The Impact of Palliative Care on Quality of Life and Cortisol Levels in HIV/AIDS Patients with Anxiety

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ABSTRACT

Background*: Individuals with HIV/AIDS often experience significant physical and mental burdens. Palliative care has emerged as a means to improve the quality of life for people living with HIV/AIDS (PLWHA). This study aims to determine the effect of palliative care on the quality of life and psychoneuroimmunoendocrine aspects in PLWHA, particularly those suffering from anxiety, as indicated by cortisol hormone levels.* ***Methods:*** *A total of 30 PLWHA with anxiety were selected based on inclusion and exclusion criteria. This study employed a quantitative design with a quasi-experimental one-group pre-test and post-test approach. The data were analyzed using descriptive statistics and a paired t-test to assess the impact of the intervention on quality of life and cortisol hormone levels.* ***Results:*** *The findings indicated a significant improvement in quality of life following palliative care ($p = 0.000$, $p < 0.05$). The cortisol levels in PLWHA with anxiety decreased following palliative care; however, the reduction was not statistically significant, suggesting that palliative care had no measurable impact on cortisol levels post-intervention ($p = 0.845$, $p > 0.05$).* ***Conclusion****: Palliative care significantly enhances the quality of life in PLWHA. However, it does not lead to a statistically significant reduction in cortisol hormone levels before and after the intervention. Factors such as patient compliance with the palliative care plan and the influence of efavirenz on cortisol levels in PLWHA are likely contributing to these results.*

Keywords: *palliative care, people living with HIV/AIDS (PLWHA), cortisol hormone, quality of life.*

INTRODUCTION

Palliative care is a comprehensive healthcare service designed to reduce patient suffering and improve their quality of life while also providing support to their families. This approach is grounded in rationality, realism, and compassion, addressing the full spectrum of patient needs, including biological, psychological, social, cultural, and spiritual aspects. It adheres to ethical principles and employs a holistic, multimodal, and interdisciplinary approach.[1] Palliative care is relevant for a broad range of patients, including those dealing with cancer, HIV/AIDS (people living with HIV/AIDS or PLWHA), chronic illnesses, and other degenerative conditions.[1] The increasing prevalence of these health challenges highlights the critical need for palliative care.

The global incidence of PLWHA continues to increase, as documented by the World Health Organization (WHO) and the Joint United Nations Program on HIV and AIDS (UNAIDS). In 2017, 36.9 million people worldwide were

living with HIV/AIDS, a number that increased to 37.9 million in 2018.[2]

In 2018, 46,659 new HIV cases reported, with an additional 22,600 cases identified by June 2019. The prevalence of AIDS cases remains relatively stable each year, indicating a growing population of PLWHA who remains in the HIV infection stage and has not yet progressed to AIDS. Notably, certain provinces in Indonesia have a higher prevalence of HIV, with DKI Jakarta leading with 60,501 cases, followed by East Java (50,060), West Java (35,529), Papua (33,458), and Central Java (29,048). In Surabaya City, 156 HIV cases were reported in March 2019. As of the same date, 3,651 PLWHA were receiving antiretroviral therapy (ART), reflecting ongoing efforts to provide care and support for PLWHA.

Biological, psychological, social, cultural, and spiritual factors all contribute to the progression of HIV infection, its impact on health, and mortality rates. These influences are associated with the development of the disease and encompass various aspects, such as the stress of learning one's HIV-positive status, denial of being infected, societal stigma, and socio-cultural elements. These factors are interconnected through psychoneuroimmunoendocrine pathways, where immune and endocrine mechanisms intersect with these diverse factors to affect the health and extended survival of PLWHA. [3–6]

