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End-of-Life Care and Bereavement Issues in HIV/AIDS

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Abstract

This review addresses end-of-life care issues characterizing HIV progression by delineating associated stages of medical and nursing care. Progression from the stage of primary medical and nursing care aimed at functional cure to the stage of palliative care is depicted first. This transition is considered in accord with the major symptoms experienced − fatigue, pain, insomnia, decreased libido/hypogonadism, decreased memory and concentration, depression, and distorted body image. From the stage of palliative care, progression is delineated onward through the stages of hospice care, death and dying, and, finally, an extension to the bereavement process (after the death of the patient her or himself).

Keywords

End-of-life; death; dying; bereavement; aging; HIV; AIDS

Key points

mortality in HIV/AIDS; stages of end-of-life care; palliative care and hospice care

This paper will address four areas over the spectrum of end-of-life issues and apply it directly to the area of HIV/AIDS: (1) palliative care; (2) hospice care; (3) death and dying and (4) bereavement. An issue with this spectrum from the outset is one of definition: there is a frequent lack of appreciation for the differences between palliative care and hospice care. Palliative care involves the evolution of a disease long-term such that it presents with a “comingled” symptom burden due to the presence of multiple medical co-morbid illnesses over time. The associated symptoms are not alleviated by the use of disease-specific medications and tend to persist – in many ways as indicators of chronic disease. Hospice care is care supporting the patient when the patient is imminently facing death and dying. These two areas of care overlap, but their goals are distinct. In the area of HIV/AIDS, where premature aging is known to occur, patients come to palliative care earlier than is expected.

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This is a result of the dramatically successful development of the antiretroviral (ARV) medication regimens for HIV infection in that the former causes of morbidity and mortality have shifted primarily from complications due to immunosuppression to those characteristic of aging in the general population. Once hospice care in older HIV infected persons has achieved its goals, then the care issues may move to the patient's experience of dying, and – with the patient's death – on to the experience of the patient's death by others (bereavement). It might be added that the hospice care stage also applies to how a patient begins to mourn her/his mounting losses of functional capacities and, ultimately, to mourn her/his own passing − in anticipation. Hence, each of the first three stages significantly overlap with one another in the patient, leaving us with the fourth stage of bereavement in the loved ones.

It has been over twenty years since the advent of effective antiretroviral therapy (ART), which had been rapidly demonstrated to dramatically reduce AIDS-related mortality and morbidity in the USA[1]. In line with the long-term impact of those well established treatment gains, it is anticipated that fully 50% of persons living with HIV infection in the USA will be age 50 or older by the year 2020. HIV-associated morbidity and mortality has melded with that of the general population – coronary artery disease (CAD) and MI; CVA; neurocognitive disorder; diabetes; and cancer. While it may occur over an extended period of time with HIV infection now, total physical and mental symptom burden eventually increase. Hence, the experience of HIV infection to the patient is eventually converted to one in which there is a generalized expression of HIV disease progression (partly, encompassed by the construct of "frailty") that – to some extent − is not due to specific disorders that can be diagnosed and effectively treated. In line with these characteristics, the associated symptoms with this chronic disease burden are less likely to become the primary focus of treatment attention by the primary care provider. Thus, there are a number of such somatic symptoms associated with the longevity of HIV infection itself (or duration of HIV serostatus). These symptoms include fatigue, pain, insomnia, decreased libido/hypogonadism, deceased memory and concentration (HIV-associated neurocognitive disorders), depression, and distorted body image. Palliative care for the chronic symptoms experienced by HIV infected patients focuses on the competent, skilled practitioners (effectiveness); confidential, nondiscriminatory, and culturally sensitive care (acceptability); collaborative and coordinated care (efficiency); flexible and responsive care (access and relevance to need); and fair access for all clients (equity). Palliative care has been associated with improved functional status in activities of daily living as well as with an improved quality of life in HIV infected persons.

