9 A Complex Case of Psychiatric Issues Associated with HIV Disorder

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Case History

A 39-year-old Italian-Canadian male, father of two young children, with a history major depressive disorder and IV drug use (opioids) presented to the family clinic after being notified that he has HIV. He was notified of the HIV infection 2 weeks ago after completing anonymous HIV testing. He acquired the infection via unprotected intercourse with a female partner whom also contracted HIV months previous. The patient is worried about how his diagnosis will affect his future relationships and about who will take care of his young children in the future if the infection progresses given he is their sole care provider. Currently, the patient's sister is a source of support for the patient's family and she is aware of the diagnosis. The patient has not used IV drugs for 2 years. The patient reports he has had a sore throat for the past 2 weeks and has experienced increased fatigue over the past month. Patient also reports starting an SSRI for low mood 2 months ago. He is taking sertraline 100 mg per day for depressed mood. On physical examination, patient has non-tender lymphadenopathy primarily involving the posterior cervical lymph nodes. The patients CD4 count is currently 320 cells/ microL.

9.1 Epidemiology of Mental Disorders among HIV Patients Focusing on the Most Common Psychiatric Disorders

Commonly seen mental disorders in patients with HIV include:
Delirium
Major depression
Bipolar disorders including mania
PTSD
Anxiety disorders
Neurocognitive disorders
Substance abuse or dependence
HIV-associated dementia

Mental health disorders among individuals with HIV are common. Overall, in the United States, nearly half of individuals with HIV have a psychiatric disorder [9]. The most common psychiatric disorders among those with HIV are major depressive disorder and substance use disorder [9, 17, 71]. HIV has also been linked to an increased likelihood of having comorbid anxiety and/or psychosis [35, 71].

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K. Shivakumar, S. Amanullah (eds.), *Complex Clinical Conundrums in Psychiatry*,
https://doi.org/10.1007/978-3-319-70311-4_9

9.1.1 Delirium

Delirium is highly prevalent in HIV-infected patients with an estimated prevalence of 40–65% and a major cause of mortality. Delirium symptoms can be characterized by changes in alertness or global impairment of cognition with disorientation; impairment of recent memory and abstract thinking; sleep-wake cycle disturbances; psychomotor disturbances including hypo or hyperactivity; and emotional changes such as anxiety, irritability, fear, depression, euphoria and apathy. Numerous factors can contribute to delirium in HIV patients including metabolic abnormalities, infection, sepsis, hypoxemia, anaemia and various CNS manifestations seen in HIV patients. A patient who is diagnosed with delirium should be considered as a medical emergency and given a full diagnostic work to exclude various general medical complications associated with HIV infection. In this group of patients, delirium treatment can be associated with major treatment challenge and high mortality (Fig. 9.1).

9.1.2 Depression

With regard to depression, studies have shown that a patient with HIV is 2X–7X more likely to experience depression than those who do not have HIV [18, 76]. In fact, between 5% and 45% of HIV-positive people experience depression at some point in their life [3, 15]. It is noteworthy, however, that many individuals with HIV are diagnosed with major depressive disorder before they contract HIV [3], implying that depression could be a risk factor to contracting the disease. The etiology of depression among HIV patients is multifactorial, and various HIV-related conditions have been associated with the development of depression including HIV-related infection, malignancy and the medications used in HIV patients. Medications including efavirenz, interferon, metoclopramide, anabolic steroids and propranolol may produce major depression or depressive syndromes.

