had similar improvements in PTSD symptoms and no differences in substance use outcomes
			RCT ^[29]	353 women, community	Seeking Safety and relapse prevention revealed similar improvements (i.e. improved PTSD, substance use and psychiatric symptoms)
			RCT ^[30]	107 women, community and clinical	
Seeking Safety plus exposure therapy	Individual 30, 1-hour sessions over 5 months On average, 21 Seeking Safety sessions and 9 exposure therapy sessions	Psychoeducation Cognitive-behavioural therapy Coping skills Relapse prevention <i>In vivo</i> and imaginal exposure	Pilot ^[31]	5 men, community	Improvement in drug use, family/social functioning, anxiety dissociation, sexuality, hostility, meaningfulness, feelings and thoughts related to safety
Concurrent Treatment of PTSD and Cocaine Dependence (CTPCD) ^[32]	Individual 16, 90-minute sessions 2 sessions per week	Cognitive-behavioural skills training Constructivist Psychodynamic Relapse prevention/12 steps Peer support <i>In vivo</i> and imaginal exposure techniques	Uncontrolled ^[33]	39 men and women, community	Decreased PTSD symptoms, cocaine use and severity

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Table 1. Contd

Psychosocial treatment	Treatment format	Key components	Study design	No. of participants, sample population	Treatment outcomes
Transcend	Group 10 hours of group therapy per week plus additional programme components (e.g. relaxation, community service) conducted in partial hospitalization treatment 12 weeks	Psychoeducation Cognitive restructuring Empowerment Skill building Peer support Trauma processing	Uncontrolled ^[34]	46 men, veterans in partial hospitalization treatment	Improved PTSD symptoms, substance use severity, hope, self-esteem and family relationships Decreased addictive behaviours
Trauma Recovery and Empowerment Model (TREM)	Group 24–29, 75-minute weekly sessions	Empowerment Cognitive restructuring Psychoeducation Coping skills	Quasi-experimental ^[35]	170 women, residential treatment setting	Improved trauma symptoms, mental health and coping with trauma
Adapted cognitive-behavioural therapy	Individual followed by group 9–12 hours per week, 3–4 times per week, for 4–6 weeks; followed by weekly group meetings for 2–3 months	Cognitive-behavioural therapy Education Breathing retraining Cognitive restructuring Relapse prevention Coping skills Aftercare planning	Pilot ^[36]	11 men and women, community	Feasible Improved PTSD symptoms Decreased substance use
Cognitive Processing Therapy-Cognitive, enhanced for heavy alcohol use	Individual 1-hour weekly sessions for 12 weeks	Cognitive-behavioural therapy Trauma focused Psychoeducation	Pilot ^[37]	5 men, veterans	Strong initial pilot data for treating PTSD and alcohol dependence concurrently Treatment completers no longer met PTSD criteria Clinically meaningful decrease in alcohol use Good retention Ease of delivery of treatment intervention No adverse events; well tolerated therapy

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Table 1. Contd

Psychosocial treatment	Treatment format	Key components	Study design	No. of participants, sample population	Treatment outcomes
Acceptance and Commitment Therapy	Individual 18 months 96 sessions	Cognitive-behavioural therapy Mindfulness Behavioural change Commitment to personal values Experiential Focus core on processes	Case report ⁽³⁸⁾	1 woman, community	Improved depression, psychological distress and substance use
Combined interventions of medication (naltrexone), BRENDA and prolonged exposure	Individual 24 weeks total Weekly BRENDA counselling sessions and weekly prolonged exposure sessions for 10 sessions over 12 weeks Bi-weekly sessions for 6 additional sessions over 12 weeks of BRENDA and prolonged exposure as well as medication maintenance (naltrexone)	BRENDA; promotes compliance with medications, motivational enhancement techniques, present focused Prolonged exposure: cognitive-behavioural therapy, <i>in vivo</i> and imaginal exposure Medication maintenance: naltrexone	Case report ⁽³⁹⁾	1 woman, community	Decreased PTSD and depression symptoms No alcohol use for last 12 weeks of treatment and decreased urges to drink
Cognitive Processing Therapy-Cognitive, enhanced for heavy alcohol use plus medication (disulfiram)	Individual 1-hour weekly sessions for 12 weeks	Cognitive-behavioural therapy Trauma focused Psychoeducation Use of disulfiram	Case report (unpublished observations)	1 man, veteran	Improved PTSD symptoms, alcohol use and severity, depressive symptoms, physical and mental health

a The four studies presented are a sample of the studies conducted on Seeking Safety.

BRENDA = biopsychosocial, needs assessment, empathetic understanding, direct advice, feedback and assessment of patient response; **RCT** = randomized controlled trial.

