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Analysis of First-Line Antiretroviral Therapy toward Patients with HIV/AIDS in Indonesia

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Abstract

Introduction: Cases of HIV/AIDS (Human Immunodeficiency Virus-Acquired Immune Deficiency Syndrome) in Indonesia increases every year. Therefore, it requires adequate antiretroviral therapy (ARV).

Objective: To analyze first-line ARV therapy in HIV/AIDS.

Methods: The research was conducted retrospectively for four years with a descriptive analysis of HIV/AIDS patients at Hajj Surabaya Hospital.

Results: 43 samples met the inclusion criteria. 90.7% of patients were given antiretroviral initiation with an initial CD4 cell count of an average of 105,35 ± 113,03 cells/mm^3 (<350 cells/mm^3), and 67.4% were in clinical stage three. Effective therapy was found in seventeen patients (39.5%) through a CD4 cell increase of 123,34 ± 96,36 cells/mm^3. 26 patients (60.5%) had therapeutic failure which was not affected by duration of therapy and adherence (p>0,05). The most common side effect was nausea (27.9%).

Conclusion: Lamivudine, zidovudine and nevirapine are well tolerated. The use of first-line ARV which is not accompanied by monitoring toward viral load after 6 months of therapy only generates therapeutic success of 17 patients (39,5%). Viral load should have monitored after one-year first-line ARV therapy.

Keywords: antiretroviral therapy; CD4; HIV/AIDS; side effect.

INTRODUCTION

Cases of HIV/AIDS (Human Immunodeficiency Virus-Acquired Immune Deficiency Syndrome) in Indonesia increases every year [1]. HIV/AIDS is a disease characterized by a gradual loss of CD4$^+$ T cells resulting in an imbalance of CD4$^+$ T cell homeostasis which causes death. The HIV virus binds CD4 molecules on the surface of Thelper cells and replicates in them. This generates in the destruction of CD4$^+$ T cells and causes a steady decline in T-cell populations [2]. Based on the guidelines, the therapy used to overcome this case is antiretroviral therapy (ARV). To start antiretroviral treatment, it can be seen from the CD4 value and clinical patients. In general, ARV is given when CD4 <350 cells/ mm^3 or HIV infected with clinical stage three or four. ARV is given with the aim of reducing the amount of HIV virus in the body in order to increase life expectancy and reduce the incidence of infection in the population. To support the success of therapy, it requires the use of adequate antiretroviral therapy, monitoring drug compliance, and therapeutic counseling related to medication adherence, the potential risk of side effects or unexpected effect [3].

The first standard of ARV therapy uses combination of active drugs including two or more classes to suppress the amount of virus. Thus, it will improve the immune status of HIV patients, reduce deaths due to opportunistic infections (OIs), extend life expectancy and improve quality of life [4,5]. In the research conducted by Kurniawan et al, the type of NRTI used during initial therapy (zidovudin/stavudin or tenofovir) was considered not to affect virological success [6]. Likewise, the type of NNRTI used, nevirapine or efavirenz, had the same virological success. In addition, the research found that the success increased CD4 lymphocyte number in the first six months after starting therapy or immunological success was more significant. HIV/AIDS patients who have succeeded in increasing CD4 lymphocyte counts > 50 cells/mm^3 were found to be five times more likely to achieve their virological success compared to an increase in CD4 lymphocyte counts which was less than initial [6]. Research regarding the analysis of ARV therapy in HIV/AIDS in Indonesia to evaluate the use of first-line therapy has not been widely reported.

MATERIAL AND METHOD

Research design

This research had been conducted for 4 years at Polyclinic's Internal Medicine of Haji Hospital. Research data were collected retrospectively using patient medical record files. The sampling technique used was Non-Probability Sampling (Purposive Sampling). This research was conducted through several stages, which were the making of proposals, research permits, implementation of ethics, data collection, data processing, data analysis, discussion, and drawing conclusions.

Sample determination

43 outpatients with HIV/AIDS who undertook ARV and met inclusion criteria aged 14-64 had ARV therapy for six months at least, diagnosed with HIV/AIDS at an early stage or advanced stage, had initial and final CD4 cell count data, and had a complete medical record including the patient's identity, diagnosis, and treatment. Exclusion criteria are incomplete medical records.

Data analysis

It was conducted monitoring toward some clinical parameters which were CD4 cell increase and IO recurrence. The data obtained was then processed with descriptive statistics. Data was performed in tabular form and the frequency and percentage were calculated.

RESULT AND DISCUSSION

Based on the observation from medical record in 4 years period, it was obtained 43 adult patients who met inclusion criteria. As shown in Table 1, the highest number of male was 27 (62.8%) compared to women of (37.2%) with age range 19-61 years with an average of 38 ± 1.671 and the last education was high school education 24 (55.8%). This data were in accordance with demographic data from the Ministry of Health of the Republic of Indonesia in 2014 with cumulative cases of HIV/AIDS showing that the number of men were higher than women in the productive category between 25-49 years [1].