Fatigue

Fatigue is among the most common and distressing symptoms in patients with HIV/AIDS, affecting 20% to 60% of patients and can be measured well with the HIV-Related Fatigue Scale.[2] It is associated with increased release of pro-inflammatory cytokines such as TNF-a, IL-1 and IL-6 from activated macrophages and with sickness behavior clinically. The pro-inflammatory cytokines, in turn, are associated with increased HIV replication and with HIV disease progression. This cause of fatigue in HIV infection is one amongst others that overlap with causes of fatigue outside of HIV infection, especially in older patients.

Common causes of fatigue include low testosterone levels, anemia, alcohol and substance use, insomnia, iatrogenic sources (e.g., prescribed medication toxicities), obesity, diabetes, CAD, renal dysfunction, hepatic dysfunction, comorbid hepatitis C virus (HCV) infection, and fevers of unknown origin. Other less common causes include cancer, COPD, thyroid disease, and toxin ingestions. Of these, it is useful to note that anemia (particularly the anemia of chronic disease) is common in HIV infection, is an important cause of fatigue, and is a known risk factor for mortality in patients with HIV disease. Erythropoietin therapy is a safe treatment that is preferred to blood transfusions; improves quality of life; and may (as a neurotrophic therapy) improve cognition and neuropathic pain (typically due to HIV-associated distal sensory polyneuropathy) as well.[3] The symptom of fatigue in HIV infection should be addressed with a complete medical/nursing work-up. Treatment should be offered for any specific, curable identified disease as well as for fatigue that may be evaluated as due to a persisting, identified disease (e.g., HCV infection), or for fatigue thought to be due directly to HIV infection itself. Treatments for fatigue reported to have success with minimal side effects in the HIV infected have been modafinil and armodafinil.[4]

Pain

Pain is a symptom that has been noted for some time to be under-identified and under-treated in HIV infected patients.[5] The most common pain diagnoses in HIV infected patients were: headache (46% of patients), joint pain (31% of patients), pain due to polyneuropathy (28% of patients), and muscle pain (27% of patients). One review of 61 studies showed that the prevalence of pain in HIV infected patients ranged from a point prevalence of 54% to 83% using a three-month pain recall period.[6] The reported pain was typically of moderate-to-severe intensity, and pain was reported in 1 - 2.5 different sites. It is common for several different disorders to contribute to the experienced pain level of an HIV infected patient at any given time. Moderate levels of pain interference with function were generally reported. All studies that reported on the adequacy of pain management recorded that there was a marked under-treatment of pain. Regarding treatment, it has been reported that HIV-infected more commonly receive opioids than HIV-uninfected persons.[7] However, HIV infected patients received fewer days of opioids than uninfected patients and were less likely to receive long-term opioids. It is not possible here to address the complexity of pain management issues in this diverse patient group with multiple sites of pain on a chronic basis. However, it can be recommended that an effort should be made to develop pain management guidelines specific to the HIV infected population, as the data to date show that HIV infected patients continue to be under-treated for pain − despite numerous studies published that document the frequent occurrence of pain in this population.

Insomnia

Insomnia is a common complaint in people with HIV and AIDS. One review reported that insomnia occurred in as many as 73% of out-patients with HIV infection.[8] Early studies reported sleep-specific EEG changes related to HIV infection, especially increases in slow-wave sleep, but these results have not been confirmed by controlled studies since that time. Reports of insomnia are reported at all stages of HIV disease. While insomnia is frequently reported as a side effect of effective ART, studies evaluating these medications have not