Therefore, this study aims to determine whether palliative care can influence the psychoneuroimmune and endocrine aspects of PLWHA, as evidenced by changes in the quality of life and cortisol hormone levels. When the patients were given psychoneuroimmunoendocrine-based interventions such as relaxation, meditation, spiritual practices, and physical therapy, there was a significant effect on reducing stress, depression, fatigue, sleep disorders while improving quality of life. These interventions also showed changes in immunological and neurological variables, such as decreased cortisol, norepinephrine, and epinephrine levels, lower IL-6 and TNF-α, and increased NK cells and leukocytes. Acute, short-term stressors have been shown *in vitro* to suppress the activation of lymphocytes in response to mitogen stimulation and to inhibit natural killer cell cytokine production.[7] This can be interpreted as an immune response that could make individuals more susceptible to illness. Furthermore, when the brain is stressed, the hippocampus, amygdala, and prefrontal cortex become vulnerable because all three regions are targets of stress hormones.[8] Specifically, the hypothalamic-pituitary-adrenal (HPA) and sympathetic-adrenal-medullary (SAM) axes are activated when the paraventricular nucleus (PVN) of the hypothalamus processes neurosensory signals, triggering the pituitary gland to release hormones. These hormones, in turn, stimulate the adrenal cortex to release glucocorticoids, which activate the sympathetic nervous system (SNS) and prompt the release of norepinephrine throughout the body. This process subsequently reactivates the PVN, creating a positive feedback loop in which continued stress leads to sustained hormone release. This cycle negatively impacts the immune system, as glucocorticoids trigger hormones that suppress immune function.

The psychoneuroimmunology of HIV/AIDS examines how psychoneuroimmunological pathways, which are immune and nueroendocrine mechanisms, connect psychosocial factors to health and long-term survival. Biological determinants such as host genetics, age, virus strain and virulence, treatment processes, and various immune response factors also influence disease progression and the psychosocial impact.[6]

A study in Psychoneuroimmunology titled An Analysis of HIV/AIDS and Cancer by Seth R. Batten (2016) found that Psychoneuroimmunology (PNI) explores how psychological factors, such as stress and depression, influence the immune system through the nervous system. Immune system cells contain receptors for both neurotransmitters and neurohormones, suggesting that neurotransmitters can regulate immune function. A decrease in serotonin levels due to depression, for instance, could impair immune function. Specifically, depression has been associated with the activation of some aspects of cellular immunity, resulting in the hypersecretion of pro-inflammatory cytokines and the hyperactivity of the HPA axis,[9] which

could contribute to immunological disturbances, anxiety, and depression. Numerous studies indicate that chronic stress and depression, through the release of glucocorticoids, cytokines, and other chemical factors, suppress various immune cells, including natural killer cells (NK), cytotoxic T-lymphocytes, tissue macrophages, dendritic cells, and Th1 lymphocytes. If these cells are damaged, it becomes easier to contract diseases. Furthermore, if an individual already has a disease, its progression may worsen because of a weakened immune system. These mechanisms have been extensively studied in the context of HIV and cancer, as both conditions inherently compromise immune function. Consequently, if an HIV or cancer patient experiences chronic stress or depression, their lifespan may be reduced. However, if these psychological effects can be effectively managed, both quality of life and life expectancy could be significantly improved.

This study aligns with the objectives outlined in the Faculty Research Master Plan, which focuses on formulating policies that benefit society, particularly individuals affected by HIV/AIDS. It represents a valuable scientific contribution by providing evidence that palliative care can improve the quality of life for PLWHA. In addition, this study supports the goals outlined in the Sustainable Development Goals (SDGs), particularly the initiative to combat HIV/AIDS by 2030. We aim to contribute meaningfully to reducing AIDS-related mortality by implementing effective and comprehensive palliative care for PLWHA. We aspire for this approach to be recognized as an innovative policy response to HIV/AIDS, ultimately aiding in the achievement of SDG targets in this critical area.

METHODS

This study is a quantitative design with a quasi-experimental one-group pre-test and post-test approach. This study was conducted from April to May 2021 at the IHAN Clinic of Airlangga University Hospital, involving 30 PLWHA with anxiety who met the inclusion criteria, as follow: (1) a confirmed HIV/AIDS-positive status, as determined by positive serological test results (ELISA or rapid test) and Western blot, as documented in their medical records; (2) a diagnosis of anxiety disorders based on medical history, physical examination, and psychological assessment using the Kubler-Ross model and the Hamilton Anxiety Rating Scale (HARS), with quality of life evaluated through the Karnofsky scale; and (3) an age of 19 years or older. The study included a total of 30 patients. Blood samples (10 mL) were collected from each participant using ethylenediaminetetraacetic acid (EDTA)-treated vacutainer tubes. Plasma was separated by centrifugation at 2,000 rpm for 10 minutes and subsequently stored at -80°C for further analysis.