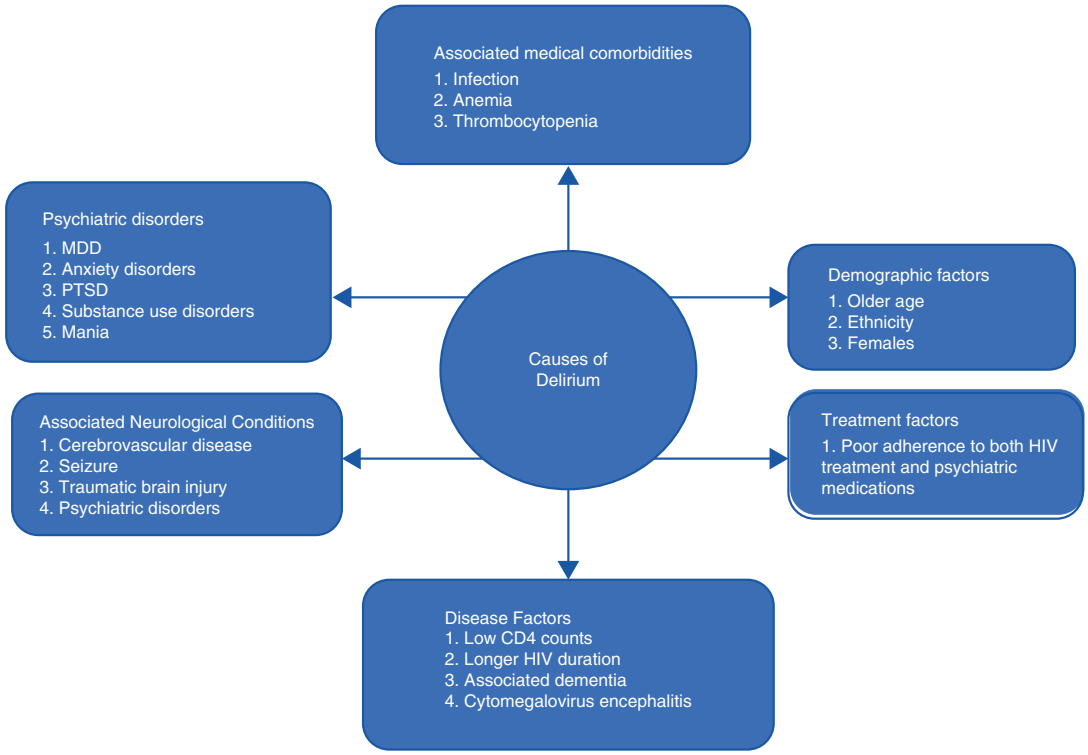

Fig. 9.1 Causes of delirium

9.1.3 Mania

Mania can occur in two distinct patterns among those with HIV. It can occur in those with HIV who have comorbid Bipolar I or as a separate manifestation called "aids mania". Among those with both bipolar and HIV, manic episodes involving, for example, grandiosity, flight of ideas and involvement in risky activities can range from producing devastating effects on one's life to mildly affecting one's functioning outside of their manic episodes [70]. Aids mania, in contrast, appears as a late manifestation of aids where mania, typically in the form of increased irritability, generally arises in those whom have never had bipolar nor experienced mania before [70] (Table 9.1).

Table 9.1 Common symptoms of depression and bipolar disorder in HIV-infected patients

Commonly seen symptoms of depression and bipolar disorder in HIV-infected patients		
	Differential diagnosis	Assessment tools
Depressive symptoms		
Low or depressed mood Loss of interest Sleep difficulties Loss of appetite Poor concentration Memory Non-specific somatic symptoms Excessive tiredness	Rule out bipolar disorder Dysphoria from PTSD Substance use disorder HIV-associated neurocognitive disorder	Center for epidemiological studies Depression scale Hospital anxiety and depression scale Phq-9 Hamilton scale for depression
Bipolar symptoms		
Mania Grandiose feelings Sleep difficulties Pressure of speech Flight of ideas Distractibility Excessive involvement in pleasurable activities	Manic or hypomanic symptoms induced by metabolic disturbances Endocrine disorders Neurological disorders Mania or hypomania associated with systemic infection Mania or hypomania associated with illicit or prescribed medication including ART (antiretroviral treatment)	Mood disorders questionnaire (MDQ) Jung mania rating scale

Adapted from Cozza et al. [23]

9.1.4 Schizophrenia

Research indicates that the prevalence of comorbid HIV with schizophrenia ranges from 4% to 19% [12, 19]. It has also been suggested that those with schizophrenia may be more likely to contract HIV than those without schizophrenia given their higher likelihood towards engaging in high risk behaviours such as unprotected intercourse with multiple partners and injection drug use [16, 56]. It is unclear whether HIV can increase one's risk of developing schizophrenia, but it appears plausible when considering the neural diathesis-stress model of the development of schizophrenia [88]. This model posits that those predisposed to developing schizophrenia may have an abnormality in dopamine (DA) neurotransmission that may be exacerbated by the cortisol release associated with an environmental stressor [88]. In line with this hypothesis, it is plausible that the stress associated with receiving the diagnosis of HIV or managing the illness could trigger symptoms of schizophrenia in those who are predisposed to schizophrenia. Research has yet to support this hypothesis. The diagnosis of schizophrenia may affect the course of HIV. For instance, those with both HIV and schizophrenia may be less equipped to cope with the stresses of the diagnosis and may be less able to afford care associated with the illness, therefore they may not fare as well as compared to those with HIV alone [80]. Furthermore, those with schizophrenia and HIV have a higher rate of morbidity and mortality than compared to those with HIV alone [85].