demonstrated a significant effect − with the exception of efavirenz [found to be an independent predictor of insomnia[9]] − and of raltegravir.[10] A large epidemiological study of insomnia prevalence among HIV infected persons demonstrated that HIV infected persons had a high prevalence of insomnia (and daytime sleepiness).[11] However, HIV infected persons did not have a significantly higher rate than matched HIV seronegative persons − although those data might be limited in generalizability to only HIV infected persons who were diagnosed and treated early. Treatment is best initiated with non-pharmacological techniques, especially given the prevalence of concern for drug-drug interactions of psychotropic agents with the ARVs in HIV infected persons. Hence, treatment should begin with sleep hygiene, relaxation training, mental imagery, cognitive behavioral therapy and self-hypnosis as well as yoga and acupuncture.[12] If pharmacological treatment is necessary, melatonin may be used without moving to prescribed agents. Amongst the prescribed agents, there is little to no HIV-specific randomized controlled trial evidence available, though a variety of agents have been identified as “first-line”. These include very low-dose doxepin, mirtazapine, oxazepam, and zaleplon (for sleep-onset insomnia).[13] More recently, ramelteon (as a melatonin agonist) should be considered for this specific indication.

Decreased Libido/Hypogonadism

A very common problem in HIV infection is the problem of decreased sexual drive and gonadal function. Moreover, the frequency with which this complication occurs in HIV infected persons is compounded by the stigma HIV infected persons face related to being active in their sexual interests. Low levels of testosterone may lead to fatigue, loss of libido, and dysphoria. Testosterone levels naturally decline with age, with about 20% of men over 60 and 50% of men over 80 having low levels of testosterone. In HIV infected persons, 30–50% have low testosterone levels, and the cause(s) remain poorly defined. Testosterone replacement can be done by multiple routes (topical, injection, or oral). Each route has its own advantages and disadvantages. Testosterone replacement for HIV infected persons has become widely accepted. Yet, recent reports have made testosterone replacement increasingly controversial.[14] Several recent studies have associated testosterone replacement with increased risk for cardiovascular complications. In fact, it has been suggested that testosterone replacement should be reserved, when possible, until additional, controlled studies of the efficacy and safety of testosterone replacement are carried out amongst the HIV infected.

Decreased Memory and Concentration (HIV-Associated Neurocognitive Disorders/HAND)

Decreased memory and concentration (and “neurocognitive impairment” [NCI], more generally) can occur in any stage of HIV disease but are most commonly seen in late stage disease/AIDS. Currently, HAND is reported to occur in approximately 50% of HIV infected persons in the USA on stable, effective ART. Of note, NCI may be the first symptom of AIDS in 10% or more of patients. The Frascati Conference re-defined HAND to be comprised by three categories: asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND), and HIV-associated dementia (HAD).[15] ANI is a condition

(not a disorder) and occurs when there is significant decline in two or more domains of neurocognitive performance assessed by standardized testing but no significant decline in activities of daily living (ADLs). It is estimated that ANI (unlike MND and HAD) has not significantly declined in prevalence in the era of effective ART. For MND, there must be mild NCI in at least two domains of cognitive performance and mild functional impairment in ADLs. For HAD, there must be moderate-to-severe NCI in two or more domains of cognitive performance accompanied by at least moderate impairment in ADLs due to the NCI. Further, HAD is an AIDS-defining clinical diagnosis.

Screening for HAND has been documented not to be accomplished well by the widely used Mini-Mental State Examination (MMSE), which is focused on cortical deficits rather than the subcortical deficits more prominent in HAND. Likewise, the Montreal Cognitive Assessment (MoCA) screening test useful in the general population for minor cognitive impairment has not been documented to be highly useful for HAND.[16] Evidence suggests that HIV-specific screening tests remain useful, including the HIV Dementia Scale (HDS)[17] − though this test has been found to be lacking in sensitivity at lower levels of impairment as well as to be culturally delimited. The International HIV Dementia Scale (IHDS)[18] is culture-fair and has somewhat greater evidence supporting its ongoing use in the era of effective ART.[19–20] However, current HIV-specific screening tests might well need to add selected, formal neuropsychological tests to optimize the screening accuracy for the presence and severity of HAND. While formal neurocognitive testing at screening is not feasible, it is worth noting that patients may be screened with a self-report measure while waiting for their clinic appointments using the Medical Outcomes Study-HIV (MOS-HIV) cognitive functioning scale,[21] though self-report tests are limited when compared with tests that objectively assess cognitive function.

