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The impact of mental health and traumatic life experiences on antiretroviral treatment outcomes for people living with HIV/AIDS

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Potent antiretroviral therapy (ART) has transformed HIV from a death sentence to a chronic illness. Accordingly, the goal of HIV care has shifted from delaying death to achieving optimal health outcomes through ART treatment. ART treatment success hinges on medication adherence. Extensive research has demonstrated that the primary barriers to ART adherence include mental illness, especially depression and substance abuse, as well as histories of traumatic experiences such as childhood sexual and physical abuse. These psychosocial factors are highly prevalent in people living with HIV/AIDS (PLWHA) and predict poor ART adherence, increased sexual risk behaviours, ART treatment failure, HIV disease progression and higher mortality rates. The efficacy of standard mental health interventions, such as antidepressant treatment and psychotherapy, has been well-defined, and a small but growing body of research demonstrates the potential for such interventions to improve ART adherence and reduce sexual risk behaviours. Despite this evidence, mental disorders in PLWHA frequently go undiagnosed and untreated. Challenges to the provision of mental healthcare for PLWHA in HIV clinical settings include time and resource constraints, lack of expertise in psychiatric diagnosis and treatment, and lack of available mental health referral services. Future research should prioritize the evaluation of mental health interventions that are cost-effective and feasible for widespread integration into HIV clinical care; the impact of such interventions on ART adherence and clinical outcomes; and interventions to identify individuals with histories of traumatic experiences and to elucidate the mechanisms through which such histories pose barriers to effective HIV treatment.

Keywords: mental illness, depression, trauma, adherence

Introduction

The introduction of increasingly potent combination antiretroviral treatment (ART) regimens over the past 12 years has dramatically reduced HIV-related morbidity and mortality in wealthy countries, with the life expectancy of HIV-infected patients on ART now approaching that of the general population.[1] With the transformation of HIV/AIDS from a practical death sentence to a chronic illness, the objective of HIV clinical care has increasingly focused on using ART to achieve sustained suppression of HIV RNA plasma levels and thereby optimize HIV health outcomes.

Health outcomes among people living with HIV/AIDS (PLWHA) on ART are heavily influenced by medication adherence. The levels of adherence required to prevent viral mutation and ART resistance are very high by the standards of other chronic illnesses,[2,3] and much research has focused on the determinants of and barriers to ART adherence and optimal HIV health outcomes. A large body of literature, recently summarized in a set of comprehensive review articles,[4,5] now demonstrates the important role of psychosocial factors, including depression, substance abuse, stress and traumatic life experiences, in influencing ART adherence and treatment outcomes for PLWHA.

Depression, trauma and other types of psychosocial adversity are highly prevalent in PLWHA.[6] Mood and anxiety disorders, particularly depression, are the most common psychiatric diagnoses,[7–10] and are 5–10 times more common in PLWHA than in the general population.[11] In the USA, approximately half of PLWHA have significant depressive symptoms and 20% to 25% meet diagnostic criteria for a depressive disorder.[12,13] Depression is twice as common in PLWHA as in comparable controls.[14] The presence of multiple rather than a single psychiatric diagnosis (e.g. co-morbid depression and substance abuse) is the norm rather than the exception.[15]

While depression is widely recognized as an important concern for PLWHA, perhaps less appreciated are the prevalence and consequences of past and ongoing traumatic experiences.[16] Numerous studies have documented substantially higher

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prevalence of childhood sexual and physical abuse, exposure to other traumatic experiences and subsequent post-traumatic stress disorder (PTSD) among both men and women living with HIV/AIDS compared with nationally representative general population samples (reviewed in Brief *et al.*[17]). This association between trauma history and HIV status may indicate a causal relationship (e.g. childhood sexual abuse has been linked to higher rates of sexual and drug use behaviours that increase the risk of HIV infection) or may reflect the concentration of HIV in marginalized and disadvantaged populations at high risk of trauma exposure.[17]

