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Post-traumatic Stress Disorder: Guiding Management with Careful Assessment of Comorbid Mental and Physical Illness

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Post-traumatic Stress Disorder: Guiding Management with Careful Assessment of Comorbid Mental and Physical Illness

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Post-traumatic stress disorder (PTSD) is a common and serious psychiatric condition in the civilian and veteran population. The lifetime prevalence of PTSD in the Canadian general population is 9.2%,[1] which, surprisingly, is not significantly different from the 7.2% lifetime prevalence rate within the Canadian Regular Forces.[2] In Canadian veterans pensioned with a medical condition the 1-month prevalence was 10.3%.[3] Given the serious functional impairment and impaired quality of life[4,5] associated with PTSD, careful assessment and treatment of PTSD is warranted. Due to the complex clinical presentation of PTSD, which can include symptoms across the continuum from adjustment disorder and subthreshold PTSD to "full-blown" PTSD, this issue of *Mood and Anxiety Disorders Rounds* is confined to a general overview of the psychiatric management of PTSD with comorbid psychiatric conditions. Despite the challenges researchers face in conducting studies on the effectiveness of treatment of this disorder,[6] if evidence-based practices are utilized using established guidelines,[7,8] remission can be achieved in 30%–50% of PTSD cases.[9]

Comorbidity: The Rule Rather Than the Exception

Over 90% of individuals with PTSD will have another Axis I disorder. Major depression, another anxiety disorder (social phobia, generalized anxiety disorder, obsessive-compulsive disorder, and panic disorder), alcohol and substance use disorders,[10] and suicidality[11] are common comorbid conditions (Figure 1). Careful assessment for personality disorders, especially borderline[12] and antisocial,[13] is required because Axis II pathology may substantially affect management. Bipolar disorder is an important consideration, because bipolar II disorder is often difficult to recognize and can be an important barrier to response to treatment. Emerging evidence shows a strong relationship between PTSD and physical health problems.[14,15] The most common medical complaints associated with PTSD include chronic pain syndromes, asthma, gastrointestinal complaints and cardiovascular disease.[15,16] These conditions should be considered when planning the management of PTSD.

Psychiatric Assessment

The psychiatric assessment should detail the presenting symptoms and elicit a trauma history, including childhood and adolescent trauma, and exposure to military trauma (combat or peacekeeping operations).[9] It should be noted that minute detail related to a traumatic event should only be gathered if absolutely necessary; the recounting of an extremely traumatic event may be highly triggering and lead to significant symptom exacerbation. If possible, history gathering should be limited to information that clarifies the diagnosis.

Editor's Note:

Dear readers,

Few debts are greater than those due to our military, who serve to keep us all safe. This issue is devoted to PTSD, an affliction common in returning veterans; CANMAT wishes to express its gratitude to the Canadian Armed Forces and hopes that this newsletter will be helpful to clinicians as they treat veterans and their families.

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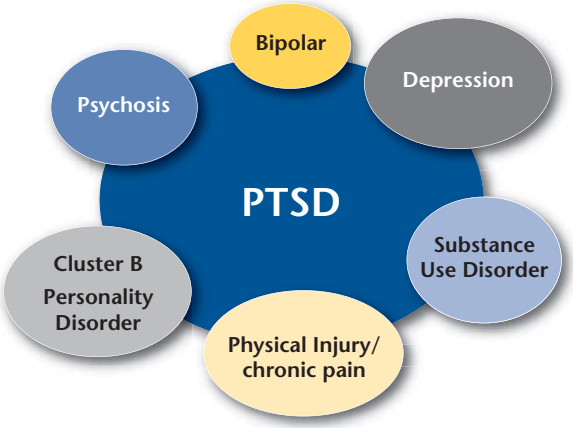
Figure 1: Important comorbid conditions to consider in the management of post-traumatic stress disorder (PTSD)