The diagnosis HAND demands a thorough medical/nursing work-up, as it remains a diagnosis of exclusion. The work-up should include CT or MRI of the brain to rule out other causes of NCI and a lumbar puncture (also to rule out other causes, as well as for an HIV load test). Metabolic causes and toxicity of alcohol, psychoactive substances and prescribed medications must also be ruled out. Regarding treatment, reducing the impact of treatable, comorbid medical/nursing and psychiatric/mental health nursing conditions is a useful place to start, such as diabetes, hypertension, chronic pain, depressive disorders and alcohol and substance use disorders. Second, the use of non-pharmacological methods should be evaluated, such as physical exercise and mental exercise as well as formal cognitive rehabilitation techniques. Teaching patients to make and use lists and to employ electronic reminders as well as to use homework assignments on web sites displaying cognitive exercises are all helpful in translating the insights from the clinic on specific cognitive deficits into improvements in a patient's ADLs. Third, pharmacotherapy may be indicated, with the use of CNS-penetrating effective ART regimens and the psychostimulants being most generally recommended.[22]

Depression

"Depression" is a non-specific term with multiple potential meanings. The most common representation is as a level of depressed mood, which we all experience in everyday life.

However, it also represents a whole spectrum of disorders in which depressed mood co-occurs with a constellation of associated symptoms and is severe and consistent enough to affect ADLs, e.g., major depressive disorder (MDD). MDD occurs at greater than three times the rate of the general population in HIV infected persons.[23] "Depression" can also refer to adjustment disorder with depressed mood, dysthymia, substance-induced depressive disorder, and other related syndromes. When an HIV-infected patient who has not yet experienced any symptoms of HIV infection experiences her/his first symptom recognized to be referable to HIV, she/he can no longer believe that HIV will never cause illness, dysfunction and death. The ensuing general uncertainty about one's own health status is associated with an increased frequency of depressive spectrum disorders – more importantly than depressed mood level taken alone. The patient must learn to cope with this new uncertainty. It is important to be aware that the manifestations of depressive disorders may be confused with those of HAND or, in reality, depressive spectrum disorders and HAND may be co-occurring − despite the fact that the diagnostic criteria for HAND do not allow for comorbid depressive disorders because of their potential impact on neurocognitive function.[15]

Regarding the impact on HIV infection itself, MDD may be treated with the same medications that would be indicated for MDD outside of HIV infection. However, important considerations are side effect profiles and the potential for drug-drug interactions. Of the SSRIs, paroxetine – which may also treat HAND[24] − has been favored as well as citalopram. Fluoxetine is best avoided because of its long half-life and the longer half-life of it primary metabolite (norfluoxetine) and because of their metabolism on both the CYP P450 2D6 and 3A4 isoenzyme systems. Of relevance to drug-drug interactions, these isoenzyme systems are also used by the ARVs. Bupropion in its higher dose range should also be avoided due to its dose-dependent seizure diathesis combined with that of HIV infection of brain itself.

It is also relevant to note that MDD has long been known to be associated with immunosuppressive effects in persons with HIV infection. MDD has been associated with decreased natural killer activity as well as increased CD8+ T cell activation in HIV infected women.[25] In numerous studies of MDD, MDD has been found to be associated with increased production of pro-inflammatory cytokines that are secreted by activated macrophages in persons with HIV infection. This relationship provides a potential ground for a true synergism between MDD and HIV infection on clinical inflammatory outcomes that are of prominent concern today due to greater inflammation-mediated rather than immunosuppression-mediated causes of morbidity and mortality amongst the HIV infected with long-term suppression of plasma viral load on effective ART regimens. Martinez et al. [26] reported on a prospective cohort of 504 HIV-infected individuals initiating their first ART regimen in rural Uganda and found that higher levels of depressive symptoms were associated with both lower levels of plasma tryptophan and a higher plasma kynurenine/tryptophan (KT) ratio over 12-month follow-up. In contrast, declines in the KT ratio and increases in plasma tryptophan levels partially explained effective ART-mediated improvements in depressive symptom severity in that study. An increased production of 3-OH-kynurenine or quinolinic acid (formed later in the kynurenine pathway), or both, is found in HIV infected persons. Relatively low levels of 3-OH-kynurenine can cause neurotoxicity by inducing oxidative stress and neuronal apoptosis. After interaction with