43 patients were obtained that 17 patients had therapeutic success and 26 patients experienced therapeutic failure. For the therapeutic failure of 26 patients in detail, 7 (26.9%) died and 19 (73.1%) were referred to other hospitals. Therapeutic failure can be caused by several things which are patient incompliance and viral load evaluation is not conducted routinely in addition to CD4 evaluation. Compliance is a major factor in achieving successful treatment of HIV infections. It was reported that adherence to take ARV drugs <80% was a predictor for the failure of HIV treatment [7]. In this study, compliance taking ARV was only 35% and there was not affected CD4 cell increase (p>0,05). In this study, incompliance was caused by environmental factors that were not supportive (57.7%), such as the distance from the hospital from the house, support from the closest family, and economical.

With early viral load test, it can detect the failure of antiretroviral therapy is more accurate than monitoring using immunological or clinical criteria, thus preventing an increase in patient morbidity and mortality [8,9]. If the viral load resulted in > 1000 copies/ml after using first-line antiretroviral therapy for ± 3 years, it can be switched to second-line therapy [9]. According to the Guidelines for antiretroviral treatment after being declared a failure in first-line treatment, it must use second-line ARV treatment [3]. Changes in therapy to the second line cause changes in medical costs because the price of second-line ARV drugs is more expensive than first-line ARV drugs [8].

Table 1. Characteristic Distribution of Patients with HIV/AIDS

Characteristic	Group	Subtotal (%)
Sex	Men	27 (62,8)
	Women	16 (37,2)
Age (year)	Range	19-61
	Mean±SD	38,4±1,671
Occupation	Work	25 (58,1)
	Do not work	18 (41,9)
Level of education	Elementary school	2 (4,7)
	Junior high School	9 (20,9)
	Senior High School	24 (55,8)
	University	8 (18,6)
Side effect	Nausea	12 (27,9)
	Diarrhea	5 (11,6)
	Anemia	5 (11,6)
	Neuropathy	4 (9,3)
	Gynecomastia	2 (4,6)
	Headache	2 (4,6)
	Insomnia	1 (2,3)
	None	12 (27,9)

Table 2. Comparison of CD4 in Pre and Post ARV Therapy

Parameters of CD4 (cells/mm³)	Mean ± SD		P value	ΔCD4 (Mean ± SD)
	Pre	Post		
CD4	105,35 ± 113,03	267,96 ± 287,86	0,000 (p<0,05)*	123,34 ± 96,36

* Significant difference between CD4 cell count pre and post therapy. Wilcoxon test.

Table 3. Analysis of the Effect of Other Variables on CD4 cell Decline

Variabel	Characteristic	ΔCD4 Subtotal (%)	P value
Duration of therapy	6 months	23 (53,49)	0,795 (>0,05)*
	12-24 months	15 (34,88)	
	≥36 months	5 (11,63)	
Adherence	Level of education	9 (34,6)	0,445 (>0,05)**
	Side effect	2 (7,7)	
	Environment	15 (57,7)	
Recurrence IO	Yes	12 (28)	0,989 (>0,05)**
	No	31 (72)	

Note : *Fisher exact test, **Man-Whitney test

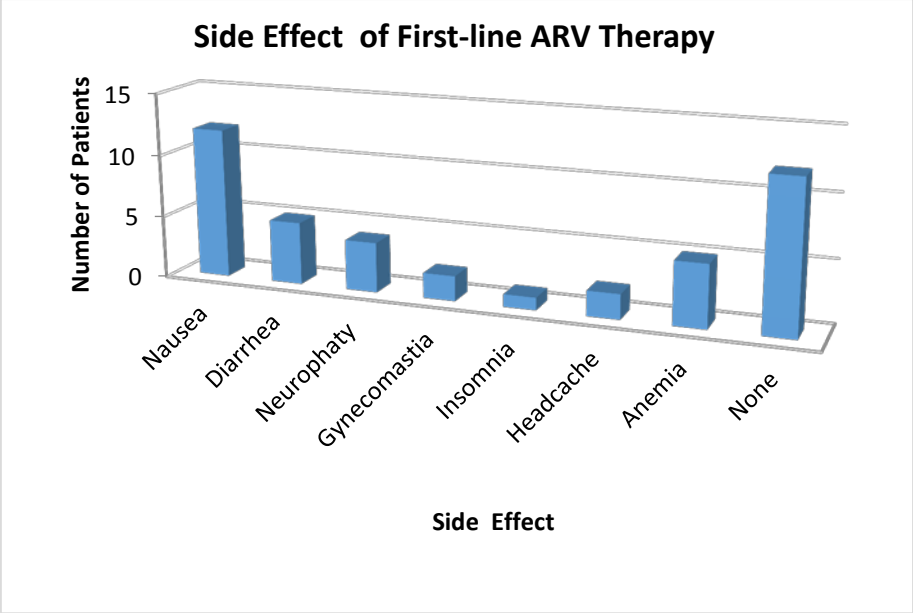

Figure 1. The side effect of Fist-Line Antitroviral Therapy (ARV)