9.1.5 Substance Abuse or Dependence

In terms of the epidemiology of substance use issues among those with HIV, approximately 40% of those with HIV have a substance use problem involving a substance other than marijuana [9]. Common substances reported to be used among individuals with HIV include alcohol, heroin, and cocaine. Amphetamine use appears to be increasingly used by this population [1]. The lifetime prevalence for alcohol use disorders and other drug use disorders among HIV patients compared with the lifetime prevalence of general population is much higher. It is also common to see an increased HIV-related mortality, morbidity and lower treatment adherence at antiretroviral therapy among the patients with substance abuse disorders and HIV.

9.1.6 Anxiety Disorders

Individuals with HIV are also more likely to have anxiety and psychotic disorders compared to the general population. Approximately 15.8% of those receiving care for HIV also have a generalized anxiety disorder while 10.5% meet criteria for panic disorder [9]. Adjustment disorder is one of the most common psychiatric disorders seen in HIV patients, especially during the early course of the illness [69].

9.1.7 Psychosis

The prevalence rate of new-onset psychosis among HIV-positive individuals ranges between 0.5% and 15% [19, 55]. New-onset of psychotic disorders among HIV patients are commonly seen in the late stages of the disease, and this may be associated with neurocognitive disorders. Common symptoms of psychosis include delusions of grandeur, somatic and persecution typically presenting during the late stages of HIV [38]. The etiology of psychosis in HIV infection is complex and multifactorial, and this may be part of the comorbid psychiatric conditions associated with HIV such as major depressive disorders, bipolar disorder, delirium, neurocognitive disorders or medication side effects.

9.1.8 Post-traumatic Stress Disorder

The lifetime prevalence rate of post-traumatic stress disorder (PTSD) has been found to be as high as 40% among those with HIV [53]. It has been posited that PTSD may develop after the diagnosis of a life-threatening illness such as HIV [53]. This may be the case particularly in those with HIV who lack adequate coping skills, social support or access to appropriate mental health services to help them manage with their illness. Furthermore, many individuals with HIV have been found to have had experienced traumatic events that triggered PTSD before the HIV diagnosis [65]. Given that research studies have produced mixed results as to whether HIV causes PTSD, more research is needed to better elucidate the relationship between the two conditions [44]. A better understanding of the relationship between HIV and PTSD is important so that healthcare providers may develop trauma prevention programmes targeting high-risk groups such as those with HIV and thus help potentially decrease rates of morbidity and mortality associated with the disease.

9.2 Pathogenesis of Mental Disorders in HIV

The pathogenesis of mental disorders in HIV is complex and varies widely depending on the type of mental disorder. For example, study findings have shown that factors such as stress, immune cell functioning, inflammation and medication interactions contribute to the development of various mental illnesses [18, 25, 40, 50, 86]. With regard to stress, individuals diagnosed with HIV are often faced many stressors in addition to the health complications that may arise throughout their illness. For instance, those diagnosed with HIV often deal with the stigma associated with the disease; make major lifestyle decisions; adjust to treatment regimens; determine when and who to

disclose their illness to; and deal with changes in family, partner or friendship dynamics following diagnosis [78, 89]. Those with HIV are more likely to develop a comorbid psychiatric disorder such as depression and anxiety than compared to those who are HIV negative because they must endure many additional stressors [18].

Immune cell dysfunction can also contribute to the development of mental illness among those diagnosed with HIV. For example, the biological mechanism of HIV, monocytes and lymphocytes entering the brain along with the production and release of inflammatory cytokines has been found to contribute to the pathogenesis of HIV-associated dementia (HAD) [57]. More specifically, macrophages, microglia and astrocytes interact with each other to release cytokines such as IL-1β, TNF- α and arachidonic acid, which are neurotoxic to the brain and said to contribute to the development of HAD [31].

