

Review Article

Depression in Patients with HIV/AIDS

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ABSTRACT

Depression is common in patients with HIV/AIDS, and its identification and treatment are critically important in disease management. Despite depression's high prevalence and major impact on patient's quality of life, questions remain regarding its epidemiology and preferred treatment. The authors of this paper summarize available

information on the epidemiology of depression in HIV/AIDS, review treatment options, and discuss possible interactions between antidepressants and other agents. This may be useful in the better management of HIV/AIDS patients.

KEYWORDS: depression, epidemiology, HIV/AIDS, treatment

INTRODUCTION

Depression is one of the major disabling factors in any chronic illness. Diagnosis and optimal treatment of depression in HIV/AIDS patients is complicated by interactions between the disease conditions as well as among the pharmacological agents used to treat them. Diagnostic challenge in many such chronic disorders is mainly due to association of similar features as the symptoms of the chronic disorder itself. HIV infection is one such condition where the disease itself may cause many symptoms resembling those of depression. On the other hand, several psychiatric conditions including depression may predispose individuals to acquiring HIV infection as a consequence of their influence on behaviour^[1,2]. Treatment of depression in HIV/AIDS patients is jeopardized not only by the inability to diagnose the condition specifically but also by poor adherence to treatment, which has many social, medical and non-medical factors. This review summarizes the current knowledge on the epidemiology and different aspects in management of depression in HIV/AIDS.

EPIDEMIOLOGY

Prevalence of depression among HIV infected population is shown to be varying from 0 - 47% in different studies. Despite this, a meta-analysis of ten studies comparing HIV-positive and at risk HIV - negative patients demonstrated a twofold increase in the prevalence of major depression in patients infected with HIV^[3]. This variation is wide enough to raise questions on the methods and criteria used in the different studies. There are conflicting results

regarding the influence of stage of HIV infection on depression and anxiety. One study showed poor correlation with severity of apathy and cognitive performance with incidence of depression^[4]. Another study conducted at a specialty HIV clinic at a tertiary health care centre in South India reported 40% of seropositive individuals suffering from syndromal depression. Anxiety severe enough to fulfill the ICD-10 criteria for generalized anxiety disorder has been found in 90% of the HIV infected individuals with depressive symptoms. Suicidal tendency among HIV patients was highest during the first week after the revelation of the seropositive status and all of those who attempted suicide had past history of psychiatric illness^[5,6]. Majority of studies done in India have reported higher rates of depression among women compared to men which is implicated to higher caregiver burden, more social stigma and poor healthcare^[7]. Greater severity of depression, on the other hand, has been found to be associated with greater frequency of injection risk behavior among depressed injection drug abusers making them more vulnerable to HIV infection^[1,2].

DIAGNOSIS OF DEPRESSION IN HIV/AIDS

Several barriers exist in diagnosis of depression in HIV/AIDS patients. Patients may be unwilling to discuss their moods and emotions with the health care provider for fear of being stigmatized further^[7]. For the health care provider diagnosis of depression in HIV/AIDS patients is not an easy task as the depressive symptoms such as fatigue, insomnia, weight loss etc. may be taken as part of

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disease itself, and serious thought to diagnose a separate psychiatric disorder is not entertained. The diagnosis may be further complicated by the presence of comorbid neurological illness, substance abuse and use of multiple drugs including antiretroviral drugs that are known to cause depressive symptom as a side effect. Importance of diagnosis of major depression in HIV/AIDS lies in the fact that response to therapy in HIV/AIDS patients is as good as in uninfected population and when not recognized it has negative impact on adherence with medical treatments, quality of life and overall outcome^[8]. To overcome the diagnostic barrier, it is recommended that health care providers should encourage expression of emotions in clinics and non-specialists need training in the assessment of psychiatric syndromes in HIV patients^[7]. Several types of clinical rating scales have been developed for diagnosis and rating of depression. Study has shown that in otherwise asymptomatic HIV infected patients physical symptoms of fatigue insomnia, weight loss are related to psychological disturbance possibly major depression^[9]. Difficulty in early diagnosis is an important issue because one study has shown that only about half of HIV infected patients in US receive antidepressants^[10].

Differential diagnosis of Major depression in HIV/AIDS

The differential diagnosis of depression includes non-pathological states of grief and mourning which may be very severe in some cases and a variety of disorders related to both psychological and physiological disturbances. Complaints of depressive syndrome can be representative of dementia, delirium, intoxication, CNS injury or infection, and other acute medical conditions. AIDS dementia and other HIV related CNS conditions can produce a flat apathetic state that is often misdiagnosed as depression. Cocaine withdrawal produces a depressive syndrome and delirium that can mimic many psychiatric conditions. CNS syphilis, otherwise a rare condition, may be misdiagnosed as a psychiatric illness in HIV/AIDS patients^[9].

Effect of depression on course of HIV infection

This is another area facing a lot of conflicts. Some studies have shown lack of association between depression and course of HIV infection while others have shown poorer outcome in patients with depression. This may be due to poor adherence to treatment regimen and self-care as well as stress induced immune dysfunction as decreased number of natural killer cells and B lymphocytes have been shown at low viral load^[7].

TREATMENT OF DEPRESSION IN HIV/AIDS

Further complicating the issue starting from diagnostic problems, treatment of depression in HIV/AIDS patients faces many limitations from both sides: patient and health care provider. Patients already on multiple drugs for HIV and other infections may have tendency to have poor compliance to antidepressants and health care provider may also be reluctant to add drugs to patients who are already on multiple drugs. Furthermore, it was seen in a trial with fluoxetine that the drug was found to be effective in comparison to placebo but the attrition rate was high. The trial also concluded that the severity of immunosuppression was not related to antidepressant response, attrition or side effects and fluoxetine treatment was not associated with change in CD4 cell count^[10].