cellular xanthine oxidase, 3-OH-kynurenine produces reactive oxygen species (such as superoxide radicals) that cause inter-nucleosomal DNA cleavage, and ultimately cell death through apoptosis. Over-production of reactive oxygen species has been associated with MDD. In addition, quinolinic acid is a potent N-methyl-D-aspartate receptor agonist, and intra-hippocampal injection of quinolinic acid in rats is known to cause substantial loss of hippocampal neurons. This links the over-production of quinolinic acid directly with the hippocampal atrophy observed in MDD. Hence, MDD-associated impacts on inflammation could well play a role in the determination of the clinical outcomes of effective ART amongst HIV infected persons.

Distorted Body Image

With the advent of the era of effective ART, one toxicity that soon became apparent was the lipodystrophy syndrome, initially termed “Crix belly” after the early protease inhibitor ARV, Crixivan/indinavir. Lipodystrophy remains an incompletely understood condition characterized by a combination of central fat accumulation, peripheral fat depletion, and metabolic disturbances. An early study of HIV-infected heterosexual women and men who have sex with men (MSMs) with lipodystrophy syndrome showed erosion of self-image and self-esteem, problems in social and sexual relations, threats to locus of control, forced HIV disclosure, demoralization, and depressed mood.[27] Two well validated instruments are the Body Image Quality of Life Scale and the Situational Inventory of Body Image Dysphoria. They successfully have been used to measure body image effects. Self-reports of decreased facial fat and sunken cheeks were associated with lower infra-orbital, buccal, and submandibular skin folds; self-report of a “buffalo hump” was associated with a greater neck circumference; and self-report of abdominal enlargement was associated with increased waist circumference.[28] Men were most commonly affected by lipoatrophy and women by lipohypertrophy.

Regarding treatment, non-pharmacological means can be effectively utilized first. A recent two-arm randomized controlled trial (RCT) (n = 44) comparing cognitive behavioral therapy (CBT) for body image and self-care compared to an enhanced treatment-as-usual condition at three and six months after baseline showed at three months that the CBT condition demonstrated substantial improvement in body image disturbance, depressed mood level, and ARV adherence.[29] The results were generally maintained, or improved, at six months. Regarding pharmacological treatment, RCTs of switching specific ARVs have not had favorable effects on the volume of abdominal adipose tissue. Several small studies of life style interventions, such as supervised aerobic and progressive resistance training, have reported modest to no reductions in abdominal adipose tissue but have yielded some improvements in associated metabolic abnormalities. While these trials have been disappointing, life style interventions are safe and appropriate to recommend as general health measures for patients with lipohypertrophy. The data do not support recommending metformin as a specific treatment for lipohypertrophy, although it may be used for abnormal glucose homeostasis in patients with lipohypertrophy who have impaired fasting glucose, impaired glucose tolerance or type 2 diabetes mellitus and mild or no lipoatrophy.[30] Similarly, testosterone repletion is not indicated solely to improve body composition in this population. However, recombinant human growth hormone (rhGH) has been used to treat

AIDS-related wasting and was known to be lipolytic. Supra-physiologic doses of rhGH reduced visceral adipose tissue by 17–20% and improved lipid profiles in placebo-controlled trials in HIV-infected patients with abdominal obesity. The most promising intervention for lipohypertrophy is tesamorelin, a synthetic analogue of growth hormone releasing hormone that yields more physiologic levels of insulin-like growth factor-1 (IGF-1) than high-dose rhGH due to preservation of the negative feedback loop at the level of the pituitary. Two phase III, placebo-controlled trials of approximately 400 patients per study have reported 11–15% reductions in visceral adipose tissue at 6 months in the tesamorelin arms.