Serological Test

Plasma samples were analyzed using a human cortisol ELISA kit (Elabscience, USA). All serological tests were performed according to the manufacturer's instructions.

Ethical Clearance

This study received ethical approval from the Institutional Ethics Committee of Airlangga University under certificate number 25-995/UN3.14/PPd/2013. All participants provided written informed consent before they participated in this study.

Data Collection and Analysis

Quality of life data were analyzed using a paired t-test. The normality of data distribution was assessed using the Shapiro-Wilk test. If the data did not follow a normal distribution, differences in the quality of life before and after treatment were analyzed using the Wilcoxon test. Cortisol level data were analyzed using descriptive statistics, including bar charts and frequency tables. The effect of the intervention on cortisol hormone levels was assessed using a paired t-test.

RESULTS

This study was conducted from April to May 2021 at the IHAN Clinic of Airlangga University Hospital, involving 30 PLWHA with anxiety who met the inclusion criteria. A quantitative design was used, employing a quasi-experimental one-group pre-test post-test approach. Cortisol

Table 1. Characteristics of PLWHA before and after palliative care according to the Karnofsky scal

Karnofsky Score	N	Min	Max	Median	Mean	SD
Pre-Test	30	60	70	60	61	3,05
Post-Test	30	70	90	85	84,67	5,71

hormone levels were measured in each patient before and after receiving palliative care to assess its impact on improving the quality of life and reducing cortisol hormone levels in PLWHA.

The analysis revealed that the average Karnofsky score among PLWHA increased from 61 to 84.67 after the treatment, indicating an improvement in the quality of life following palliative care. Before palliative care, the lowest Karnofsky score was 60, and the highest was 70, with an average of 61 $\pm$ 3.05 and a median of 60. After palliative care, the lowest score was 70, and the highest was 90, with an average of 84.67 $\pm$ 5.71 and a median of 85. This descriptive analysis suggests that palliative care contributed to a notable improvement in the quality of life of PLWHA.

Differences in Quality of Life in PLWHA Before and After Palliative Care

The normality test results ($p < 0.05$) indicated that the data on the Karnofsky scale were not normally distributed. Therefore, the differences in the Karnofsky scores were analyzed using the Wilcoxon test.

The analysis revealed significant differences in the Karnofsky scores of PLWHA before and after palliative care, with a p-value of 0.000 ($p < 0.05$) at a 5% significance level. The mean of the Karnofsky score in the pretest was 61, with a median of 60, while the mean in the post-test increased to 84.67, with a median of 85. The difference in the Karnofsky scores before and after palliative care was 23.67. Statistically, this result indicates that palliative care improved the quality of life, as evidenced by the increase in the Karnofsky scores.

Table 2. Wilcoxon test results for Karnofsky scores before and after palliative care

Karnofsky Score	Median	Mean	Standard Deviation	*P*
Pre-Test	60	61	3,05	0,000*
Post-Test	85	84,67	5,71	

Characteristics of Cortisol Hormone Levels in HIV/AIDS Patients

This study aims to determine the effect of palliative care on psychoneuroimmunoendocrine aspects in PLWHA, as indicated by cortisol hormone levels measured through serum cortisol levels (ng/ml).

Palliative care, which uses a psychoneuro-immunoendocrine model, focuses on 5 human dimensions, namely biological, psychological, social, cultural, and spiritual (holistic treatment).

Biological Dimension: Patients received treatments related to nutritional management and symptom relief, addressing issues such as pain, nausea, vomiting, dyspepsia, anorexia, cachexia, general weakness, fatigue, secondary infections, and others.

Psychological Dimension: Supportive psychotherapy interventions, including cathartic ventilation, reassurance, CBT (cognitive behavioral therapy), ACT (acceptance and commitment therapy), general relaxation, guided imagery, and self-hypnosis, were implemented to help alleviate psychological issues, such as sadness, anxiety, and depression.

Social Dimension: By addressing biological and psychological needs, patients were better able to perform activities of daily living (ADL) and participate in work and social activities according to their abilities.

