



Correlation of Drug Eruption with the Number of CD4 In the HIV-Infected Patient at Haji Adam Malik General Hospital

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Abstract : Background: Incidence of HIV is increasing in some Asian countries, and new infections are still emerging. Antiretroviral drugs (ARVs) use a combination of three or more drugs called High Activity Antiretroviral Therapy (HAART) to improve the quality and life expectancy of people with HIV. Factors associated with an increased risk of drug eruption were CD4 cell counts ≤ 200 cells / mm³, CD8 > 460 cells / mm³, gender and previous drug eruption history.

Purpose : To investigate the association of drug eruptions with CD4 cell counts in HIV patients.

Methods: A cross sectional study with observational analytic design. Using secondary data from medical record of RSUP H. Adam Malik at Poliklinik of Pusyansus and Poliklinik SMF of dermatology and venereology.

Results: Total subjects of the study were 474 patients, of whom 121 were erupted. Subjects most experienced drug eruption is men 69.14% and women 30.57%, the most age group is 25 - 49 years as many as 85.94%. Clinical features of most drug eruptions experienced were morbiliform eruption 57.85%. The drugs that cause the most drug eruption are ARVs with Nevirapine content 61.98%, and Efavirenzis 38.02%. The results of the analysis test found a significant relationship between drug eruption incidence with CD4 cell count ≤ 200 cells / mm³ with p value 0.012 ($p < 0.05$).

Conclusion: CD4 cell count is significantly associated with drug eruption in HIV patients. More men who experience drug eruption in the age group of 25-49 transcendental factor that predominate HIV patients are heterosexual or free sex. ARV drugs containing Nevirapine cause the most drug eruption compared to Efavirenz.

Keywords : HIV, drug eruption, antiretroviral, CD4.

Introduction

Incidence of HIV is increasing in some Western European and Asian countries, and new infections are

still emerging.¹ In Indonesia, HIV was first discovered in the province of Bali in 1987. Until now HIV has spread in 365 cities across provinces in Indonesia.²

In 1996, antiretroviral drug (ARV) therapy was introduced using a combination of three or more drugs Called High Activity Antiretroviral Therapy (HAART) to improve the quality and life expectancy of HIV infected patients.³

In the 1980s, antibiotics were the most responsible drug for drug eruptions used as a treatment and prophylaxis against opportunistic infections. The emergence of adverse drug reactions caused not only by ARV drugs but also drugs used to treat opportunistic infections.⁴ Drug hypersensitivity reactions occur at a higher rate in HIV patients than in the general population and cause significant morbidity. HIV / AIDS patients are 100 times more likely to get heavy drug eruptions than the general population.^{3,6} The diagnosis and treatment of drug hypersensitivity reactions in HIV patients is difficult due to the use of multiple drug regimens to treat patients.⁷ Skin and liver are the organs most frequently involved in drug hypersensitivity reactions.⁵ Cutaneous drug eruptions are the most common manifestation of drug hypersensitivity reactions.⁸ Patients may appear to have systemic absent exanths or drug hypersensitivity syndromes, which typically manifest as maculopapular erythema eruptions.^{3,4,8,9} Drug eruptions with immunologic mechanisms are called immunologic drug eruptions or allergic drug eruptions. One kind of eruption can be caused by a variety of drugs, while one drug can cause various eruptions.¹⁰⁻¹² Eruptions of allergic drugs include erythema multiforme, maculopapular eruption, urticaria, blister or pustular. The development of reactions may vary, for example the specific diagnosis is drug rash with eosinophilia and systemic symptoms (DRESS), Fixed drug eruptions, acute generalized exanthematouspustulosis (AGEP), Steven-Johnson syndrome (SSJ) and toxic epidermal necrolysis.¹³ Incidence of cotrimoxazole drug eruption is higher in HIV patients (40-80%) compared with healthy subjects (3-5%). The risk of allergic drug eruption from antibiotics is increased in HIV patients due to immunologic factors and susceptibility to exposure to antibiotics.⁸

Experimental

This research is a cross sectional study with observational analytic design. Using secondary data from medical records of HIV patients in departement of dermatology and venereology Haji Adam Malik General Hospital during the period January 2015 - December 2016. Recording of basic data conducted by researchers is:

1. Patient Identity:

- a. Age
- b. Gender
- c. Risk factors are infected with HIV

2. ARV drugs; based on data written on the medical record.

3. Laboratory results of patient CD4 cell count before starting antiretroviral treatment; based on data written on the medical record.