Patients with PTSD present with 4 symptom clusters: re-experiencing the traumatic events, avoidance of reminders, emotional numbing, and hyperarousal symptoms.[7,17] Avoidance of reminders and emotional numbing are grouped together as a symptom cluster in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV),[17] but are seen as distinct and will likely be denoted as such in DSM-V. Patients may relive their trauma via intrusive recollections during the day, including flashbacks, or at night as bad dreams or nightmares. Many complain of both physical and emotional symptoms of anxiety when exposed to reminders of their traumatic event. They may avoid reminders of the trauma and describe emotional numbness or an inability to experience a normal range of emotions. Common hyperarousal symptoms include insomnia, irritability, poor concentration, and hypervigilance. According to the DSM-IV-TR, acute PTSD has a duration of 1–3 months, and the disorder is considered to be chronic if its duration exceeds 3 months.[17]

The Primary Care PTSD Screen, a 4-item self-report yes/no instrument, is easy to use in clinical practice. The instrument has a sensitivity of 78% and specificity of 87% for PTSD in patients who answer 'yes' to ≥3 items (Table 1).[18] Patients who screen positive should be assessed for PTSD using the DSM-IV-TR diagnostic criteria, or by using a more specific screening instrument. The Clinician Administered PTSD Scale (CAPS)[19] may be too detailed for most clinicians and is more commonly used in research centres. A more practical approach is to use a self-rating scale such as the PTSD Checklist, which has a military and a civilian version,[20] and then to confirm the self-report rating and the nature of the traumatic experience(s) with a clinical interview. Some patients may present with some symptoms of PTSD without meeting the full diagnostic criteria.[21,22] Even if the full criteria are not met, studies indicate that these individuals may experience significant functional impairment,[23] and may also benefit from treatment.

Determining the presence of psychiatric comorbidity, as part of a thorough PTSD assessment, is critical.[23] PTSD often presents with comorbidities such as depression and substance abuse and dependence.[10,24] Studies have estimated that >50% of PTSD patients have symptoms of a major depressive disorder,[10] but in the veteran population the percentage may be much higher.[25,26]

A risk assessment for both suicidal and homicidal ideation is essential. The presence of PTSD increases suicidal ideation and the risk of completed suicide.[11,23] The presence of comorbid depression further increases suicide risk.[11,27] In the veteran population, aggression and anger are well documented.[24,28] During the initial PTSD assessment, military members may report violent thoughts and aggressive behaviour, including homicidal thoughts. Assessing comorbidity, suicidal or homicidal ideation, and extent of social support is imperative in order to determine the need for urgent, inpatient treatment.[7] In particular, a high risk for suicidal behaviour should prompt strong consideration for inpatient admission. Enquiry should also be made into family functioning as the family plays an important role in the treatment process.[7]

Treatment

Table 2 describes the initial steps in the management of PTSD. Substantial comorbidities, whether psychiatric or physical, should be managed simultaneously with the PTSD.

Psychoeducation

Once a firm diagnosis has been established, psychoeducation regarding diagnosis and treatment is critical for both patients and

CASE 1: Military-related PTSD with physical injury and depression

A 27-year-old veteran was referred with persistent depressed mood, insomnia, and panic attacks. He was nonresponsive to citalopram 30 mg daily. He was recently released from the Canadian Forces (CF) after serving 8 years. He first noticed symptoms after returning home from his deployment in Afghanistan where he was exposed to major combat. He was the driver in the second vehicle of a convoy when the lead vehicle hit a roadside bomb. He tried to rescue his comrade from the burning vehicle, but they were ambushed by the Taliban. During the firefight he was shot in his right leg; he was evacuated first to the Kandahar Airbase and was transferred to an American hospital in Germany, then back to Canada.

Within 6 months of returning to Canada, the patient reported reliving the events in Afghanistan in intrusive recollections and recurrent nightmares. He became preoccupied with the safety of his family, especially his children. He started to fear going to bed and was drinking increasing amounts of alcohol to help him sleep and smoking marijuana to control pain. He started to become nervous in crowds and became afraid to leave his home. He was irritable, frequently getting into fights at work and at home with his wife. His moods were low; he had lost interest in most activities and complained of fatigue, low energy, diminished appetite, and no sex drive. After his release from the military, he finally went to see his family doctor who started him on citalopram and zopiclone to help him sleep. At first he noticed some improvement in anxiety, but these periods were short-lived. He continued to use alcohol regularly for sleep and he was still having frequent anger outbursts. Finally, after losing his job and reporting increased thoughts of suicide, his family doctor convinced him to see a psychiatrist.