Mania is another symptom of mental illness that can occur in those with HIV. Mania may be related to a comorbid bipolar disorder, caused by substance use or secondary to HIV infection, HIV medication, or HIV-related infection [14, 42, 61]. The exact mechanism of how HIV infection is related to the development of manic symptoms is unclear; however, it has been posited that HIV is neurotoxic and disrupts brain structure and function which leads to manic symptoms [51, 66]. Another study highlighted the potential role of CD4 cells in the pathogenesis of mania secondary to HIV. The study findings found that those with HIV had lower CD4 counts than compared to those without manic symptoms [51]. Therefore, perhaps CD4 cells may influence whether a patient with HIV experiences symptoms of mania or not.

Certain antiretroviral medications have been found to cause mental illness. For example, mania has developed secondary to the use of antiretroviral medications such as zidovudine and didanosine [14, 54]. In contrast, one study found that if antiretroviral medication was able to reach the CNS it was protective effect against the development of manic symptoms among those with HIV [58]. More studies with larger sample sizes would be helpful to better elucidate the relationship between mania and antiretroviral medication.

9.3 Psychosocial and Behavioural Risk Factors for Depression and Anxiety

There are a number of factors that may predispose individuals with HIV to developing depression and anxiety. Nakimuli-Mpungu et al. [60] examined risk factors for depression among those with HIV living in Southern Uganda. Their research findings showed that HIV-positive patients with depressive disorders were more likely to have difficulty adhering to their antiretroviral medication regimens, have less social support and were less likely to have feelings of self-efficacy compared to those with HIV whom did not have depression [60]. According to their study, those with HIV and comorbid depression were also more likely to have tuberculosis and experience manic episodes than those with HIV and no depression [60]. In another study involving HIV-positive individuals in Uganda, research findings showed that factors such as being female, a family history of psychiatric illness, the use of poor coping strategies, alcohol use, stress and food insecurity were predictive of major depressive disorder [45]. In terms of factors that correlated with anxiety, Pappin et al. [67] found HIV-positive patients who experienced adverse effects from their antiretroviral medications, engaged in avoidant coping styles or were subjected to stigma related to their diagnosis were more likely to develop symptoms of anxiety.

9.4 Assessing Depression and Other Comorbid Psychiatric Conditions: The Role of Screening Instruments

According to the research literature, depression affects approximately 4–40% of those living with HIV [17, 59, 69]. Currently, there is no gold standard for examining depression among HIV-positive individuals. Typically the diagnosis of depression among people living with HIV in clinical settings is made with information obtained from a clinical interview based on either the International Classification of Diseases (ICD;

[92]) or Diagnostic and Statistical Manual of Mental Disorders criteria (DSM 5; [5]). A structured clinical interview such as the Structured Clinical Interview for the DSM-5 (SCID, [28]) or the Composite International Diagnostic Interview [91] is the most commonly used assessment when examining depression in research settings [82]. Symptom severity scales are often utilized to monitor change in symptomology over a course of time. The Center for Epidemiologic Studies Depression Scale (CES-D-20; [72]) and the Beck Depression Inventory [8] are symptom severity scales that have been used extensively with HIV populations.

The CES-D-20 is a well-validated tool used to examine depression in the general population [72]. Zhang et al. [94] tested both the shorter version of the CES-D-20 and the CES-D-10, with HIV-positive people in British Columbia, Canada, and found the internal consistency reliability coefficient to be adequate with a coefficient alpha of 0.88. Furthermore, the researchers found high levels of sensitivity (with 95% CI) at 91% and specificity (with 95% CI) at 92% [94]. Therefore, the study determined that the shortened 10-item CES-D scale was adequate and comparable to the CES-D-20 in its utility when examining depression symptoms among those with HIV.