4. Diagnosis of drug eruption; based on data written in the medical record Polyclinic pusyansus that was considered to the departement of dermatology and venereology.

The patient characteristic data were analyzed descriptivel. Correlation of the drug eruption with CD4 cell count in HIV patients was analyzed using Chi square test. In this research, there is no intervention on the sample of research because the data used in this research comes from medical record. Prior to the research, the protocol will be requested Ethical Clearance from the Committee of Ethics Haji Adam Malik General Hospital.

Result and Discussion

From the data collection, 670 new patients with HIV / AIDS registered in Polyclinic of Pusyansus Haji Adam Malik General Hospital during January 2015 - December 2016 periode. There were 196 patients with incomplete data including list of drugs and laboratory results CD4 cell count, so it is excluded from the study sample. So the total subject of research is 474 people. There were 121 patients referred toimmunodermatology

in department of dermatology and venereology and diagnosed with drug eruption. Characteristic features observed from all study subjects included sex, age group, clinical features, CD4 cell count, drugs obtained from polyclinic Pusyansus and HIV transmission factors.

In this study, it was found that the distribution of research subjects ie new HIV patients by sex the most were males, ie 285 patients (60.1%) and women as many as 189 patients (39.9%).

Table 1 Distribution of research subjects by sex

Sex	Drug Eruption		No drug eruption Amount		Total
	n	%	n	%	
Male	84	17.72	201	42.40	285 (60.12)
Female	37	7.80	152	32.06	189 (39.86)
Total	121	25.52	353	74.47	474 (100)

Based on research in Indonesia, most of the results show that the number of male patients more than women. As the study conducted at RSCM Jakarta in 2013 the number of male HIV patients is 81.2% and women 18.8% .59 The high rate of HIV infection in men is due to the lifestyle and mobility of men more outside the home than women. Men also have more sexual partners outside freely than women.

In the age group of 25-49 years old, the age group experienced the most drug eruption was 382 patients (80.59%), and in the age group 20 -24 years old as many as 11 patients the age group ≤ 50 years of drug eruption occurred as many as 6 patients (4.9%) This can be observed in Table 2.

Table 2. Distribution of research subjects of drug eruption patients by age group

Age	Drug eruption		No drug eruption		Total (%)
	n	%	N	%	
< 5 yo	0	0	5	1.05	5 (1.05)
5 – 14 yo	0	0	7	1.47	7 (1.47)
15 – 19 yo	0	0	2	0.42	2 (0.42)
20 – 24 yo	11	2.32	43	9.07	54 (11.4)
25 – 49 yo	104	21.94	278	58.64	382 (80.59)
≥ 50 yo	6	1.26	18	3.79	24 (5.06)
Total	121	25.52	353	74.47	474 (100)

Mean age of drug eruption patient

\bar{x} : 4.96 Min : 20 yo
SD : 0.374 Maks : 57 yo

Mean age of no drug eruption patient

\bar{x} : 4.80 Min : 1 yo
SD : 0.750 Maks : 64 yo

The age group of 25-49 years is a productive age group with high levels of sexual activity. Thus, high HIV infection in the 25-49 year age group is due to the very high sexual activity causing the spread of HIV infection most commonly found in that age group.

The results of the analysis in this study are the most commonly found clinical manifestations are morbiliform / maculopapular eruptions, followed by generalized exfoliative dermatitis, urticaria / angioedema, stevenjohnson syndrome and fixed drug eruption.