Cultural and Spiritual Dimensions: Patients received psychoeducation on fostering a positive self-image and overcoming stigma. Additionally, they were provided with guidance on achieving a

Table 3. Characteristics of Hormone Cortisol Levels of PLWHA Before and After Palliative Care

Description	Pre-test	Post-test
Minimum	64,67	133,96
Maximum	513,93	562,56
Mean	296,06	289,74
SD	112,57	118,28
Median	287,51	258,37

fulfilling life and strengthening personal integrity through motivation and religious approaches.

Holistic palliative care is expected to improve the patients' quality of life by addressing these interconnected dimensions.

Based on **Table 3**, the average cortisol hormone levels of PLWHA at the IHAN policlinic of Airlangga University Hospital were 296.06 ng/ml before being given palliative care, with the lowest cortisol hormone level of 64.67 ng/ml and the highest of 513.93 ng/ml. Before treatment, 50% of PLWHA had cortisol levels above 287.51 ng/ml. After receiving palliative care, the average PLWHA's cortisol hormone levels decreased to 289.74 ng/ml, with the lowest cortisol hormone levels of 133.95 ng/ml and the highest of 562.56 ng/ml.

This study found that 60% (n=18 of 30) of PLWHA experienced a decrease in cortisol levels after receiving palliative care. However, this decrease was not statistically significant, and 50% of PLWHA still had cortisol levels above 258.37 ng/ml after palliative care. Descriptively, the average cortisol hormone levels of PLWHA decreased by 6.32 ng/ml after palliative care. However, further statistical analysis is required to determine whether this decrease is significant, using a paired sample t-test, provided that the data meet the normal distribution value based on the Kolmogorov-Smirnov test.

Differences in Cortisol Hormone Levels in HIV/AIDS Patients Before and After Palliative Care

The differences in cortisol hormone levels in HIV/AIDS patients before and after receiving palliative care were measured using a paired sample t-test under the condition that the data were normally distributed. The results of the Kolmogorov-Smirnov test showed that cortisol hormone levels before palliative care had a p-value of 0.200 ($p > 0.05$), indicating that the data were normally distributed. Similarly, cortisol hormone levels after palliative care had a p-value of 0.157 ($p > 0.05$), indicating that the data were normally distributed. Consequently, the differences before and after palliative care were measured using a paired sample t-test with the following results.

Table 4 shows the results of the paired sample t-test, which indicated no significant differences in cortisol hormone levels in PLWHA before and after receiving palliative care, with a p-value of 0.845 ($p > 0.05$). Therefore, it can be concluded that there was no statistically significant difference in cortisol hormone levels before and after palliative care at a 5% significance level. These results suggest that the decrease in cortisol levels from 296.06 ng/ml to 289.74 ng/ml after palliative care was not significant, indicating that palliative care had not been optimally carried out in reducing anxiety in PLWHA.

Table 4. Characteristics of cortisol hormone levels in PLWHA before and after palliative care

Description	Pre-test	Post-test
Mean	296,06	289,74
SD	112,57	118,28
P	0,845	

Paired sample t-test ($p < 0,05$ = *Significant*)

DISCUSSION

People Living with HIV (PLWH) experience numerous burdens in physical, psychological, social, spiritual, and cultural. Data from Moens and colleagues' systematic review (2014) showed that the most prevalent physical symptoms in PLWH are pain (30-98%), followed by nausea and vomiting (41-57%), fatigue, tiredness, and weakness (43-95%), sleep disturbances (40-74%), diarrhea (29-53%), breathing problems (43-62%), constipation (19-35%), and anorexia (82%). Meanwhile, the most prevalent psychological symptoms in PLWH are depression, depressed mood, sadness, and bad mood (17-82%) followed by anxiety, nervousness, and agitation (13-76%).[10]