Following a comprehensive psychiatric evaluation, the initial plan was to focus on stabilization by aggressively treating his comorbid addiction and major depression. An initial first step, as the patient was concerned with potential sexual side effects, was to add bupropion XL 150 mg in combination with citalopram and start low-dose (15 mg) mirtazapine RD at bedtime to assist with his sleep. He was also provided with extensive psychoeducation and psychotherapy focussing on depression and addiction. Once his symptoms were better controlled, he could benefit from trauma-focussed psychotherapy.

Table 1: Primary Care PTSD Screen[18]

In your life, have you ever had any experience that was so frightening, horrible, or upsetting that, ***in the past month***, you:

1. Have had nightmares about it or thought about it when you did not want to?
2. Tried hard not to think about it or went out of your way to avoid situations that reminded you of it?
3. Were constantly on guard, watchful, or easily startled?
4. Felt numb or detached from others, activities, or your surroundings?

Screen is positive if patient answers "yes" to any three items.

Table 2: Important principles in the management of PTSD

1. Develop a therapeutic alliance
2. Assess the safety and suicide risk
3. Consider the setting of treatment (outpatient, inpatient, or day program)
4. Assess and manage physical conditions that could exacerbate PTSD symptoms (eg, thyroid problems, chronic pain conditions)
5. Conduct careful psychoeducation related to PTSD
6. If there is a current comorbidity (eg, substance use disorder, mood disorder, or borderline personality disorder), prioritize treatment of this/these condition(s)
7. Choose pharmacotherapy based on the presence of any comorbidities
8. Once the comorbid condition(s) has/have been stabilized, then consider a trauma-focussed cognitive behaviour therapy.

their families. Educating patients regarding the phases of treatment and understanding of what is to be expected, particularly when to expect treatment benefits, helps to avoid frustration and hopelessness associated with inappropriate treatment expectations.

Symptom stabilization

The main goal of stabilization is to manage acute symptoms and improve current functioning. Stabilization usually requires psychoeducation, anxiety management training, and medication (Table 3). Once symptoms stabilize, patients are more able to engage in psychotherapy,[29] such as prolonged exposure and other evidence-based forms of cognitive behavioural psychotherapy (CBT). Regardless of the treatment modality, stabilization is critical. The initiation of "trauma-focussed psychotherapy" prior to stabilization may exacerbate both PTSD symptoms and pre-existing or comorbid symptoms of depression and substance abuse.

For mild to moderate PTSD without significant comorbidity, and where minimal stabilization is required, CBT may be initiated prior to medication. However, for the typically more severe and chronic cases referred to psychiatrists, CBT should follow acute symptom stabilization with medication. CBT requires the ability to learn and apply new information. When severe depression or anxiety symptoms are present, cognitive impairment is common and often has a significant impact on new learning. CBT specifically for PTSD typically involves close to 20 sessions emphasizing a combination of cognitive restructuring of maladaptive trauma-related beliefs and exposure techniques.[30]

Pharmacological management

As demonstrated in Table 3, a number of medications have been employed to treat PTSD. Selective serotonin reuptake inhibitors (SSRIs) and the serotonin norepinephrine reuptake inhibitor (SNRI) venlafaxine have the most empirical evidence for efficacy in the treatment of PTSD and are usually considered as a first-line treatment for PTSD.[7,31-35] SSRIs and venlafaxine are also effective agents for the treatment of comorbid mood and anxiety disorders commonly associated with PTSD. Education about the potential risk of increased suicidal thoughts associated with antidepressant medication, particularly at the time of initiation of treatment, should also be reviewed with the patient.[31]

Other dual acting antidepressants such as mirtazapine, bupropion, and, more recently, duloxetine are widely used to treat major depression and other anxiety disorders, but have less empirical data demonstrating their efficacy for the specific treatment of PTSD.[36-40] In PTSD they are considered as second- and third-line treatment options for patients who have failed to respond to first-line treatment. However, since SSRIs have not demonstrated their efficacy in subpopulations of combat-related PTSD[32,41] and due to the high rate of comorbid major depression and other anxiety disorders, dual-acting antidepressants should also be considered as first-line treatments, especially in PTSD with comorbid major depression.