This tapestry of adversity has important implications for patients' success in HIV clinical care. Current mental illness, especially depression and substance abuse, predict lower ART adherence,[18] a greater likelihood of failing ART[19] and increased mortality.[20] Similarly, patients with more lifetime trauma exposure are less adherent to ART,[21] have more emergency room visits and hospitalizations[22] and have faster rates of HIV disease progression and mortality.[23,24] These associations have generally shown consistent dose–response relationships: the odds of ART non-adherence[21] and the incidence of opportunistic infections[24] increase with each additional lifetime traumatic experience, and PLWHA with chronic depression over years of follow-up have higher mortality rates than those with intermittent or no depression.[20]

The evidence linking depression to adverse HIV-related behaviours and outcomes is striking in its strength and consistency.[5] The studies that have focused on trauma exposure and PTSD in HIV, particularly as they relate to behaviours and health outcomes, are relatively few in number.[17] The definition of the PTSD diagnosis has engendered much debate, especially related to the 'criterion A problem' (which types of events should be allowed as potential precipitators of PTSD),[25] the 'threshold problem' (whether PTSD represents the upper end of a continuous spectrum of psychological response to extreme stress or a clearly bounded pathological state qualitatively distinct from non-pathological stress responses)[26] and the veracity of self-report.[27] However, a broad consensus supports the existence of the PTSD diagnosis, and a number of psychometrically sound instruments exist to measure both trauma exposure and PTSD symptomatology.[25,28]

The pathways through which mental illness and lifetime trauma influence HIV treatment outcomes have not been fully elucidated. Greater severity of depressive symptoms was linked to faster CD4 decline even before the era of highly active ART,[29] and some studies have suggested a direct influence of depression on the immune system,[30] possibly mediated by diminished natural killer cell counts.[31,32] However, the effect of these psychosocial factors on virological, immunological and clinical outcomes is presumed to operate primarily through reduced ART adherence. Past trauma may influence adherence through current mental health or substance use, trust in the healthcare system, coping styles, social support or self-efficacy, although adjustment for measures of these constructs in observational data has generally not explained the associations between trauma, adherence and outcomes.[21] Nevertheless, the evidence supporting the relevance of trauma history and mental illness for HIV treatment outcomes is compelling.

Mental health treatment for PLWHA

Effective interventions to address mental health disorders in PLWHA have been well-defined.[33,34] Recent systematic reviews have underscored the efficacy of standard antidepressant and group therapy-based treatment modalities in depressed PLWHA.[35,36] Strategies to address more complicated psychiatric presentations, such as co-morbid mental health and substance abuse disorders, have also shown promising results in reducing psychiatric morbidity.[37] Interventions targeted specifically at addressing PTSD in HIV-infected survivors of childhood sexual abuse are also effective in reducing psychiatric symptoms and improving coping skills.[38,39]

Further, there is accumulating evidence that treating mental health disorders leads to improved HIV behaviours and clinical outcomes for depressed PLWHA. A small number of randomized clinical trials have shown beneficial effects of various psychotherapy-based interventions for PLWHA on HIV medication adherence and sexual risk behaviours.[39–42] Antidepressant treatment for depressed PLWHA has also been associated with improved HIV medication adherence in retrospective observational data,[43–45] although no experimental data on this question have been published to date.

Challenges for clinical care

Despite the relevance of mental health disorders for HIV outcomes and the availability of proven mental health interventions, the available evidence indicates that mental disorders in PLWHA frequently go undiagnosed and untreated. In a large cohort of patients experiencing HIV care in the USA, nearly half of those meeting criteria for major depression had no record of such a diagnosis in their medical record,[46] and one-third of those needing mental health services were not receiving them.[47] These deficiencies in diagnosis and treatment likely reflect a number of dynamics. In wealthier countries, HIV is primarily affecting disadvantaged populations with limited interaction with the healthcare system. For many HIV patients, therefore, their HIV provider effectively serves as their primary care physician, and HIV clinical care is the primary point at which a mental illness could be identified and an intervention could be pursued. Providers trained as infectious diseases specialists, however, may perceive themselves as ill-equipped to look for and treat psychiatric illnesses and therefore may be reluctant to fill such a role. When a mental illness is identified, HIV providers may make a referral to a mental health specialist, yet patients may fail to complete the referral for a variety of reasons, including the stigma of mental health services and financial and time barriers.