Several small studies have evaluated other comprehensive behavioural treatments for alcohol dependence and PTSD, including Transcend, TREM and collaborative care. Transcend^[34] is a group treatment that integrates a variety of treatment approaches (e.g. cognitive-behavioural, constructivist/dynamic theory, relapse prevention/12 steps, peer support). In an initial study of this treatment, participants were required to have completed a substance rehabilitation programme in the prior 6 months. Significant improvements in PTSD symptoms and substance use outcomes were found at the end of treatment and were maintained post-treatment. TREM^[53] was originally developed for female trauma survivors with severe mental disorders, many of whom had substance use disorders. TREM is a group treatment focusing on psychoeducation, cognitive restructuring, empowerment, skill building and peer support.^[54] A modified version of TREM was evaluated in a residential setting and compared with treatment as usual.^[55] Significantly, the authors found that addressing trauma using trauma-focused treatment was both safe and effective and led to improvements in multiple domains including trauma-related symptoms, mental health functioning and substance abuse treatment. Collaborative care^[55] is a *preventative* treatment for PTSD and alcohol use disorders. It is delivered prior to the development of PTSD. For example, collaborative care is given to individuals who have experienced a traumatic life event and presented to the hospital for surgery related to the trauma. It consists of case management, motivational interviewing to target potential alcohol use, pharmacotherapy and cognitive-behavioural therapy. One randomized controlled trial comparing collaborative care with usual care^[55] revealed positive outcomes in terms of PTSD symptoms and alcohol use that were maintained over 1 year.

One pilot study of cognitive-behavioural therapy^[36] suggests that adapting an intervention designed for PTSD for use in substance abuse treatment can lead to significant improvements in both PTSD and substance use severity.^[36] Another pilot study found improvements in PTSD symptoms and alcohol use with the use of cognitive processing therapy-cognitive (CPT-C), enhanced

to address heavy alcohol use, for the treatment of veterans diagnosed with PTSD and alcohol dependence.^[37]

Results from a single case report,^[38] of over 1 year of Acceptance and Commitment Therapy for the treatment of PTSD and co-morbid substance use, demonstrated support for the use of this therapy with concurrent substance abuse. In another case report,^[39] the use of prolonged exposure and naltrexone (supported by intervention-promoting medication compliance and motivational enhancement techniques) was effective for the treatment of an individual with PTSD, alcohol dependence and major depression. Additionally, another case was reported (unpublished observations) in which CPT-C, enhanced for heavy alcohol use, and disulfiram was found to be an effective treatment combination of psychosocial and pharmacological interventions for a veteran diagnosed with PTSD and alcohol dependence. Of note, in all three case reports, the behavioural therapy was administered *concurrently* with an intervention to treat the substance use disorder.

Overall, these studies suggest that interventions designed specifically for PTSD and co-morbid alcohol dependence are effective. In addition, behavioural interventions designed specifically to treat non-co-morbid PTSD can be modified and administered safely and effectively in individuals with co-morbid alcohol dependence. The key element seems to be including an intervention (either by modifying the existing therapy or by using a concurrent therapy) to specifically address alcohol dependence. The combination of psychotherapy and pharmacotherapy also seems feasible and potentially effective (unpublished observations).^[39]

2.2 Pharmacotherapy

The US FDA has approved the use of the selective serotonin reuptake inhibitors (SSRIs), sertraline and paroxetine, for use in PTSD. In addition, there are three medications approved by the FDA to treat alcohol dependence: disulfiram, naltrexone (as tablets and a long-acting injectable formulation) and acamprostate. Some data on the use of these medications, specifically disulfiram and naltrexone, in individuals

with PTSD and co-morbid alcohol dependence do exist.

Given the overlap between symptoms of depression and PTSD, it is not surprising that the SSRI antidepressants are the first line of therapy for PTSD. There is a small amount of literature on the use of these agents in co-morbid individuals. Following a small study that suggested the SSRIs may be effective in individuals with co-morbid PTSD and alcohol dependence for symptoms of PTSD and alcohol use outcomes,^[56] a larger study was initiated. This larger, placebo-controlled study (n=94) had more mixed results.^[57] In this study, there was no significant overall effect of the SSRI sertraline on symptoms of PTSD or alcohol use. However, a cluster analysis suggested that outcomes differed for subtypes of alcohol-dependent individuals: specifically, those with early-onset PTSD and late-onset alcohol dependence were the individuals who benefited from the medication.^[58]

Although not approved by the FDA, a body of research is suggestive that the noradrenergic medications might be effective in PTSD and are a promising new direction for the treatment of PTSD with co-morbid alcohol dependence. Adrenergic drugs such as the β -adrenoceptor antagonist, propranolol, the α_2 -adrenoceptor agonists, clonidine^[59-61] and guanfacine, and the tricyclic antidepressants (TCAs)^[62] have shown some promise, although the studies are limited by open-label design or small sample size. More recently, the α_1 -adrenergic receptor antagonist prazosin has shown promise in the treatment of nightmares in both veteran^[63] and non-veteran populations,^[64] although its effect on overall symptoms of PTSD is less clear. There is also a recent pilot study in individuals with alcohol dependence, without comorbidity, suggesting prazosin might have promise in the treatment of alcohol dependence.^[65] Prazosin has been identified as an ideal medication to study in a co-morbid population and clinical trials are under way (see www.clinicaltrials.gov).