Tabel 3. Distribution of clinical manifestation of drug eruption

Clinical Manifestation	CD 4 count				Total	
	≤ 200		> 200			
	n	%	n	%	n	%
Morbiliformis eruption	57	47.10	13	10.74	70	57.85
Urticaria / angioedema	7	5.78	4	3.30	11	9.09
Acute generalized exanthematouspustulosis (AGEP)	5	4.13	1	0.82	6	4.95
Fixed drug eruption (FDE)	2	1.65	0	0.00	2	1.65
Steven Johnson Syndrom(SJS)	5	4.13	1	0.82	6	4.95
Generalized exfoliative dermatitis	22	18.18	4	3.30	26	21.48
Total	98	80.98	23	19.02	121	100

The results of research that have been done in Indonesia, Nababan and Faiz research at RSUP H. Adam Malik found the most clinical picture is eksantematous eruption 82%, followed by steven Johnson syndrome 9.8%, erythroderma 1.6% and others 6.6% .16 In the study in RSUD dr. Soetomo Surabaya found 46.3% who suffered morbiliform eruption skin disorder From the results of this study found that most subjects who experience drug eruption get a drug with combination ARV and ATD where there are 25 patients who received a combination containing Nevirapine and 18 patients who received a combination containing Efavirenz. It also occurs in patients who get the most antiretroviral combination of ARV + ATD + chemoprophylaxis is the subject of ARVs containing Nevirapine versus Efavirenz.

Table 4. Distribution of drugs and combination

Drugs	CD 4 count				Total	
	≤ 200		> 200			
	n	%	N	%	n	%
Duviral (AZT + 3TC) + Neviral / AZT FDC	1	0.82	1	0.82	2	1.65
THE / StocrinHiviralTenofovir)	2	1.65	1	0.82	3	2.47
HiviralTenofovirAluvia	0	0.00	0	0.00	0	0.00
Duviral + Neviral /AZT FDC + ATD	21	17.35	4	3.30	25	20.65
THE /StocrinHiviralTenofovir + ATD	15	12.39	3	2.47	18	14.86
Duviral + Neviral /AZT FDC + kotrimoksazol / klindamisin / fluconazole	17	14.04	5	4.13	22	18.17
THE / StocrinHiviralTenofovir + kotrimoksazol (pehatrim) / klindamisin / fluconazole	9	7.43	2	1.65	11	9.08
Duviral + Neviral /AZT FDC + kotrimoksazol /klindamisin / fluconazole + ATD	22	18.18	4	3.30	26	21.48
THE / StocrinHiviralTenofovir + kotrimoksazol (pehatrim) /klindamisin / fluconazole + ATD	11	9.09	3	2.47	14	11.56
Total	98	80.99	23	19.01	121	100

Duviral: Zidovudine (AZT) + Lamivudine (3TC); Neviral: Nevirapine; AZT FDC: Zidovudine +Lamivudine+Nevirapine; THE: Tenofovir + Hiviral + Efavirenz; Stocrin :Efavirenz; ATD: Anti Tuberculosis drug.

According to the Indonesian National Guidelines, HIV patients who start antiretroviral 200 cells / mm³ are advised to take therapy with a CD4 cell count of chemoprophylaxis for 2 weeks. In clinic Pusyansus Haji Adam Malik General Hospital administration of chemoprophylaxis according to national guidelines, where patients are given cotrimoxazole for 2 weeks as prophylaxis then followed by antiretroviral drugs, if the CD4 cell count > 350 cells / mm³ then cotrimoxazole is discontinued.

The analysis test using Chi square test with 95% confidence level p value 0.012 (p <0.05) value of X² count (pearson Chi square) is 6,319 (value X table 3,841). Based on p value there is a significant relationship between drug eruption incidence and CD4 cell count. This can be seen in Table 5

Table 5. Analysis of drug eruptions with CD4 cell counts in HIV patients with drug eruption and without drug eruption

	Diagnosis		Total
	Erupsiobat	Tanpaerupsiobat	
CD 4 ≤ 200	98	244	342
> 200	23	109	132
Total	121	353	474

Chi square test with confidence level 95% p value 0.012 (p <0.05), value of X² count (pearson Chi square) is 6,319 (value X² table 3,841).

The results of this study found a significant relationship between drug eruption events with CD4 count ≤ 200 cells / mm³. Based on the literature, the incidence of drug eruption in HIV patients increased 100 times compared to normal people, this is due to the immune system dysregulation characterized by decreased CD4 cell counts in HIV-infected patients. One of the trigger factors ≤ 200 cells / mm of drug eruption in HIV patients is the CD4 cell count in which immunity occurs in the introduction of drug hapten by the body.^{3,14}

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