CHANGES IN THE LEVEL OF ACTH, CORTISOL AND LYMPHOCYTE T COUNT AFTER ESTABLISHING DIAGNOSIS OF HIV AND AIDS

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ABSTRACT

Ever growing problem relating to HIV is its high morbidity and mortality. PLWAs usually are facing 3 (three) stressors; biological stressor due to HIV intervention, psychological stressor, and psychosocial stressor. ACTH and Cortisol are two interrelating hormones in order to maintain normal level due to various influences including stressful micro environment. Based on those facts, this study require specific approach through psycho-neuro-immunological paradigm to reveal the changes in ACTH and Cortisol level and lymphocyte T count after revealing of HIV and AIDS diagnosis in HIV patients with high risk population without HIV infection. In every subject from both groups we conducted follow-up for 30 days. We used panel study as our study design, in the same subject we conducted other study at different times. ACTH level in those with HIV infection has tendency to increase on day 7th and day 31st. In negative HIV group, we found dramatic decrease on day 7th and steep increase on day 31st. The increase in ACTH level is still below ACTH level in the first examination. In this study diagnosis of HIV infection is an influence to the increase of hypothalamic-pituitary-adrenal (HPA) axis activity. Impact on various body cells, causing changes in ACTH and cortisol level, and lymphocyte count. These changes beside caused by HIV biological stressor, also due to psychological stressor caused in turn by diagnosis revealing, with the latter has a predominant over acute stress.

***Keywords**: diagnosis of HIV Infection, ACTH, cortisol, lymphocyte T*

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INTRODUCTION

HIV&AIDS as infectious disease until recently is a global health problem. The growing problem related to HIV&AIDS infection is its high morbidity and mortality (Hirschel 2003). Data taken from Infectious Disease Intermediate Care Unit (IDICU) PLWA has better than predicted life quality. This condition is influenced by earlier acceptance process. It is regarded as important in relation with more effective coping mechanism. People living with HIV&AIDS (PLWA) in common, are faced with three stressors, biological stressor due to HIV intervention, psychological stressor due to diagnosis revealing of HIV & AIDS infection, and psychosocial stressor due to stigma and discrimination either from the family or society. Cortisol is a hormone produced by fasciculate, spongiosa zone of adrenal cortex with strong contribution in cell immunity under stress influence. Excessive cortisol level in prolonged time on the contrary has immunosuppressant effect with influence in lymphocyte count, but changes in ACTH and cortisol level after revealing of HIV&AIDS diagnosis is not yet fully understood. ACTH and cortisol are two interrelating hormones in order to maintain normal level due to various influences including stressful micro environment.

We have achieved advances in medicine and pharmacy, also preventive approach has been taken. Therefore, morbidity to HIV and AIDS related death should have been decreasing. In fact, on the contrary, morbidity and mortality is still high with tendency of ever increasing. Diagnosis revealing of HIV infection is a stressor to person which could trigger stress with potential influential changes in ACTH, cortisol, lymphocyte count and progression of disease. On the other hand, if the changes in ACTH, cortisol level, and lymphocyte count is not investigated immediately, patient's management will not be optimally done, which in turn will influence individual defense mechanism in HIV infected person, progression of HIV infection to AIDS is unchecked, and even becoming a major public problem.

There are various factors which determine the progression of HIV infection. One important factor is the weakening immune system, marked by decreased T lymphocyte count. Immune status of a patient is influenced by psychological stressor due to diagnosis

revealing of HIV&AIDS infection. Diagnosis revealing of HIV&AIDS infection can influence the hypo-thalamic-pituitary-adrenal axis (HPA), along with Serum level of ACTH and cortisol (Oppenhim 2003; Ransohoff 2003). Changes in cortisol level will, in turn, influence the function of immune system (Bailey 2002; Scholz 2001; Tanaka 2001). Based on those facts, this study needs approach using psychoneuroimmunology paradigm to reveal the changes of ACTH, cortisol serum level, and lymphocyte count after diagnosis revealing of HIV&AIDS infection. Therefore, patient's management will be optimum, HIV morbidity and death due AIDS can be suppressed.

MATERIALS AND METHODS

This study was an observational study by observation and measurement in ACTH, cortisol serum level and lymphocyte count in subjects. The subject in this study is HIV&AIDS infected patients. The purpose of this study was to observe the changes in ACTH, cortisol serum level and lymphocyte count after diagnosis revealing of HIV&AIDS in high risk group with HIV infection with those in high risk group without HIV infection as comparison. In every subject from both group 30 days follow-up were performed. Study design in use was panel study, the same subject undergoing other examination in different time.

