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Success Of Syphilis Therapy In Hiv/Aids Patients Related To Cd4 Level

Andre Yuindartanto[1] , Afif Nurul Hidayati[1,2*] , Diah Mira Indramaya[1] , M. Yulianto Listiawan[1] , Evy Ervianti[1], Damayanti[1] , Erwin Astha Triyono[3]

[1] Department of Dermatology and Venereology, Dr. Soetomo General Academic Teaching Hospital, Surabaya, Indonesia.

[2]Department of Dermatology and Venereology, Universitas Airlangga Teaching Hospital, Surabaya, Indonesia.

[3] Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.

ABSTRACT

Background: Syphilis and human immunodeficiency virus (HIV) infection are diseases that can be transmitted through sexual intercourse, so it is not surprising that someone has both at the same time. Syphilis can increase the risk of contracting the Human immunodeficiency virus (HIV) where HIV-negative people exposed to syphilis will increase the risk of contracting up to 3-5 times. Objective: This study aims to determine the success of syphilis therapy in HIV/AIDS patients related to CD4 levels.

Methods: This study was conducted using a quantitative analytic design, the type of research carried out was retrospective by collecting data that had been collected previously. The population in this study were all patients with HIV in Dr. Hospital. Soetomo Surabaya. The sample in this study was selected using a total sampling technique involving 25 people with HIV. The data of this study were sourced from secondary data, namely medical record data from the inpatient and outpatient of UPIPI RSUD Dr. Soetomo Surabaya in 2019. The CD4 levels obtained were analyzed by descriptive statistical tests and T-tests, while Duncan's test was used to determine VDRL levels.

Results: The results of this study indicate that syphilis therapy has been shown to increase CD4 levels. This increase was obtained based on the results of calculations before and before syphilis therapy. An increase in CD4 cells in HIV patients through syphilis therapy was also accompanied by a decrease in VDRL. Based on the test results, it is known that there are significant differences before and before therapy where VDRL decreases every time the experiment starts from 1st titer to 4th titer with the average obtained (1st titer = 11.04), (2nd titer = 4.72), (3rd titer = 4.08) and (4th titer = 1.84).

Conclusion: Syphilis therapy has been shown to be able to increase CD4 levels in syphilis patients with HIV and reduce VDRL levels.

Key words: syphilis, HIV/AIDS, CD4, treatment, sexually transmitted infection.

BACKGROUND

Syphilis and human immunodeficiency virus (HIV) infection are diseases that can be transmitted through sexual intercourse, so it is not surprising that someone suffers from both at the same time (Aini, et al., 2020). In some developing countries until 1998, syphilis was still considered an important cause of death, and in relation to the spread of HIV infection was shown to increase the sexual transmission of HIV (Agustina et al., 2011). Several government programs have been implemented, but syphilis cases in Indonesia continue to increase. One of the causes of an increase in syphilis cases is an increase in HIV status. So that the provision of information regarding the prevention of syphilis is emphasized in patients who are more at risk, play an important role in prevention efforts, and can increase the success of syphilis therapy.

Penicillin G is still the treatment of choice for all stages of syphilis. The therapeutic regimen used depends on the stage of the disease. Early syphilis (primary, secondary or early latent) can be treated with a single injection of 2.4 million units of benzathine penicillin G intramuscularly (IM). Late syphilis (late latent syphilis) is treated with injection of benzathine pencilin G 2.4 million units IM weekly for a total of three injections (Messahel A et al., 2009).

There are several other antibiotics that can be used if there is an allergy to penicillin. Doxycycline is effective for early syphilis (100 mg orally twice daily for 14 days) and for late syphilis (100 mg orally twice daily for 28 days). Ceftriaxone (1–2 g daily IM or intravenously (IV) for 10–14 days) can also be used as an alternative to penicillin (Ghanem KG, 2010). Several studies have shown that there is a reciprocal relationship between syphilis and HIV infection. This relationship means that syphilis can increase the incidence of HIV infection, and vice versa HIV infection can cause the incidence of syphilis. Based on the pathogenesis of the two diseases, it can be seen that the syphilitic lesions accumulate inflammatory cells, especially CD4+ cells. Where cells that have CD4+ receptors are targets of the HIV virus, making it easier for HIV infection to occur in syphilis patients. This is in accordance with research by Agustina et al (2011), which mentions several factors in syphilis that are thought to have contributed to the process of HIV transmission. The factors in question are the breakdown of the epithelial barrier as the entrance (or exit) of HIV; the arrival of a large number of macrophages and T cells creates a rich environment for HIV receptors; Cytokine production by macrophages stimulated by treponemal lipoproteins can increase HIV replication. Pallidum can induce HIV-1 gene expression from monocytes and macrophages; and T. pallidum lipoprotei can induce CCR5 from monocytes which is the main co-receptor for HIV transmission (Agustina et al., 2011). This study aims to determine the success of syphilis therapy in HIV/AIDS patients related to CD4 level