Benzodiazepines are not recommended as monotherapy for the treatment of PTSD,[9,42,43] but are sometimes used for the treatment of insomnia[7] or, in combination with an antidepressant, to treat acute anxiety. They might also be useful to manage early side effects associated with some antidepressants or antipsychotics, including restlessness, jitteriness, or agitation. There is a risk of rebound insomnia or anxiety when a benzodiazepine is discontinued, especially after long-term use.[44] The use of benzodiazepines among patients with PTSD who have comorbid substance abuse should be avoided.

Combining psychotherapy and pharmacotherapy

Although there is limited research evaluating combination treatment,[45,46] many clinicians prescribe psychotherapy and pharmacotherapy either concurrently or sequentially during the course of treatment. There is also evidence that psychotherapy improves outcomes in patients with chronic PTSD who have demonstrated a partial response to pharmacotherapy.[47]

Assessing treatment response

Despite the lack of a generally accepted definition for recovery or remission in PTSD, assessing treatment response remains critical. Response to treatment for PTSD can be assessed objectively, using the self-rated PTSD Checklist (Military or Civilian Version) and comorbid depression can be assessed objectively using the Hamilton rating scale for Depression (HAMD-7)[48] or the self-rated Patient Health Questionnaire (PHQ-9).[49]

Dosing considerations

PTSD patients often present with marked anxiety, and they may be very sensitive to the potential heightened anxiety or agitation sometimes associated with early antidepressant treatment. Patients benefit from a "start low, go slow" approach to medication titration. Consider initiating treatment at 25%–50% of the usual starting dose and then gradually increasing to a therapeutic level.[50,51] While the initiation of medication might be slow and cautious, ultimately the dose should be titrated to full symptom remission, at maximum tolerated doses.

Treatment adherence/compliance

Medication compliance is crucial for treatment to be effective. False beliefs or fears about medications should be explored and

Table 3: Recommendations for PTSD pharmacotherapy

First line	Fluoxetine, paroxetine, sertraline, venlafaxine XR
Second line	Fluvoxamine, mirtazapine, moclobemide, phenelzine Adjunctive: risperidone, olanzapine
Third line	Amitriptyline, imipramine, escitalopram Adjunctive: carbamazepine, gabapentin, lamotrigine, valproate, tiagabine, topiramate, quetiapine, clonidine, trazodone, buspirone, bupropion, prazosin, citalopram, fluphenazine, naltrexone
Not recommended	Despipramine, cyproheptadine Monotherapy: alprazolam, clonazepam, olanzapine

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confronted prior to starting treatment and addressed regularly during treatment follow-up. Providing a safe environment and a positive doctor-patient interaction will help develop trust and improve medication compliance.[52,53] Engaging and educating all care providers, including the family, is essential. Peer social support programs can play a valuable role in encouraging treatment adherence.[54]

Patients may wish to discontinue their medication once they start to feel better or can no longer tolerate side effects such as weight gain or sexual dysfunction. However, studies have demonstrated that patients with PTSD continued to show improvement with pharmacotherapy up to 36 weeks after treatment initiation and early discontinuation leads to a high rate of relapse.[55] Therefore, in most cases, long-term medication treatment may be recommended.[45]

There are no published guidelines specifying the length of pharmacological treatment for anxiety disorders; however, existing guidelines for major depression suggest that the medication should be continued for at least 6 months to 1 year after symptom remission has been reached.[56]