First-line ARV drug used including nucleoside reverse transcriptase inhibitors (NRTI) groups and non-nucleoside reverse transcriptase inhibitors (NNRTI) groups, which were zidovudin, lamivudin and nevirapin. Based on research conducted by Riyadi et al, this combination could increase CD4 cell counts to 109.02 cells/mm³ [11]. Lamivudin is a synthetic nucleoside analog while zidovudin is a synthetic nucleoside analog. Zidovudin and lamivudin have several advantages which can be used in patients who are contraindicated relative or absolute to the kidneys and have good CNS penetration. Thus, it can be given to patients with HIV-associated neurologic deficits [12].

The use of ARV therapy enables the side effects. However, each individual has a different response [13]. Of the 43 patients using ARV therapy, it was found six types of drug side effects as listed in Figure 1. The most common type of drug side effects was nausea that occurred in 12 patients. These side effects appear in the first few weeks after taking ARV therapy. The second most common side effect was anemia which appeared after four weeks of taking ARV. Although all patient used the same ARV (zidovudin + lamivudin + neviral) therapy, there were different responses. The emergence of mild side effects with first-line therapy in patients did not need to be replaced. However, in patients with severe side effects (stage 3), second line replacement could be conducted.

To see the therapeutic success, it can be seen from the CD4 value. CD4 cell counts are important predictors of antiretroviral therapy such as knowing the right time for the initiation of antiretroviral therapy, monitoring disease progress and monitoring responses to antiretroviral therapy [14]. If it is used for monitoring clinical parameters, CD4 cell counts can be an early indicator of disease progression because CD4 cell counts fall before clinical conditions. For the initiation of ARV therapy, a recommended CD4 value was <350 cells/mm^3 [5]. The average baseline CD4 count before ARV therapy was 105,35 ± 113,03 cells/mm^3 (Table 2). 90.7% patients were given ARV therapy with a CD4 value <350 cells/mm^3. This was conducted in order treatment failure did not occur because patients who started ARV therapy with CD4 counts <200 cells/mm^3 showed treatment failure nearly doubled [15]. Besides based on CD4 cells, the initiation of ARV therapy can also be determined based on clinical stage where as many as 67.4% in clinical stage three (WHO, 2016). The higher the CD4 cell count of HIV/AIDS patients when starting treatment, the higher the CD4 cell count increase [16,17]. To find out the effectiveness of ARV therapy, it can be seen from CD4 because CD4 T cells produce cytokines and interact with other immune cells to regulate the immune response. All patients received ARV with a duration of therapy between 6-48 months. The increase in baseline and late CD4 cell counts was 123,34 ± 96,36 cells/mm^3. From the results of this increase, effective ARV therapy was given to patients with HIV/AIDS because according to WHO, an increase in CD4 50-150 cells/mm^3 after a year given ARV therapy shows the effectiveness. Although there was an increase in CD4 cell counts there was no relationship with duration of therapy and compliance (p>0,05) (Table 3).

Another clinical parameters seen to determine ARV therapy effectiveness is IO recurrence. 72.1% patients given this first-line ARV therapy were found that there was no recurrence of OI. According to Wingfield & Wilkins, initiation of ARV therapy with CD4 <200 cells/mm^3 can cause IO recurrence [17]. In theory, the aim of ARV therapy is to increase CD4 T cells to prevent IO activation and avoid the direct effects of the HIV virus. Antiretroviral therapy also results in clinical damage from the immune system through inflammatory recovery syndrome (IRIS) [18]. In this study same results with research conducted by Yogani et al, 2015 explained that there was no relation between opportunistic onfection with an increase in CD4 counts in HIV patients who were given ARV therapy in the first six months [19,20].

CONCLUSION

After six months, first-line ARV therapy shows the effectiveness enhancement in CD4 with an average of 123,34 ± 96,36cells/mm^3. The use of first-line ARV therapy without monitoring of viral load only results in therapeutic success in 17 patients (40%) because it was possible to find out whether antiretroviral therapy failed or not. Viral load should have monitored after one-year first-line ARV therapy. Furthermore, a larger sample size within routine viral load evaluations requires to ensure the effectiveness of first-line ARV therapy.

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