METHODS

This research was conducted using a quantitative analytic design, the type of research carried out was retrospective by collecting data that had been previously collected (Sugiyono, 2013). The population in this study were all patients with HIV in Dr. Hospital. Soetomo Surabaya. The sample in this study was selected using a total sampling technique involving 25 people with HIV. The data of this study were

sourced from secondary data, namely medical record data from the inpatient and outpatient rooms of UPIPI RSUD Dr. Soetomo Surabaya for the period January-December 2019. The data obtained were analyzed by statistical descriptive analysis followed by a T test to determine whether there was CD4 success in HIV patients. VDRL data of HIV patients obtained during the study were then analyzed using Analysis of Variance (ANOVA) and tested using the Duncan-Tukey test to determine the effect of the treatment which was very significant.

RESULTS

1. Descriptive Statistics Test

Table 1. Comparison of CD4 cells before and after syphilis therapy

CD4 levels	**Before Syphilis Therapy**		**After Syphilis Therapy**	
	n	%	n	%
> 500	2	8%	2	8%
200-500	14	56%	23	92%
< 200	9	36%	0	0%
Total (n) (%)	25	100%	25	100%

Based on table 1. the incidence of HIV/AIDS with syphilis coinfection had the highest CD4 levels at >500 as many as 2 people with a percentage of 8%. Furthermore, patients with CD4 levels with a number of 200-500 cells/uL were found in 14 people with a percentage of 56%, followed by patients with CD4 levels at <200 found in 9 people with a percentage of 36%. After being given treatment for 12 months, the success of CD4 therapy in HIV patients increased with the highest CD4 levels being >500 by 2 people with a percentage of 8%, then the CD4 levels of patients with a number of 200-500 as many as 23 people with a percentage of 92%, and not no one has CD4 < 200. The Indonesian Ministry of Health revealed that there was a decrease in CD4 levels between 70-100 cells/mm3/year in HIV/AIDS patients. The following is a picture of the difference in CD4 levels before and after syphilis therapy.

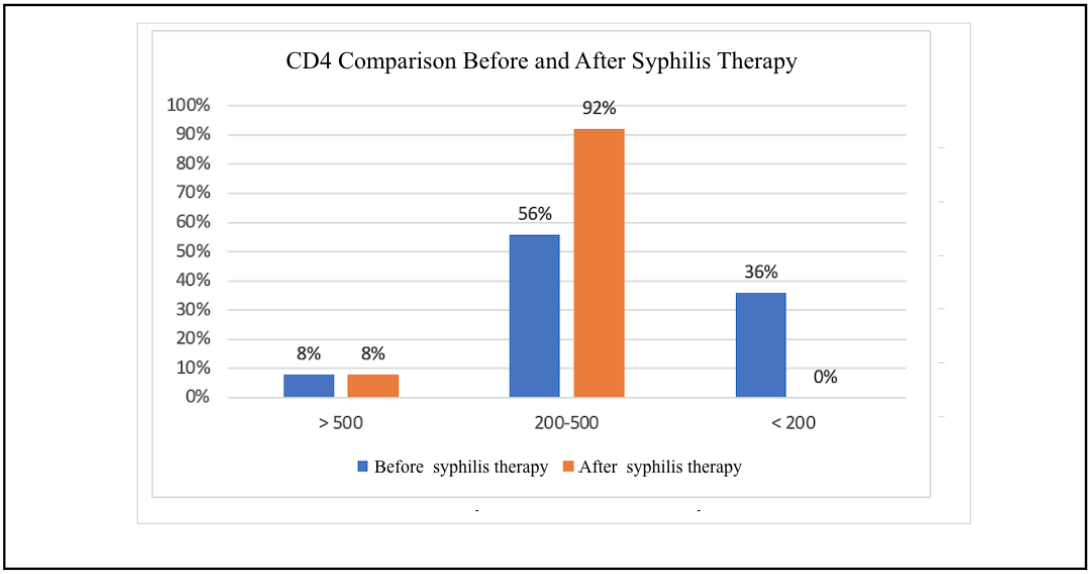

Figure 1. Differences in CD4 levels before and after syphilis therapy

Normality test

Before the t-test was conducted to determine the success of CD4 administration, a normality test was carried out first. The normality test in this study used the Kolmogor of Smirnov test with the following criteria:

1. If the significance score (Sig.) > 0.05 then the data is normally distributed

2. If the significance score (Sig.) < 0.05 then the data is not normally distributed

Based on the test results, it is known that the data obtained are normally distributed

One-Sample Kolmogorov-Smirnov Test

		Before Syphilis Therapy	After Syphilis Therapy
N		25	25
Normal Parameters[a,b]	Mean	278.7600	336.7600
	Std. Deviation	107.98159	101.73261
Most Extreme Differences	Absolute	.147	.129
	Positive	.147	.129
	Negative	-.124	-.099
Test Statistic		.147	.129
Asymp. Sig. (2-tailed)		.173[c]	.200[c,d]

Figure 2. Normality test results

This different test model is used to analyze the pre-post research model or before and after. Different tests are used to evaluate certain treatments on the same sample in two different observation periods (Pramana, 2012). Paired sample t-test is used if the data is normally distributed. The basis for making the decision to accept or reject Ho in this test is as follows.

1. If t count > t table and probability (Asymp. Sig) < 0.05, then Ho is rejected and Ha is accepted that syphilis therapy in HIV patients has a significant effect.
2. If t count < t table and probability (Asymp. Sig) > 0.05, then Ho is accepted and Ha is rejected, that syphilis therapy in HIV patients has no significant effect.

The following presents the results of the t-test data analysis of the success of syphilis therapy in HIV patients.

		Paired Differences					t	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference			
					Lower	Upper		
Pair 1	Before_ Syphilis_ Therapy After_ Syphilis _Therapy	-58.00000	18.20714	3.64143	65.51554	-50.48446	15.928	.000

Figure 3. Print CD4 t-test before and after therapy

Based on the results of the T test, it is known that the sig. which is obtained is 0.000, thus syphilis therapy in HIV/AIDS patients is proven to be able to improve the immune system for people with HIV. The success of syphilis therapy was also found in the mean difference before and after CD4 administration. It is known that the average CD4 cell count in 25 HIV patients before treatment for syphilis was 278,7600. After treatment for syphilis, the CD4 levels of HIV patients increased by 58 to 336,7600. The following describes the differences in CD4 levels of HIV patients before and after syphilis therapy is given in the following table.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Before_ Syphilis_ Therapy	278.7600	25	107.98159	21.59632
	After_ Syphilis _Therapy	336.7600	25	101.73261	20.34652

Figure 4. Print screen of paired CD4 test before and after therapy

VDRL Anova Test

The ANOVA test or Analysis of Variance Test is used to see the variances that arise due to several treatments to conclude whether or not there is a difference in the average in the population. The basis for taking is:

1. F count < F0.05, H0 = there is no difference between treatments.
2. F count > F0.05, H1 = there is at least 1 difference between the 4 different treatments

ANOVA

VDRL

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1167.160	3	389.053	4.709	.004
Within Groups	7931.200	96	82.617		
Total	9098.360	99			

Figure 5. Print screen of ANOVA test for VDRL levels before and after syphilis therapy

Based on the results of the ANOVA test for VDRL levels, it is known that H1 is accepted where there is a difference between the 4 treatments carried out. To find out more about the difference in results between VDRL titer tests, the Duncan Turkey test was carried out. Based on the test results, it is known that there is a significant difference before and after being given therapy where the VDRL decreases every time it is tested starting from 1st titer to 4th titer.

VDRL

Duncan[a]

Titer	N	Subset for alpha = 0.05	
		1	2
4th Titer	25	1.840	
3rd Titer	25	4.080	
2nd Titer	25	4.720	
1st Titer	25		11.04
Sig.		.296	1.000

Means for groups in homogeneous subsets are displ

Figure 6. Duncan VDRL test print screen before and after syphfilis therapy

Figure 6 shows the results of the Duncan test in HIV patients through syphilis therapy, the average VDRL obtained in 1st titer was 11.04, then in the second titer it decreased by 6.32 with an average gain of 4.720. continued at the 3rd titer, the average VDRL was 4.08 and there was a significant decrease in the 4th titer with an average VDRL of 1.84.