Managing treatment-resistant PTSD

In cases of treatment-resistant PTSD, it is important to reassess the patient to ensure that the diagnosis is correct and that comorbid conditions have been considered in the management. Although there is no treatment algorithm for the pharmacological treatment of PTSD, for patients who demonstrate a partial response (25%–50% improvement) after 6-8 weeks of treatment with the first antidepressant trial, optimization of monotherapy is a critical first step. This generally entails titrating the agent to maximally tolerated doses, so long as each dose increase produces some benefit. If after dose optimization a response to treatment (≥50% improvement) is not evident, the initial agent should be switched to another first-line agent. If optimizing the initial agent leads to treatment response but not full remission, combination strategies may be considered. There is some evidence to suggest that combining 2 agents early in the treatment of depression might be more effective than monotherapy to induce remission,[57] but it is unclear if this strategy would be similarly effective in PTSD.

When considering combination strategies, discuss potential risks as well as expected benefits with the patient.[50] Common combination treatments include adding an antidepressant with a different mechanism (eg, mirtazapine or bupropion) to an SSRI or SNRI. The utility of adding an atypical antipsychotic (eg, risperidone, quetiapine, aripiprazole, or olanzapine) in combination with a primary antidepressant has been suggested in several small studies.[58-61] These agents appear to be beneficial in managing hyperarousal symptoms such as hypervigilance and irritability, as well as for severe dissociation symptoms.[32] There is significant evidence for the addition of an atypical antipsychotic for treatment-resistant depression,[62] which often presents as a complicating factor in PTSD. There is no established role for the use of conventional antipsychotics in the treatment of PTSD.

Anticonvulsant medications (eg, carbamazepine, valproate, topiramate, and lamotrigine) are increasingly used in combination with antidepressants to treat symptoms of depression, mood instability, and impulsivity;[63-68] however, controlled trials have, to date, failed to confirm the utility of these agents for PTSD.[69] These agents are generally reserved as third-line agents, and used in combination with first- or second-line agents.

Insomnia is extremely common, persistent, and severe for most PTSD patients. If symptoms of insomnia persist with the use of therapeutic doses of antidepressants, a trial of low-dose mirtazapine (15 mg) or trazodone (50-100 mg) may be helpful. Alternative non-benzodiazepine hypnotics

CASE 2: PTSD with social phobia

A 28-year-old single woman was referred for assessment of anxiety symptoms. She described worrying throughout the day, and was experiencing nightmares and concentration problems. She had experienced intimate-partner violence from her ex-boyfriend, who had hit her and forced her to have sex with him on a number of occasions. She reported nightmares about these attacks. She could not sleep in her own bedroom, where the attacks had occurred. The anxiety symptoms were so disabling she had difficulty functioning at work. She also described a long history of being shy and described high anxiety in social situations. She was not suicidal, and denied a history of drug or alcohol abuse. Her mother had life-long social phobia. There was no childhood history of sexual or physical abuse.

The patient was treated with a combination of pharmacotherapy and psychotherapy. She responded to individual cognitive behaviour therapy with a focus on exposure and response prevention. She also found that the anxiety symptoms were substantially reduced with a combination of venlafaxine XR 300 mg per day, trazodone 25 mg at bedtime, and clonazepam 1 mg at bedtime. This approach not only improved the PTSD symptoms, but also reduced her social phobia. With her symptoms of anxiety better controlled, the patient was now ready for trauma-focussed psychotherapy.

include zopiclone. There is also some evidence demonstrating the benefits of using prazosin, an adrenergic inhibitor specifically to reduce nightmares.[70,71] A sleep study should also be considered in cases where a specific comorbid sleep disorder such as sleep apnea is suspected.

Conclusion

The presentation of PTSD is often complicated by comorbidity. Understanding the impact of trauma can help the clinician appreciate the challenges faced by the patient, which is essential to establishing a trusting therapeutic alliance. Treatment often involves a combination of medications, making compliance more challenging. Although remission is not always possible, pharmacological interventions assist with symptom reduction and improve functioning and quality of life. Pharmacological interventions, especially with comorbidity, can also assist with stabilization and facilitate psychotherapeutic interventions such as trauma-focussed psychotherapy.

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