Palliative care can also help patients address cultural challenges, such as stigma, and spiritual issues by encouraging the PLWH to build personal integrity through enhancing their spirit and religious support.[10] Palliative care aims to improve the quality of life of PLWH and their families through prevention, assessment, and treatment of the physical, psychological, social, spiritual, and cultural symptoms. Research has shown that palliative care can significantly alleviate symptoms in PLWH, including pain

and other symptoms, psychological distress, and issues related to cultural and spiritual well-being. A study conducted by A. G. Baidowi which entitled the Relationship between Social and Spiritual Support for HIV/AIDS Sufferers and the Quality of Life of HIV/AIDS Sufferers, found that 27.90% of respondents who reported moderate spiritual support also had a moderate quality of life. Additionally, there were no respondents (0.00%) who reported poor spiritual support alongside a poor quality of life. This suggests that higher levels of spirituality are associated with an improved quality of life among individuals living with HIV/AIDS. Previous studies have consistently reported a very strong and significant positive unidirectional relationship between the level of spirituality and the quality of life in people with HIV/AIDS.[11]

Social discrimination causes people living with HIV/AIDS to experience difficulties in interpersonal relationships and social environments. For patients whose early symptoms are not obvious, the psychological impact can be more profound than physical pain. Therefore, PLWH require the holistic support provided in palliative care to help them navigate life challenges and alleviate psychological anxiety and distress.

Psychoneuroimmunoendocrinology is an interdisciplinary field that explores the interactions between psychological, neurological, immunological, and endocrine components. These systems interact through neuronal and endocrine signaling pathways, influencing immune responses and overall physiological function of the endocrine system and central nervous system. The discipline emphasizes understanding how physiological and psychosocial factors affect immune regulation. Disruptions in the interactions among the nervous, endocrine, and immune systems contribute to the development of pathogenic symptoms.[4] Psychosocial factors such as anxiety are particularly relevant in the worsening and progression of HIV infection, affecting morbidity and mortality rates in patients with AIDS.[3]

The HPA axis plays a critical role in stress response and immune regulation. It comprises 3 key components: the PVN (Paraventricular nucleus) of the hypothalamus, the anterior pituitary gland, and the adrenal cortex. Neurons residing in PVN produce CRH and AVP, which are released into the pituitary portal vein under the influence of higher regulatory centers, including the hypothalamic suprachiasmatic nucleus (SCN), which controls central circadian rhythms. Released CRH and AVP stimulate the secretion of ACTH from corticotrophs of the anterior pituitary gland. ACTH then stimulates the production and secretion of glucocorticoids (cortisol in humans and corticosterone in rodents) from adrenocortical cells located in the zona fasciculata of the adrenal gland. Circulating glucocorticoids exert negative feedback on the PVN and pituitary gland, forming a self-regulating feedback loop.[12]

During injury, disease, or infection, the immune system is activated, releasing cytokines - proteins which work as mediators of the innate immune responses. Inflammatory cytokines, such as TNF-α, IL-1, and IL-6, are produced and secreted locally by various immune cells in the area of inflammation during the first phase of the immune response. These 3 cytokines have the most regulatory effects on HPA activation, leading to increased cortisol secretion and other glucocorticoid hormones from the adrenal glands. Cortisol, in turn, suppresses the production and release of pro-inflammatory cytokines. Likewise, psychosocial stressors, including depression and anxiety, stimulate HPA activity, resulting in increased cortisol secretion. This further suppresses the production and release of pro-inflammatory cytokines by macrophages, T cells, and B lymphocytes.[13,14]

Cortisol inhibits the production of interleukin (IL)-12, interferon (IFN)-gamma, IFN-alpha, and tumor-necrosis-factor (TNF)-alpha by antigen-presenting cells (APCs) and T helper (Th)1 cells. Conversely, it upregulates IL-4, IL-10, and IL-13 secreted by Th2 cells, which results in a shift toward a Th2 immune response. It also prevents the proliferation of T-cells by rendering the interleukin-2 producer T-cells unresponsive to IL-1 and unable to produce the T-cell growth factor (IL-2) (Samuel & Gill, 2018). Reducing stress levels can help restore balance in the HPA axis, as the negative feedback regulation of the

CRH and ACTH secretion is mediated by type II glucocorticoid receptors.[14] This underscores the importance of psychological and social support in managing stress-related immunosuppression in PLWHA.

The psychological domain consists of both positive and negative emotions, cognitive processes, self-esteem, body image, and an individual's sense of purpose. The prevalence of anxiety disorders affects approximately 16% of HIV/AIDS patients. Differences in psychological quality of life scores may be attributed to the duration of illness, as prolonged suffering often leads to increased fear of death and psychological distress (negative feelings). Long-term HIV infection can contribute to mental health deterioration, negatively impacting the overall psychological quality of life of PLWHA.