Transmission factor of HIV influence disease progress, which is believed will influence outcome of the study (CD4 count), therefore it is necessary to stratify the nature of risk factors. This is meant to achieve more homogeneous subgroup (strata). Randomization was done in every separate stratum, and then chosen subjects will be regrouped in appropriate group. Therefore in this patient, stratified randomization was used, by using simple random sampling method.

Fourteen subjects were enrolled in this study. Peripheral blood sample was taken three times: Initial examination (Baseline), peripheral blood sampling was taken in the first day when inclusion criteria had been fulfilled, but the patient had not been told of their HIV infection status. The patient expressed their consolation for enrolment in study procedure and signing informed consent as subject and agreement for blood sampling. The second examination was conducted in the seventh day. Day seven was chosen based on consideration that the most severe acute stress after diagnosis revealing of HIV infection occurred at this time. The third examination was conducted on day thirty-one, under auspices that acute stress usually happened from two hours until day fifteen after stressor, and then gradually adapts from thirty to sixty days after diagnosis revealing of HIV infection. Every subject was given appropriate pre test and post test of HIV serology.

Three times examination was meant to produce data concerning free variable and restricted variable. In order to achieve external validity, this study subjects were taken from available population, the patients admitted or hospitalized in IDICU and from available population to target population, high risk persons who were the second external validity.

RESULTS

This study was meant to observe the changes in the levels of ACTH, cortisol and lymphocyte count after diagnosis revealing of HIV infection in high risk group with HIV infection compared to high risk which serologically not infected with HIV as comparison.

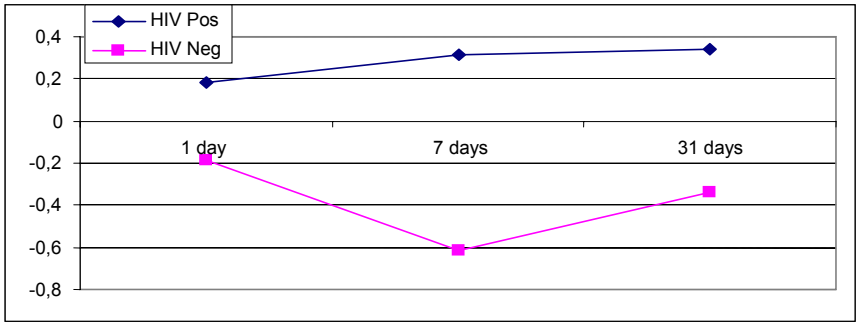

Figure 1. Changes of ACTH level after day 1, 7 and 31

ACTH level in HIV infected group was tended to increase on day one, seven, and thirty one. In negative HIV infection there was a sharp decrease on day seven, and tendency to increase on day thirty one. The increase in ACTH is still under the baseline of ACTH level (Figure 1)

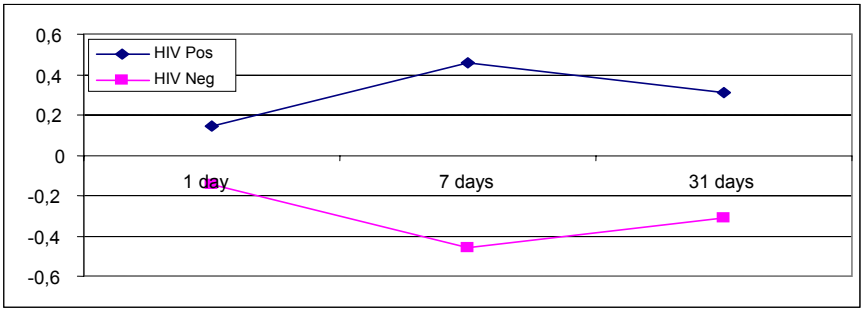

Figure 2. Changes in cortisol level after day 1, 7 and 31

HIV positive group has tendency to increase in cortisol level on the seventh day and tendency to decrease on the thirty-first day. HIV negative group has a decrease in cortisol level on the seventh day, increasing on day thirty-first, but didn't gain the same level as the baseline examination. The difference of cortisol level in the second examination was concurrent with the influence of acute stress, triggered by stressor of diagnosis revealing of HIV infection as an acute stress trigger. Acute stress usually happening in the first week from the beginning of stress exposure, with peak on the seventh day. In line with the revealing, on the second examination after diagnosis revealing of HIV infection, there was a significant difference between HIV infected group and those who serologically uninfected (12.377 ± 4.046 vs. 8.650 ± 3.213). HIV infected patient had an increase in lymphocyte count on day seven and sharp decrease on the thirty-first day. In HIV negative group there was a decrease on day seven, with sharp increase on day thirty-one (Figure 3).