In HIV lipoatrophy, a meta-analysis of six placebo-controlled trials found that pioglitazone therapy was more effective than placebo for increasing limb fat mass, but rosiglitazone was not significantly more effective. A meta-analysis of 16 trials concluded that rosiglitazone should not be used in HIV-associated lipodystrophy. Pioglitazone was also reported to be safer, but any benefits appeared to be small. Metformin was the only insulin-sensitizer to demonstrate beneficial effects on insulin resistance, lipids, and body fat redistribution.[31]

A variety of plastic surgery procedures have also been used.[32] For lipoatrophy, free flaps, lipotransfer, or commercial fillers or implants have been used to replace adipose tissue. Types of dermal fillers include poly-L-lactic acid (PLLA; Sculptra), a semi-permanent injectable filler; polymethylmethacrylate (PMMA), consisting of 80% bovine dermal collagen plus 20% PMMA microspheres; and calcium hydroxylapatite (CaHA; Radiesse), a soft-tissue filler consisting of 30% calcium hydroxylapatite microspheres and 30% carboxylmethylcellulose. A five-year study has shown that a polyacrylamide hydrogel-based filler is a safe and effective treatment for facial wasting. Other filler options include injectable bovine and human collagens, hyaluronic acid, and autologous free fat transfer. Further research is required to fully understand the psychosocial impact of lipodystrophy and to develop strategies that help individuals cope.

Hospice Care for HIV Infected Persons

We have been focused on how palliative care could be approached simultaneously with primary medical and nursing therapies aimed at long-term disease control and a functional cure in HIV disease. However, there comes a point in the trajectory of HIV disease progression in which palliative care begins to overlap with hospice care more than with primary medical and nursing care. In palliative care, the approach is to improve the quality of life of patients and their families facing the problems associated with life-threatening HIV disease progression through the prevention and relief of suffering by means of early identification, assessment and treatment of pain and other symptoms as well as other aspects of symptom burden (psychological and spiritual). In hospice care, the focus is on the end-of–life. Thus, the see-saw swinging up to palliative care from primary medical and nursing care converts to a new see-saw in which there is a swing up to hospice care from palliative care over time.

The stage of hospice care is one in which patients are provided with support to enter into the death and dying process (generally with a prognosis of six months or less to live).[33] Prior to the introduction of the ARVs with zidovudine (or azidothymidine/AZT) monotherapy in the

late 1980s, hospice care in HIV/AIDS was routine, though it also addresses the palliation of symptoms and provision of comfort for patients. With the subsequent evolution of ARV therapy into the dual nucleoside reverse transcriptase inhibitor therapy (NRTI) era, followed by the early era of “highly active antiretroviral therapy” (HAART), a shift occurred in the care from dying with HIV/AIDS to living with HIV/AIDS. Thus, the move away from hospice-based care grew rapidly to the point that this form of care came to be perceived as “irrelevant” in HIV/AIDS. With the more recent growth of HIV prevalence in the older population, the acceptance of the need for hospice care of the HIV infected has re-emerged.[34] Currently in HIV history, an interplay between palliative care and hospice care is more relevant than ever before. Health care providers must employ a truly multi-disciplinary (rather than a “multiple discipline”) integration of knowledge to align and re-align between a focus on a goal of primary medical and nursing care (and “functional cure”) of HIV/AIDS versus one focused on the goal of caring for the patient in need of symptom palliation and later in terms of a focus on anticipation of the death and dying process. The entire process occurs together with the need to plan with the patient and her or his loved ones for an increasingly uncertain future that continuously seems to waiver between a disposition toward an appropriately targeted, longer-term medical and nursing management approach versus a more intense, shorter-term caretaking approach. To a large extent, this shifting process of care is mediated by the variable impact of the aging process over time.