The neuroendocrine system plays a significant role in the progression of HIV. HIV-1 establishes chronic infections in lymphoid cells, allowing the virus to directly influence the neuroendocrine system through its host cells. As a result, this interaction indirectly affects neuroimmune responses, which are crucial in regulating the body's anti-viral immune mechanisms. The hypothalamic-pituitary-adrenal (HPA) axis serves as a critical physiological signaling pathway that mediates the psychosocial effects of HIV progression. Although modern antiretroviral therapies have significantly reduced the risk of severe opportunistic infections, such as Kaposi's sarcoma or Pneumocystis carinii pneumonia, individuals living with HIV/AIDS still experience distressing physical symptoms. These symptoms—such as neuropathy, fatigue, and diarrhea—can hinder workplace functioning and discourage individuals from returning to employment. Research findings on the impact of disease markers on employment status are inconsistent.

Blalock *et al* (2022) conducted a cross-sectional study involving 200 men and women with HIV/AIDS attending an urban public outpatient clinic. The study found that unemployed individuals (60% of the sample) were significantly more immunocompromised and had lower mean CD4 counts compared to employed individuals.[15] However, other studies have not found a direct correlation between CD4 cell count, viral load, and employment status.[16,17] Overall, the mixed results suggest that factors beyond physical health, such as psychosocial and neuropsychiatric influences, may also impact decisions regarding workforce reintegration.

The stress response is regulated by the HPA axis, which consists of three key components: the hypothalamus, the anterior pituitary gland, and the adrenal cortex. When an individual encounters a stressor, the signal is transmitted to the hypothalamus, prompting the release of Corticotropin-Releasing Hormone (CRH) and Arginine Vasopressin (AVP) hormones. These hormones stimulate the pituitary gland to secrete Adrenocorticotropic Hormone (ACTH) into the bloodstream, which then prompts the adrenal cortex to produce and release glucocorticoids, including cortisol.[18] During stress, neurons located in the paraventricular nuclei (PVN) of the hypothalamus secrete corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP) into the hypophysial portal system, where they reach the anterior lobe of the pituitary gland. CRH and AVP bind to their cognate transmembrane receptors, triggering the synthesis and secretion of adrenocorticotropic hormone (ACTH) by the corticotroph cells in the anterior pituitary gland. Increased circulating ACTH concentrations activate the biosynthetic pathway of glucocorticoids (cortisol in humans and corticosterone in most rodents) in the zona fasciculata. Glucocorticoids are the final hormonal products of the HPA axis, playing a key role in modulating the body's response to stress.[9]

According to research conducted by Evans et. al (2002), anxiety and depression are known to be significantly associated with an increase in the number of activated CD8 T lymphocytes and viral load. In early HIV disease, evidence suggests that populations of T lymphocytes expand, which is believed to be compensatory of the immune response to control HIV infection by inhibiting viral replication and lysing HIV – infected cells.[19] As also mentioned by Famularo (1997), CD8 cells can efficiently suppress HIV replication through major histocompatibility complex (MHC)- restricted cytotoxic killing of infected cells (destruction of CD4-infected cells/

lysing HIV infected cells), particularly during primary infection, and through HIV-suppressing soluble factors. In HIV–HIV-seropositive women, depression is associated with significant increases in subsets of CD8 cells. These findings appear consistent with recent evidence suggesting that the CD8 T-lymphocytes may play a beneficial role in early HIV infection, but could be detrimental to the host in the later stages of the disease. In individuals with advanced HIV disease where the viral load is very high, CD8 T lymphocytes can have detrimental effects because they can mediate injury to several organs, especially tissue-infiltrating CD8 lymphocytes, which contribute to CD4 cell destruction.[20]

It is known that glucocorticoids interfere with the activation process of T lymphocytes by causing excessive and persistent activation.[19] This overactivation of T lymphocytes is considered one of the main pathogenic mechanisms in HIV infection, as it accelerates lymphocyte turnover and ultimately reduces CD4 cell counts.[21] In addition, cortisol leads to decreased production of interleukin-2 and interferon (IFN)-γ and increased levels of IL-4, a pattern associated with faster progression of HIV infection.[22] Moreover, cortisol suppresses IL-1 production by macrophages, preventing Th2 activation, which in turn inhibits IL-2 formation, and subsequently affects IL-4, IL-5, and IL-6 production, impairing B-cell differentiation into plasma cells and reducing IgG formation.