How can mental health disorders be addressed more systematically in HIV clinical care? First, to address the under-diagnosis of such disorders, HIV clinics should screen all presenting patients at regular intervals for mental health problems. Several mental health screening instruments have been adapted successfully for such purposes, including instruments that were designed for and validated in HIV patient populations.[48] Such instruments can usually be rapidly administered and scored by a nurse, assistant or other clinic staff member as part of a standard check-in process. This class of screening instruments generally has relatively high sensitivity but somewhat lower specificity, implying that positive screens require follow-up from a provider with some level of mental health training, such as a licensed social worker, to confirm the presence of a diagnosis.

Once a mental health disorder is identified, mental health treatment options must be in place. While referral to speciality

psychiatric services will be required for some patients, the integration of mental health treatment into HIV clinical care settings will likely have the greatest potential for effectively engaging and retaining patients in mental healthcare. While several examples exist of the successful integration of HIV and psychotherapy-based mental healthcare,[37,49,50] the large-scale adaptation of such psychotherapeutic interventions into HIV clinical care remains challenging because of staffing requirements and resource constraints.

Mental health interventions that equip existing HIV clinic staff with the tools to effectively prescribe and monitor antidepressant treatment may be more readily scaled up into widespread practice. One promising approach, known as measurement-based care (MBC),[51,52] is an evidence-based strategy for providing depression treatment in non-psychiatric settings by giving clinical coordinators the tools and supervision needed to accurately identify and effectively manage depression. In the MBC approach, the clinical coordinator provides decision support to the treating non-psychiatric clinician, addressing the lack of psychiatric expertise that is the norm in most HIV treatment settings without requiring the on-site presence of a psychiatrist. These clinical coordinators perform initial assessments, monitor symptoms and side effects using standardized tools at regular intervals and make dosing recommendations to the treating physician based on best-practices guidelines. The clinical coordinator role can be effectively filled by a social worker or nurse given appropriate training and supervision,[53] giving this model the potential to be replicated in a wide range of resource-constrained HIV treatment settings. MBC has been shown to be effective in treating depression in primary care settings[54] and has been successfully adapted to resource-constrained environments,[53] although it has not previously been tested in HIV patients. Such approaches parallel the recent efforts in chronic disease models such as cardiovascular disease and diabetes care to empower 'care managers' to safely and effectively implement much of the day-to-day disease management with appropriate oversight from specialty medical providers.

Future directions

Research has demonstrated the high prevalence of mental health disorders as well as traumatic and severely stressful experiences in the lives of PLWHA. Individuals with mental illness, particularly depression and histories of traumatic experiences, are at increased risk of poor HIV medication adherence, HIV treatment failure and adverse clinical outcomes. While the need for comprehensive, accessible and effective mental health services for PLWHA is clear, the challenges are equally evident. At least three areas suggest themselves as high priorities for future research. First, mental health interventions should be developed and evaluated that are affordable, cost-effective and feasible for widespread integration into HIV clinical care. Second, evidence should be gathered on the effectiveness of such interventions not only in improving mental health but also in impacting HIV medication adherence and clinical outcomes so as to guide policy decisions on the appropriate allocation of limited resources. Third, particular attention is warranted for interventions to identify individuals in HIV clinical settings with histories of traumatic experiences and to understand and address the mechanisms through which such histories pose barriers to effective HIV treatment. In this era of highly effective long-term HIV treatment, addressing the mental health burdens of PLWHA will be an essential component of strategies to achieve optimal treatment response and health outcomes in HIV clinical care.

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