The Process of Death and Dying

As the pendulum of HIV disease progression shifts more regularly toward hospice care, the predominant clinical focus eventually becomes entry into the process of death and dying. This is the stage of the disease in which isolation of the patient from others both occurs more frequently − due to lack of comfort with the death and dying process by others, and it is most keenly felt. Ongoing assessments of spiritual well-being and meaning are integral to the death and dying process. Facilitation of this process requires “being present”; “listening actively”; assisting with advanced care planning needs (which should begin in early HIV disease); providing support for a patient’s delineation of her/his desires; and guiding the patient, her/his family, and other loved ones through the death and dying process. While the stage of palliative care might be considered complete by some at this point, the needs of HIV-infected persons for symptom palliation persist throughout the illness to the time of death. However, it is true that it is the stage of hospice care that predominates here and carries forward the process to the stage of imminent death. Thus, begins the stage of death and dying − a phase of the evolution of medical and nursing care that remains far too frequently overlooked today in HIV/AIDS.

An unusual, recent study of this phase of the process took a phenomenological approach to the research participants in sharing their living experiences in confronting death and dying through story telling.[35] Qualitative analytic methods were used to uncover three common narrative themes in this phase: making choices, transformation of fear, and meaning in death. The fear of dying was noted to be transformed into an energy directed toward living – while being cognizant that death remains present as a part of what defines life.

It has been over 20 years since life-saving combination ARV treatments became available. The life expectancy among the subset of people living with HIV infection who had optimal therapy initiated early is now close to that of the general population. One million [830 000–1.2 million] people died from AIDS-related illnesses in 2016, worldwide. In the United States, 6,721 people died from HIV/AIDS in 2014, and HIV/AIDS was the 8th leading cause of death for those aged 25–34 and the 9th for those aged 35–44. Late diagnosis remains a key issue.[36] Meanwhile, UNAIDS has set highly ambitious treatment targets for all countries: by 2020, governments will commit to ensuring that in any key population 90% of people living with HIV will know their HIV status, 90% of people with diagnosed HIV infection will receive sustained effective ART, and 90% of people receiving effective ART will have durable viral suppression. While these are laudable goals to strive for at the population level, at the individual level it is incumbent upon us to recognize that people continue to die from HIV/AIDS in the USA – much more so worldwide – in the year 2017.

Bereavement

Beyond the death and dying stage of HIV/AIDS lies the emptiness left in the lives of those left behind by the deceased patient. This “stage”, the loss of the deceased patient [bereavement], is not generally included in studies done on the patient with a lethal complication of HIV/AIDS or HIV-associated non-AIDS (HANA) conditions. Rather, it is considered outside of this scope, as it relates to loved ones of the patient rather than the patient her or himself. However, bereavement is a potent life stressor with demonstrated chronic impacts on associated psychological distress (grief), neuroendocrine measures, immunological status, and physical and mental clinical health status.[37] As bereavement is no longer a frequent life stressor among HIV seropositive persons, these effects have lost their former noteworthy focus of study in the literature. Yet, bereavement in the setting of HIV/AIDS still does occur and remains tremendously impactful.[38]

Research differentiating grief from depressed and anxious mood showed an 18% prevalence of unresolved grief in HIV-positive and HIV-negative MSMs.[39] Psychological distress is quite common in the year following loss.[40] Various time periods have been examined with respect to the development of complicated grief disorders. In fact, two, four, six, and eight-week periods as well as six, 12, and 14-month periods have been used. Despite this wide span of time examined post-loss, the data show that the chronicity of grief itself does not appear to mediate the occurrence of complicated grief reactions. However, a close aggregation of losses as well as discrimination, homophobia, low social support, lack of partner recognition for financial benefits and medical care rights, and greater difficulties in resocialization then those experienced in the general population are well known to increase the deleterious impact of bereavement among MSMs. Although the majority of post-bereavement depressive symptoms experienced, indeed, are transient,[41] a significant sub-group eventually develops bereavement-associated MDD.