Only a few studies have been conducted evaluating these medications to treat alcohol dependence in individuals who have co-morbid PTSD. A study conducted in veterans (n=254) comparing naltrexone with disulfiram alone and a combi-

nation of the two agents suggested that alcohol-dependent individuals with PTSD have better alcohol use outcomes when receiving active medication than when receiving placebo, although there was no advantage with the combination over monotherapy. Additionally, individuals with PTSD did particularly well on medication when compared with other dually diagnosed individuals with Axis I disorders including affective disorders, schizophrenia, schizoaffective disorder and anxiety disorders.^[66] Since there was no advantage of one medication over the other, clinically, therapist and patient preference could be taken into account when prescribing medication. Since naltrexone and disulfiram do not treat symptoms of PTSD, individuals were maintained on a stable psychiatric regimen for PTSD prior to randomization to naltrexone or disulfiram. This is another study that suggests the importance of therapeutically addressing both disorders in co-morbid individuals.^[66]

The use of antiepileptic drugs represents a novel approach to treatment that may target symptoms of both alcohol dependence and PTSD. Topiramate has been successfully used as an add-on agent to treat veterans with refractory symptoms of PTSD who were receiving a variety of medications (such as antipsychotics, TCAs, benzodiazepines, SSRIs, valproate and carbamazepine),^[67] and as a monotherapy to treat non-combat symptoms of PTSD.^[68] Two open-label studies suggested that topiramate may be effective in treating nightmares and insomnia in PTSD,^[69,70] although two randomized, albeit small, studies failed to confirm its efficacy.^[68,71]

Topiramate is one of the most promising new medications to treat alcohol dependence.^[72,73] In the first randomized controlled trial, topiramate (maximum 300 mg/day) reduced alcohol use and craving, as well as the negative consequences of drinking alcohol, and significantly improved physical health and quality of life compared with those receiving placebo.^[73] In a larger, multisite, randomized, placebo-controlled trial, the results were similar; topiramate significantly reduced alcohol consumption per drinking day and number of heavy drinking days, and increased the percentage of days abstinent.^[74] These studies were

conducted in participants with alcohol dependence *without* co-morbid psychiatric disorders. The interest in topiramate is growing, and several trials are under way evaluating its efficacy in individuals with alcohol dependence and co-morbid psychiatric disorders, such as bipolar disorder and borderline personality disorder. In the only study of topiramate in individuals with PTSD and co-morbid alcohol dependence, the drug was administered in an open-label fashion for 8 weeks as an add-on therapy in 29 subjects, of whom 35% were heavy alcohol drinkers. Topiramate reduced the general symptoms of PTSD and measures of alcohol consumption.^[75] These studies together suggest that topiramate may be an effective treatment for PTSD with co-morbid alcohol dependence.

3. Conclusions

Co-morbid alcohol dependence in individuals with PTSD is a common clinical occurrence that complicates the clinical picture and is associated with worse outcomes than in individuals with single diagnoses. Some evidence is emerging that can help guide clinicians in planning treatment for their co-morbid patients. Both psychosocial and psychopharmacotherapeutic options to treat PTSD, alcohol dependence and the co-morbidity have been developed. The evidence to date suggests several principles that should be followed. Given the high rate of co-morbidity of alcohol dependence in individuals with PTSD, all individuals presenting for treatment of PTSD should be screened for an alcohol use disorder. For those individuals who do have an alcohol use disorder, individuals (and clinicians) can opt for a psychotherapeutic or pharmacological intervention. There is some promising evidence to suggest that the two can complement each other.

While there are specialized psychosocial treatments available that were developed for the treatment of co-morbid PTSD and alcohol dependence, most notably, Seeking Safety, some evidence suggests that adapting existing treatments, such as cognitive-processing therapy or prolonged exposure, can be effective in co-morbid individuals. This *does* require adding an intervention for addressing the alcohol dependence, either by mod-

ifying the existing treatment or with adjunctive therapy. The intervention to treat co-morbid alcohol dependence can be either behavioural or pharmacological. If the patient and clinician opt for using pharmacotherapy, simultaneously addressing both disorders (e.g. using medications to treat PTSD such as the SSRIs in conjunction with a medication to treat alcohol dependence, such as naltrexone or disulfiram) seems optimal. The development of medications that may be effective for both disorders, such as prazosin and topiramate, is under way.

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