In the context of this research, the study is an experiment because the researcher intervened in the causal variable being studied, utilizing a quasi-experimental design without a control group. It was observed that there was a reduction in the mean cortisol levels during the post-test (289.74 ng/ml) in comparison to the pre-test (296.06 ng/ml). This descriptive analysis illustrates that, on average, the cortisol hormone levels of PLWHA decreased by approximately 6.32 ng/ml following the administration of palliative care. However, the statistical analysis did not demonstrate a significant impact of palliative care on the cortisol levels of HIV patients experiencing anxiety, as indicated by a p-value of 0.845 ($p > 0.05$).

Multiple factors are presumed to underlie the outcomes observed when testing the research hypothesis that "palliative care has no impact on cortisol levels in HIV/AIDS patients with anxiety.":

The level of patient compliance in following the prescribed home-based palliative therapy, designed to address anxiety through catharsis or ventilation, reassurance, relaxation (deep breathing and stretching), positive coping strategies, guided imagery, and self-hypnosis, remains suboptimal.

Over 50% of patients use a combination of Antiretrovirals (ARV) with Efavirenz (EFV). A study conducted by Collazos, Ibarra, and Loureiro (2004) found that patients receiving Efavirenz therapy exhibited higher cortisol levels compared to those who did not use the drug (24.2 vs. 20.2 mcg/dl, $p < 0.0001$).[23]

Evafirenz stands out as a frequently prescribed Antiretroviral (ARV) medication for PLWHA. While research has demonstrated its effectiveness in suppressing the virus, Efavirenz has also been widely associated with significant neuropsychiatric effects. These include issues like insomnia, dizziness, and mood-related conditions such as anxiety and depression. Occasionally, it has also been linked to suicidal ideation, particularly during the initial week of treatment.[24]

There is one study that showed higher cortisol levels in PLWHA who used certain ARV therapies without the consumption of other drugs that could affect cortisol levels. Patients taking Efavirenz therapy had higher cortisol levels compared to those not taking the drug (24.2 vs 20.2 mcg/dl, $p < 0.0001$), and patients receiving Ritonavir therapy also showed higher cortisol levels than those not receiving the drug (23.5 vs 20.5 mcg/dl, $p = 0.01$).[14]

This phenomenon may be attributed to the fact that Ritonavir acts as an inhibitor of cytochrome P450, which can disrupt enzymatic systems responsible for cortisol metabolism. In contrast, Efavirenz functions as a cytochrome P450 inducer. However, it is worth noting that Efavirenz can also impact certain enzymatic systems, making the relationship between Efavirenz and cortisol metabolism complex and

variable. The effects of Efavirenz's interactions with different cytochrome P450 isoforms should not be disregarded as a potential factor contributing to increased cortisol levels.[23]

Efavirenz has the potential to act as both an inhibitor and an inducer for CYP3A. Acute exposure to Efavirenz produces an inhibitory effect on the CYP3A enzyme in vivo, while prolonged exposure produces an inducer effect. The inhibitory and induction effects of Efavirenz may depend on the duration of exposure, vary significantly, and be difficult to predict.[25]

To effectively address these issues, we propose that future studies consider increasing the treatment frequency, such as conducting three meeting sessions per week, to facilitate improved monitoring of palliative care outcomes in patients. Furthermore, we recommend categorizing patients into groups based on their use of specific medication to assess the impact of palliative care on cortisol levels in HIV patients with anxiety, considering the potential influence of medication on cortisol metabolism. For instance, these patient groups may include individuals using Efavirenz, those using Ritonavir, and those not taking any medication.

CONCLUSION

Palliative care could effectively improve the quality of life in HIV patients, but no significant differences in cortisol hormone levels were observed before and after the care. Several factors are considered to have influenced this outcome, including patient compliance with the palliative care plan and the influence of Efavirenz on increasing cortisol levels in HIV/AIDS patients undergoing this treatment.

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CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

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