Grief is now typically designated as involving two types of affective processes - depressed mood and traumatic distress (with “avoidance” and “intrusions”). Yet, separation distress as a “third type” of affective process might be the most prominent type of distress in bereavement vis a vis the occurrence of complicated grief reactions. Separation distress

refers to a set of symptoms with direct relationship to the loss as the organizing factor (e.g., having difficulty acknowledging the death; assuming symptoms related to the deceased person; and experiencing excessive irritability, bitterness, or anger related to the death). Of note regarding bereavement, an RCT conducted with HIV-positive and HIV-negative homosexual men experiencing a loss over the prior six months who were randomly assigned to a semi-structured group intervention (with groups separated by HIV status) showed a significant effect on overall psychological distress and specifically on grief level when compared to community standard-of-care, bereaved control participants.[42] Moreover, the effects persisted when control variables were applied. In addition, an ad hoc Complicated Grief Index that was analyzed in that study showed a significant intervention condition reduction for both HIV-positive and HIV-negative individuals. Ultimately, it appears that supportive therapy for grief may not be necessary (but may nevertheless prove helpful) in cases of uncomplicated grief. However, supportive interventions, particularly those developed specifically for complicated grief reactions,[43] may be critical to provide for future functioning. Resilience may not only be attained but also may be promoted through intervention.[44] The purview of end-of-life care for those with HIV/AIDS should be extended beyond the sphere of the patient her or himself to the deceased patient's loved ones and social support network as well. Thus, such interventions might not only be targeted to ameliorate the negative impact of bereavement (including the reduction of the allostatic stress load of chronic loss burden) but also to extend beyond such targets to treat to a target of positive mental health and true wellness. The use of established stress management interventions together with social support groups and coping skills enhancement training could be used to achieve such a goal in the future.

Synthesis and Conclusions

The HIV/AIDS epidemic has changed perhaps more dramatically than any other disease over as short a period of time since its initial description. CDC began tracking cases of AIDS in 1981, and there was no direct treatment for HIV infection whatsoever until 1987, when the FDA approved zidovudine (then called "AZT"). Since that time, the number of ARVs has mushroomed, and the ability to monitor and control the progression of the disease has made amazing strides. Morbidity and mortality from HIV/AIDS has been tremendously reduced in high-resource countries. This work reviews the current status of end-of-life care issues in HIV/AIDS. While the progress in the treatment of the disease has been impressive and the projected life span for infected patients has been greatly increased, the impact of these developments is felt differently around the world.

This paper reports on the end-of-life care issues in HIV/AIDS as a stage-like, yet overlapping process in which the patients generally start at a stage from the point of diagnosis in which the focus is primary medical care to suppress plasma viral load to non-detectable levels and deter the development of any symptoms. Eventually, a sub-group of symptoms do occur and predominate which do not reflect any specific HIV-associated disease but rather the generalized progression of HIV infection itself. This is the stage of palliative care characterized by the symptoms of fatigue, pain, insomnia, decreased libido/hypogonadism, decreased memory and concentration (HAND), depression, and distorted body image. Next, the stage of hospice care is discussed from a historical vantage point

related to its current status today. We then discussed how the stage of hospice care leads directly to entry into the death and dying process and the prominent issues that are frequently neglected in that end-of-life stage. Finally, we take the typical endpoint for the discussion of end-of-life care issues one step beyond the usual framework to consider the impact of the death of the patient on others – that is, the potent impact of bereavement on a patient's loved ones and entire social support network. With this depiction, it is hoped that preparation for and treatment of end-of-life care issues will not only be undertaken as adeptly clinically as was done in times past but will also be better informed by the development of the end-of-life literature to the present day.

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