Kalichman et al. [43] used the Beck Depression Inventory II (BDI II; [7]) to examine depression among those with the HIV infection. The items on the BDI II can be split into two subscales: affective symptoms and somatic symptoms of depression. It is important to note that while the BDI is a very common tool to use to examine depression, research findings suggest that the BDI places more emphasis on somatic symptoms compared to other measures of depression [82]. To illustrate, Kalichman et al. [43] found, via factor analysis, that there was a positive relationship between somatic symptoms of depression, the number of acquired immunodeficiency syndrome diagnoses and the number of HIV-related symptoms. There was also an inverse relationship between somatic symptoms of depression rating and the number of T-helper cells [43]. These findings indicate that one's level of depression may be strongly linked to the disease status and symptomology. Thus, when using the BDI to assess depression symptoms in those with HIV, it is important to consider the patient's symptomology, diagnostic information and life stressors and how these factors may be influencing their depression score. The Hamilton Rating Scale for Depression (HAM-D; [36, 37]) also emphasises somatic depression symptoms as compared to other measures of depression such as the CES-D-20 [82].

Another study examined the use of two other measures of depression symptom severity called the Patient Health Questionnaire-9 (PHQ-9) [46] and its short version Patient Health Questionnaire-2 (PHQ-2) [47] with those with HIV living in Western Kenya. The PHQ-9 and PHQ-2 are a nine-item and a two-item measure, respectively, both based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition's (DSM-IV; [4]) criteria for depressive disorders. The researchers found that both measures have adequate psychometric properties when used with this population. The coefficient alpha for the PHQ-9 was reported to be 0.78 and when using a cut-off point ≥3, the PHQ-2 was shown to have high sensitivity (91.1%) and moderate specificity (76.8%) for diagnosing PHQ-9 major depressive disorder. It is important to note that more studies must be conducted to confirm the measure's utility with other HIV populations beyond those residing in Western Kenya.

Despite the lack of a gold standard for examining depression among those with HIV in the clinical setting, it appears that a clinical interview based on the DSM-5 or ICD-10 criteria is the best method for diagnosing depression. Additionally, the BDI II, CES-D-20, CES-D-10, PHQ-9 and PHQ-2 may be helpful tools when monitoring depression symptoms over time. Patient demographics, culture, stage of HIV disease, life stressors and symptomology should all be considered when choosing an interpreting the measurement tool of depression in those with HIV.

In order to assess for other comorbid psychiatric conditions among HIV-positive individuals, the research literature suggests to first begin by taking a thorough history, which includes infor-

mation obtained from both the patient, and collateral sources regarding the patient's health status, and history of medications, illnesses, substance abuse, and sexual behaviours [27]. The clinician should also perform a mental status examination, the Folstein-McHugh Mini-Mental Status Examination [29], and determine the patient's level of executive function [27]. Screening questionnaires that assess a broad range of psychiatric illnesses may be helpful among those with HIV. The General Health Questionnaire [32] can be useful when used to examine mental illness among HIV-positive individuals. It is a common clinical practice to use a combination of assessment tools such as General Health Questionnaire and Becks Depression Inventory to increase the case detection. Any mental health concerns that arise during the clinician's initial assessment should be further assessed using more specific measurement tools.

Case History Continued

- Eight years later the patient relapses with IV drugs (opioids) and reports that he has been injecting opioids for the past month.
- Patient reports having difficulty adhering to the treatment regimen and that he has been taking his antiretroviral medication intermittently.
- HIV associated dementia develops with deficits in fine motor speed, information-processing speed, executive functioning and apraxia.
- The patient's CD4 counts are <200 cells/microL.
- Magnetic resonance imaging (MRI) and T2-weighted images show cerebral atrophy of the caudate in the basal ganglia.

9.5 HIV-Associated Neurocognitive Dysfunction (Hand)

HIV associated neurocognitive dysfunction refers to neurocognitive impairment that is either symptomatic or asymptomatic [10]. There are three main subtypes of HAND: Asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND) and HIV associated dementia (HAD) [21]. Asymptomatic neurocognitive impairment is diagnosed when neurocognitive decline is evident in at least two domains (i.e., work, activities of daily living) but there is no functional impairment [2]. In contrast, MND and HAD are described as the presence of minor and major neurocognitive impairment, respectively, with the presence of functional decline [10]. HIV associated dementia also typically involves motor abnormalities such as tremors, gait ataxia and loss of fine motor skills, and behavioural problems such as mania and emotional lability [10, 57].