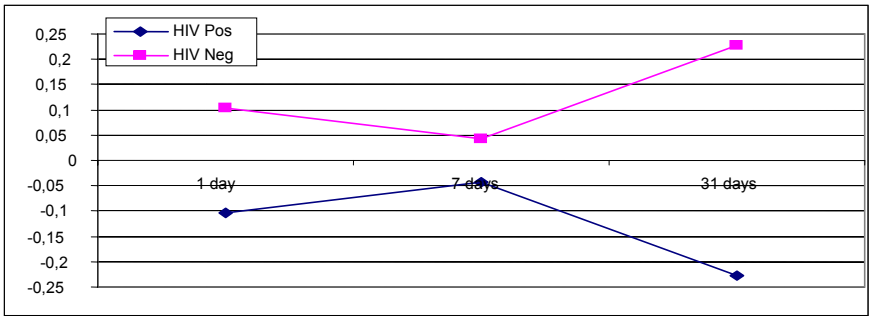

Figure 3. Changes in lymphocyte count after day 1, 7 and 31

DISCUSSION

HIV is a biological stressor and internal stress, with can even influence and causing cell stress. Perception and stressor influence to cell is very individualistic with positive or negative influence in the survival of the cell, depending on defense mechanism through coping mechanism. If cells could maintain its homeostatic balance to stressor, adaptation would be achieved and not influencing the live survival of the cell. Cell response to stressor, stress and adaptation will determine whether cell would survive, ill or even dead. Cell, of course, always interacts with environment both inside and outside in order to maintain homeostasis. Fellowship program is expected to lessen the stress degree.

One of the main targets of HIV cell is T lymphocyte because of its CD4 receptor along with CXCR4 and CCR5 co-receptor. HIV intervention can suppress lymphocyte to decrease its amount. Lymphocyte decrease due to HIV biological influence of HIV, psychological and psychosocial pressure will influence HPA axis. Interaction of HPA axis component is influenced by coping mechanism of PLWA. Whether this mechanism is effective, is very individualistic and influencing level of ACTH, cortisol and lymphocyte. Guillemin and Rosenberg (1955) have shown the

influence of hypothalamus to pituitary gland through corticotropin releasing factor (CRF) or corticotropin releasing hormone (CRH) or corticoliberin. Working mechanism of CRH is through activation of adenilat cyclase, binding with receptor in pituitary gland and in due course changing ATP to cAMP, which in turn will stimulate release of adenocorticotrophin hormone (ACTH). ACTH is a single chained polypeptide which consists of 39 amino acids, from pro-opiomelanocortin (POMC) in pituitary gland.

Results from the first, second and third examination from HIV infected group and serologically uninfected with HIV did not show any significance. This phenomenon could be due to both groups having the same level of annoyance and fear. Both groups (serologically negative and positive in this time) realized having the same risk for HIV infection. Serologically uninfected with HIV had two meanings, truly uninfected which requiring another test in the next two or three months. The second possibility was that they were in the window period, therefore in their test, the antibody result was negative, due to inadequacy of antibody level to respond the antigen.

As soon as the diagnosis of HIV was revealed, it became a psychological stress. This was because neuron in the paraventricular nuclei (PVN) accepting impulse from various locations, such as limbic system and cerebral cortex. Signal impulse initiated from psychological trigger was believed to achieve the PVN through the limbic system, while those originating from physical trigger through the cerebral cortex (Putra 1999; Suryohudoyo 1999).

In this study, ACTH level from the HIV infected group tended to increase in the seventh and thirty-first day. This increase was triggered by increase in ACTH activity in hypothalamus and POMC due to anterior pituitary gland as a result of psychological stressor after revealing of HIV diagnosis. In HIV negative group there was a sharp decrease of ACTH level in the seventh day, with tendency to increase in the thirty-first day. ACTH increase was still under baseline level. Decrease of ACTH was due to coping mechanism. On the other hand, the tendency of ACTH decrease until day seven was followed in the thirty-first day but this increase did not quite achieve the level during diagnosis showing the existence of coping mechanism.

Changes in ACTH level will influence the activity of spongiosa in the fasciculate zone of the adrenal cortex in regulating production and secretion of cortisol. In HIV positive group there was an increase of ACTH level there was an increase of cortisol level in the seventh day and decreasing in the thirty-first day. This tendency to increase since diagnosis revealing until the seventh day was due to anxiety, stress and unstable feeling in acute stress which influenced the micro environment. This situation was responded by the limbic system, hypothalamus (PVN), anterior pituitary (POMC), and spongiosum of adrenal cortex which stimulate production increase of cortisol with subsequent increase in the circulation. Tendency to decrease after the seventh day was due to the fellowship program, care and treatment in IDICU with impact on more stable coping mechanism, causing hyperactivity in HPA axis is controllable. In HIV negative group there was a decrease in cortisol level on the seventh day, tendency to increase after the thirty-first day but never achieve the same level as the baseline. These changes in cortisol level on the second examination were triggered by stressor due to diagnosis of HIV infection as an acute stress trigger. Acute stress usually occurred in the seventh day after revealing of HIV diagnosis.