Selective Serotonin Reuptake Inhibitors (SSRIs) now are the most widely used drugs for treatment of depression in general population because of their favorable safety profile and convenient once a day dosing. SSRIs have been found to be effective in treating depression in HIV/AIDS patients^[10,11]. Choice of antidepressants in HIV infected patient is still not guided by evidence as controlled trials comparing SSRIs are lacking and it is suggested that most SSRIs can be used in HIV positive adults. When drug-drug interaction is a concern, sertraline, citalopram and escitalopram may be considered^[11]. A study examining ethnic differences in response to antidepressant treatment showed that attrition rate was greater among Latinos than either blacks or whites. Black patients were more likely than whites to be nonresponders to fluoxetine. Latinos were more likely to respond to placebo compared with blacks and whites. Ethnic groups did not differ in the presence of treatment-emergent side effects^[12]. Dehydroepiandrosterone (DHEA) has been shown to be efficacious in treatment of non-major persistent depression in patients with HIV/AIDS being superior to placebo in reducing depressive symptoms. The trial had showed not only low attrition rate in the group of physically ill patients but also there were requests for extended open label treatment showing high acceptance of the preparation^[13]. But another controlled trial with testosterone did not show any benefit over placebo in terms of reduction of depressive symptoms^[14].

DRUG INTERACTIONS

Since HIV/AIDS patients, when indicated, receive multiple drug therapy for HIV infection itself or for prophylaxis or treatment of opportunistic infections there is high chance of drug-drug interaction producing unfavorable outcome.

Because protease inhibitors (PIs) produce favorable long-term suppression of viremia, elevation of CD4 lymphocyte count and retard disease progression with improved survival when combined with other antiretroviral agents, they form an integral part of Triple therapy in HIV infection. Interaction of PIs is mainly due to inhibition of Cytochrome P450 enzymes CYP3A4 and CYP2D6. Potency of enzyme inhibition varies among different PIs, ritonavir being the most potent one. PIs other than ritonavir mainly inhibit CYP3A4 while ritonavir inhibits CYP2D6 enzyme. PIs have been reported to increase the concentration of bupropion, nefazodone and fluoxetine to toxic levels and to increase the concentration of desipramine by 100 to 150 percent^[15]. However, one pharmacokinetic study concluded that dose of ritonavir need not be reduced in patients concomitantly receiving fluoxetine^[16]. In patients receiving antiretroviral therapy along with fluoxetine, serotonergic syndrome has been reported and this should be suspected in patient on any serotonergic drug taking cytochrome P450 enzyme inhibitors such as PIs, non-nucleoside reverse transcriptase inhibitors and grapefruit juice. Serotonergic syndrome is characterized by mental status change, autonomic dysfunction and neuromuscular abnormalities^[15]. PIs may also increase the plasma level of some benzodiazepines such as alprazolam, midazolam, triazolam and non-benzodiazepine hypnotic zolpidem^[16]. Ritonavir, nelfinavir and amprenavir are also moderate inducers of some of the hepatic enzymes including CYP3A4. This may complicate the interaction on long term and therapeutic drug monitoring should be taken as guide for antidepressant therapy and dosing when required. Furthermore, since generalized anxiety is very common in depressives having HIV infections, along with antidepressants anti-anxiety agents may be required. Significant interactions between antidepressants and anxiolytics include:- tendency of fluvoxamine to increase the plasma concentration of oxidatively metabolized benzodiazepines, and sertraline along with fluoxetine increasing the level of benzodiazepines. Nefazodone potentiates benzodiazepines other than lorazepam and oxazepam^[16]. It has also been shown to increase plasma level of indinavir and efavirenz^[8]. These interactions may be important in HIV patients because the higher level of benzodiazepine may mask the improvement obtained by the use of antidepressants in terms of somatic as well as psychological symptoms. Fluvoxamine and fluoxetine increase the plasma level of most of PIs along with that of delavirdine and efavirenz. On the other hand, nevirapine decreases the plasma level of both the antidepressants^[8].

Additional Issues

HIV/AIDS is not only responsible for individual morbidity and mortality but also is a familial and social burden by itself. Treatment of HIV infection is costly and complicated. High incidence of depression and anxiety further aggravates the complication. Besides pharmacotherapy, supportive psychotherapy has an important part to play in the treatment of those patients who interpret their symptoms to be reaction to the diagnosis of HIV infection. Other forms of useful psychotherapy are interpersonal psychotherapy and cognitive-behavioral psychotherapy and they are more effective when combined with pharmacotherapy for treatment of severe depression^[8].

CONCLUSION

Diagnosis and management of depression is an important factor for optimal outcome of HIV/AIDS patients. Safe and effective treatment of major depression, one of the most common comorbid conditions in individuals infected with HIV, significantly lowers morbidity and mortality of HIV disease. While possibilities of underdiagnosis and over-diagnosis exist, optimum management should be guided by correct diagnosis.

Important drug-drug interactions exist among the antiretrovirals, antidepressants and anti-anxiety agents which sometimes may lead to serious consequences such as serotonin syndrome. To avoid these consequences therapy should be undertaken in a specialty clinic whenever possible and alternatives to proper antidepressants such as DHEA should be considered in moderate depression particularly for debilitated patients when the antidepressants are less likely to be tolerated.

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