In order to determine whether the patient has HAND, a clinician should first characterize the degree of functional impairment, take a thorough history of the symptoms, determine whether the patient is on antiretroviral treatment and, if possible, obtain collateral information from family members or from those close to the patient. The clinician should also develop a differential diagnosis for HAND including disorders such as substance use disorder, major depressive disorder and schizophrenia. A patient's level of cognitive impairment can be characterized by using bedside cognitive testing and, if necessary, neuropsychological testing [2]. Some options for bedside cognitive testing include using the MiniMental Status Exam (MMSE) [2], the Montreal Cognitive Assessment (MoCA) [62] and the International HIV Dementia Screen [21].

These measures are not specific for HAND; however, the tools can be quite helpful when assessing cognitive decline in those with HIV [74]. There is no standard battery to use to assess neurocognitive impairment in those with HAND; however, literature suggests repeating assessments at least biannually in order to better understand changes patient's cognitive functioning [21]. The next step in the investigation for HAND depends on the stage of HIV and whether the patient is on antiretroviral medication. Those with more severe cognitive decline and who are not on medication for their HIV are more likely to benefit from neuroimaging, an examination of biomarkers of inflammation, and a lumbar puncture

to determine the extent of central nervous system (CNS) involvement. Staging and assessment of HIV can be completed by performing a complete blood count, electrolytes, urea, fasting blood glucose, creatinine, liver function tests, amylase and lipid panel, and screening for syphilis, hepatitis A, B, C, and sexually transmitted diseases [27].

Researchers have yet to find sufficient evidence for using these above-mentioned modalities and laboratory diagnostics with those receiving antiretroviral therapy to help understand the degree of CNS involvement [2]. Instead, these tests are useful to help rule out other diseases that may be the contributing to the observed neurocognitive decline. In the past, indicators such as viral load were strongly linked to HAND, particularly HAD; however since the advent of combination antiretroviral therapies, the viral load is less indicative of cognitive decline because of antiretroviral medication's influence on viral load [90]. Furthermore, among those that are not receiving antiretroviral therapy, CD4 levels also appears to have some utility, particularly in determining whether a patient with HAND has or will develop HAD [90]. Neuroimaging (MRI), cerebral spinal fluid analysis and certain laboratory investigations such as B12 levels are typically reserved to help rule out other diseases that may be the contributing to the observed neurocognitive decline.

9.6 Treatment of Major Psychiatric Disorders in HIV Infected People

The following is a guideline on treatment major psychiatric disorders in HIV-infected individuals. This section highlights key tools to aid in clinicians' decision-making when they are developing treatment plans for those with HIV and comorbid mental illness.

9.6.1 Antidepressants

The use of psychopharmacological management techniques for patients with HIV and depressive symptoms is a common method of treatment often used in combination with psychotherapeutic intervention (McDaniel et al. 2000). There are some considerations that must be taken into account before starting psychopharmacological treatment such as antidepressants. For instance, clinicians should determine whether the depressive symptoms can be ameliorated using other means besides the use of antidepressants. For instance, the patient's depressive mood may be due to recent changes in the patient's medical condition, new life stressors or side effects of other medications which need to be addressed by the clinician.

In addition, before starting an antidepressant in those with HIV, the patient's medication profile including over-the-counter products, recreational medications and natural remedies should be reviewed in order to predict any drug-drug interactions, particularly if the patient is on a complex cocktail of HIV medications [26]. Serotonin reuptake inhibitors, tricyclic antidepressants and psychostimulants have all been shown to be beneficial in treating depressive symptoms among those with HIV [64]. It has been suggested that patients with HIV should be prescribed these medications in a similar fashion as when prescribing to another medically ill population with careful attention paid to the dose of medication prescribed and route of administration selected (McDaniel et al. 2000). Low doses of antidepressants should be given initially and slowly titrated up with careful monitoring along the way [26].

Significant interactions between certain antidepressants and antiretroviral medication have been documented. Typically, either the antidepressant or the antiretroviral medication increases the presence of the other medication in the patient's system by affecting drug metabolism pathways [84]. Patients should be routinely monitored for side effects of antidepressant medication such as insomnia and loss of appetite or weight, and side effects should be treated aggressively. One reason to treat side effects aggressively is because untreated depression among those with HIV leads to lower levels of adherence to HIV medication thus worsening the patient's symptoms, which is often more debilitating than the side effects of the antidepressant [64] (Table 9.2).