Acute stressor in this study was defined as diagnosis establishment (revealing to the subject that he was infected by HIV), with impact on cortisol level. This means that in the second examination, besides biological stressor from HIV, there was also psychological stress caused by the revealing. But the psychological was more predominant. In this case the body responded through cerebral cortex as a physical response to HIV stressor and through lymbic system responding the psychological stressor. Activation of hypothalamic-pituitary-adrenal axis (HPA), with influence to various body cells includes influence to paraventricular nucleus (PVN) in hypothalamus, with result of molecular signal in the form of corticotropin-releasing factors (CRF). CRF acted as stress response coordinator. Various neurons were also producing CRF, but the highest level was found in the PVN (Black, 1994). In a short time (minutes) in acute stress will increase mRNA CRF, followed by increase in CRF level in the PVN. CRF will eventually migrate alongside the axon to the medial part of the hypotalamus and finally released at the terminal end of capillary vessel in venous hypophysial portal plexus which is the port end of the anterior pituitary gland, and inducing proopiomelanocortin (POMC) polyprotein which, after translation producing ACTH,α,β,γ melanocyte stimulating hormone (MSH), and β endorphin. ACTH stimulates spongiosa in the fasciculate zone of the adrenal cortex as a stress hormone (Chrousos 1995; Seeley 1998; Viviani 2001). ACTH hormone follows the systemic circulation, influencing spongiosa (fasiculata cortex zone cell) of the adrenal, causing trigger of the cortisol level, influencing the chromatine cell of the adrenal medulla causing increase of the cathecolamine (epinephrine,

norepinephrine, dopamine) in the circulation (Chrousos 1995; Nair 2000; Seeley 1998).

T lymphocyte is an HIV target, therefore its level will decrease as seen in this study. The HIV positive group has an increase of lymphocyte count on the seventh day examination and sharp decrease in the thirty-first day examination. Effort to increase this lymphocyte count did not seem to be fully successful because this decrease is triggered by the biologic intervention of HIV followed by psychological pressure due to diagnosis that the person has HIV infection, made more severe by psychosocial stressor caused by discrimination. In the HIV negative group, in the thirty-first day examination there was a sharp increase.

Self defense method in the form of effective coping-behavior, although the stress is increased, it psychopatologically can be prevented. This success was due to natural coping, accelerated by continuous counseling and fellowship. The result was unincreased ACTH level in this study. Every human has natural coping which is a response from various phenomena. This can affect the learning process in various parts of the brain, causing astrocyte, mycroglia, and neuron to decrease production and secretion

In reference to terminal illness and death acceptance process stated by Dr. Kubler-Ross (denial and isolation, anger, depression, bargaining, and acceptance), natural defense mechanism with effect of counseling and fellowship is hoped to shorten the process from denial to bargaining even acceptance. Impact of this acceleration will influence coping mechanism and HPA activity. Decrease of HPA activity will influence in decrease of neuromodulator secretion production and cortisol secretion and neurotransmitter. Further on, there will be a decrease in production and secretion of cortisol by spongiosum of the fasciculate zone of adrenal cortex.

The ability of HIV patient in maintaining his cell homeostasis in this study was marked by low cortisol level. Decrease of psychological and psychosocial stress will affect the activity of lymbic system, HPA axis and decrease of cortisol level such as seen in the result of this study. Death and terminal illness acceptance process will be suffered by individuals. This process, as that stated by Dr. Elizabeth Kubler-Ross (2005), was denial and isolation, anger, depression and withdrawal, bargaining, and acceptance. Natural coping followed by counseling and fellowship in HIV infected patient will shorten the process from denial directly to bargaining for the eventual result of acceptance. Effective natural coping can decrease this acceptance process, therefore cortisol level will decrease and immunity will be benefited. Defense mechanism is quite effective due to

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CONCLUSIONS

In this study, diagnosis of HIV infection is a stressor capable of influencing the activity of hypothalamic-pituitary-adrenal axis (HPA). The impact on various body cells causes changes in ACTH, cortisol and lymphocyte count. Changes in ACTH, cortisol and lymphocyte count aside from HIV biologic influence was also due to psychological stress from revealing of diagnosis of HIV infection. However, the psychological stressor can be predominant in acute stress. To prevent acute stress, the revealing of Diagnosis of HIV infection should be done precisely in the right time but using stages (one at a time). It is recommended that to prevent psychological stress, voluntary counseling and testing have to be done to every client. To maintain level of ACTH, cortisol and total lymphocyte count in normal level, optimum care support and treatment should be given, and to evaluate influence of stages in diagnosis revealing of HIV infection in changes of cell behavior, it is necessary to conduct further study concerning changes in molecular signal and death of T lymphocyte.

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