Table 9.2 Commonly used antidepressant medications in the HIV patients

Antidepressant	Comments
Selective Serotonin Reuptake Inhibitors(SSRI's)	
Citalopram	Potential for arrhythmia in doses over 60 mg Prolongation of QTc intervals
Fluoxetine	Prolongation of QTc intervals with certain ART drugs Very long-acting metabolite
Fluvoxamine	High discontinuation rate due to insomnia, gastrointestinal disturbance, anorexia behavioural changes, and sedation [33]
Selective Norepinephrine Reuptake Inhibitors(SNRI's)	
Desvenlafaxine	Low likelihood of interactions with HIV antiretrovirals Potential for hypertension, weight gain, and sexual dysfunction
Venlafaxine (extended release)	Prolongation of QTc intervals Ritonavir may increase serum levels of venlafaxine Potential for hypertension and weight gain
*Levomilnacipran**	Weight neutral Potential for: hypertension and sexual dysfunction Serum levels of levmilnacipran may be increased by protease inhibitors
Duloxetine	Potential for: hypertension Sexual dysfunction
Novel Antidepressants	
Mirtazapine	Potential for weight gain Anti-nausea Sedation Least potential for clinical interactions with ART
Trazodone	Sedating effect Often used a sleep aid Protease inhibitors may increase serum levels
Tricyclic Antidepressants(TCA's)	
Amitriptyline	Known for multiple side-effects such as constipation, dry mouth, weight gain Toxicities include arrhythmia, Potential for anticholinergic delirium All protease inhibitors may increase TCA serum levels to toxicity Use therapeutic drug monitoring
Doxepin	Features in common with TCA

*preferentially inhibiting reuptake of NE over 5-HT
Adapted from Cozza et al. [23]

Table 9.3 Commonly used anxiolytics

Anxiolytic	Comments
Benzodiazepines such as clonazepam	Can be prescribed for relatively mild-to-moderate cases of anxiety Used as a sleep aid Treating delirium Can be used as a first-line agent for the treatment of anxiety in patients with HIV
Non-benzodiazepine anxiolytics such as buspirone	Potent CYP3A4 inhibitors may increase buspirone serum levels

Adapted from Cozza et al. [23]

9.6.2 Anxiolytics

Anxiolytics, particularly benzodiazepines, are commonly prescribed to treat anxiety among those with HIV [87]. Research studies have shown the possibility of a significant interaction arising when a patient takes benzodiazepines along with antiretroviral medication [34]. For example, ritonavir, an antiretroviral medication, can inhibit the effects of the CYP3A enzyme; which breaks down the short-acting benzodiazepine alprazolam leading to a disruption in the clearance of alprazolam [34]. At this time, more research is needed to further examine the use of psychotropic medication such as anxiolytics among those with HIV to determine the best practice guidelines (Table 9.3).

9.6.3 Mood Stabilizers

Preliminary research findings have shown the benefits of mood stabilizers among those who are HIV positive. One study by Parenti et al. [68] treated ten HIV-positive homosexual men with lithium carbonate, and eight of the patients withdrew from the study because they developed drug toxicity. In contrast, pilot studies have found that mood stabilizers such as lithium and valproic acid are well tolerated and may even improve cognitive functioning when used in conjunction with antiretroviral therapy ([48, 77]. Researchers also studied the use of anticonvulsants in treating acute manic episodes in those who are HIV positive. Romanelli et al. [73] found that anticonvulsants may interact with anti-

Table 9.4 Common side effects of mood stabilizers

Mood stabilizer	Comments
Lithium	Lithium is exclusively dependent on renal excretion If renal function is compromised or if there is hyponatremia, lithium levels can be affected Common side effects include fatigue, slower cognition, weight gain and skin changes Symptoms of lithium toxicity (serum levels >1.5 mEq/L) include tremor, nausea, vomiting, diarrhoea, vertigo and confusion which may mimic HIV symptoms Plasma levels >2.5 mEq/L require haemodialysis and may lead to seizure, coma, cardiac arrhythmia and permanent neurological damage [20]
Valproic acid	Prone to complicated drug interactions such as hepatotoxicity, thrombocytopenia, hyperammonemia, weight gain and metabolic syndrome Lowering VPA serum levels may be seen due to metabolic induction by ritonavir and lopinavir/ritonavir combination [24]
Carbamazepine	Potent pan-inducer with the potential to reduce the levels of protease inhibitors and NNRTIs [63, 93]
Lamotrigine	Used for bipolar and unipolar depression but it has not been extensively studied in persons with HIV

Adapted from Cozza et al. [23]

retroviral medication by competing for protein binding, affecting drug metabolism and increasing viral load [73]. More research is needed to better understand the safety and efficacy of using mood stabilizers among those with HIV (Table 9.4).

9.6.4 Antipsychotics

According to a study by Hill and Lee [39], typical antipsychotics such as haloperidol and chlorpromazine appear to be initially helpful in treating delirium and improving cognitive functioning among those with HIV; however, this change appears to be short lived and dissipates within 24–48 h. Caution should be taken when prescribing antipsychotics to those with HIV because studies have indicated that HIV-positive individuals are particularly susceptible to developing extrapyramidal side effects following the initiation of antipsychotics [41]. Studies have also indicated the potential benefit of using atypical antipsychotics such as clozapine and risperidone to treat HIV related psychosis [49, 79]. Similar to the field of research examining mood stabilizers and anxiolytics among those with HIV, research aimed at understanding the use of antipsychotics with those receiving care for HIV is quite limited at the moment (Table 9.5).

Table 9.5 Common side effects of antipsychotics

Antipsychotic	Comments
Aripiprazole	Less risk of EPS, metabolic syndrome and QT interval prolongation Potential of increasing aripiprazole's serum levels when used with inhibitors such as protease inhibitors
Asenapine (Saphris)	QTC prolongation Not recommended in patients with severe hepatic impairment
Brexpiprazole	Increased risk of akathisia
Clozapine	Risk of agranulocytosis Cardiac risks: Bradycardia, syncope QTc prolongation, myocarditis/ cardiomyopathy, orthostatic hypotension Risk of seizures
Olanzaepine	Co-administration of fosamprenavir/ ritonavir may reduce olanzapine levels
Paliperidone	Risk of QTc prolongation Gastrointestinal narrowing and dysphagia
Quetiapine	Associated with QTc prolongation

Adapted from Cozza et al. [23]

9.6.5 Non-Pharmacological Approaches in HIV Associated Psychiatric Disorders

Psychotherapy for those with HIV and psychiatric manifestations is often prescribed alone or in conjunction with psychopharmacological treatments. Cognitive behavioural therapy (CBT), a type of psychotherapy, has shown promising results among those with HIV and mental illness

such as depression, substance use issues and anxiety. In fact, Clucas et al. [22] conducted a systematic review of interventions for anxiety in people with HIV and found that, in general, CBT and cognitive behavioural stress management interventions were more effective in treating anxiety than pharmacological interventions.

Cognitive behavioural therapy involves teaching patients skills so that they are able to change their maladaptive thoughts and behaviours to be more adaptive [30]. A study by Safren et al. [75] found CBT given to those with HIV and depression over the course of 10–12 sessions was helpful in both increasing adherence to medication and decreasing depressive symptoms. It was also reported that improvements were maintained at the 1 year follow-up. Interestingly, telephone-based CBT also appears to show merit when used with individuals with HIV suffering from major depressive disorder [11]. A randomized control study found telephone CBT to be just as effective as face-to-face CBT. The results of the study also indicated that telephone CBT increased patient adherence to HIV medication to a greater extent than compared to face-to-face CBT [11]. Another study examined the effectiveness of CBT, contingency management and CBT with contingency management among homosexual and bisexual men with HIV who abused methamphetamines [81]. Contingency management involves the use of positive reinforcement to reshape the behaviour of an individual and in the case of the study, to decrease the use of methamphetamines. The study found the combination of CBT and contingency management and contingency management alone both significantly reduced drug use among participants as compared to CBT alone.

Another psychotherapy called interpersonal psychotherapy (IPT) also appears to be effective in treating mental illness among those with HIV [52]. Interpersonal psychotherapy involves examining how the patient's mental illness affects their interpersonal context. Often the patient's past and current relationships are examined to identify how their mental illness has influenced their relationships and what interpersonal changes can be made in the future. Studies have tested interpersonal psychotherapy with groups of HIV-positive individuals, and researchers have generally found that this type of psychotherapy was helpful in reducing depression symptoms [6, 13, 83].

Disclosure Statement The authors do not have any disclosures.

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