DISCUSSION

Syphilis infection can increase HIV viral load, which can cause CD4 levels to fall. Successful treatment of syphilis therapy can prevent an increase in viral load and prevent a decrease in CD4 levels. Syphilis patients with HIV/AIDS infection who are successfully treated for syphilis and undergoing ARV therapy will help increase the patient's CD4 levels. The number of CD4 cells in the blood is a reliable indicator for monitoring the severity of the immune damage caused by HIV, and makes it easier for us to make decisions about antiretroviral treatment. HIV generally infects CD4 cells. HIV's genetic code becomes part of that cell. When CD4 cells multiply (replicate) to fight off any infection, they also make copies of HIV. CD4 cells are a type of white blood cell or lymphocyte. These cells are an important part of our immune system. CD4 cells are sometimes referred to as T-cells. There are two kinds of T-cells. T-4 cells, also called CD4 cells and sometimes CD4+ cells, are 'helper' cells. T-8 (CD8) cells are 'suppressor' cells, which terminate the immune response. CD8 cells are also referred to as 'killer' cells, because they kill cancer cells or cells infected with viruses.

CD4 is a marker or marker that is on the surface of human white blood cells, especially lymphocyte cells. CD4 is a very important indicator because a reduced CD4 count indicates a decrease in the immune system, white blood cells or lymphocytes that should play a role in fighting infections that enter the body are also reduced. The CD4 value in people with a good immune system is between 600-1500 cells/mm3 (Andersen, Pramudo, & Sofro, 2017). In patients with compromised immune systems due to HIV infection, the CD4 count may continue to decline as the disease progresses (Swanson, 2010). Therefore, the CD4 cell count can be an indicator to assess the level of the immune system in patients with HIV/AIDS (Yogani, Karyadi, Uyainah, & Koesnoe, 2015).

Once infected with HIV and have not started antiretroviral therapy (ART), the CD4 cell count will decrease even more. This is a sign that the immune system is getting damaged. The lower the CD4 count, the more likely you are to get sick. If there is a decrease in the number of CD4 cells that increases accompanied by an increase in viremia, this indicates the end of the asymptomatic period. Generally, the CD4 count will start to rise as soon as we start ART. But the speed varies greatly, and sometimes slow. If your CD4 count is below 50 when you start ART, your CD4 count may not increase to normal (above 500).

Maintaining CD4 levels to remain high or close to normal is important in HIV/AIDS patients because the higher the CD4 count, the lower the risk of fatigue in HIV/AIDS patients. Based on research conducted by Yogani et al (2015) it was concluded that patients receiving Highly Active Antiretroviral Therapy (HAART) experienced changes in their CD4 count, although this was dependent on their initial CD4 count, adherence to ART medication, and TB infection. Adherence to taking medication is important in the management of HIV/AIDS patients because it is related to the progression of HIV disease (Yogani et al., 2015).

CD4 T cells are the main target of HIV infection as a site for viral replication. CD4 lymphocytes function to coordinate a number of important immunological functions. This loss of function leads to a progressive impairment of the immune response. In primary HIV infection, the virus enters the bloodstream and invades CD4 T cells. Virus will bind via glycoprotein gp120 on the surface of the virus and CD4 on the surface of CD4 T cells. The glycoprotein gp41 will bind to the chemokine co-receptor CXCR-4 on

the surface of CD4 T cells. The viral nucleocapsid then enters the cytoplasm of CD4 T cells and releases viral RNA. With the help of the enzyme reverse transcriptase, viral RNA will be reverse transcription (reverse transcription) into a double-stranded DNA copy of the virus. The resulting viral DNA will integrate with CD4 T cell DNA and is now known as a provirus. A decrease in the number of CD4 T cells is one of the hallmarks of HIV infection and a major indicator of disease progression.

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The results of this study support the research conducted by Li Tong, et al (2017) with the results showing that HIV/AIDS patients with syphilis coinfection had a slower response to VDRL serologic titer reduction and more treatment failures than HIV negative syphilis patients after 6 months. -12 months of therapy with benzathine penicillin G. Treatment is considered successful if the VDRL titer falls. If the VDRL titer rises, reinfection is possible, then repeat therapy and treat the patient as a new infection. If the VDRL titer remains the same or even drops, the treatment is considered successful so that the patient is adequately monitored 24 months after therapy.

In the study by Kathuria S et al. (2016) and Kibaru EG et al. (2018) stated that haematological abnormalities changed significantly within 6 months of antiretroviral therapy with a significant increase in Hb levels. This is due to the effectiveness of ART drug administration where there is an increase in CD4 and a decrease in viral load so that the hematopoiesis process can run effectively. Non-protonema tests such as Venereal Disease Research Laboratory (VDRL+). To determine the antibodies in the body against the

entry of Treponema pallidum. The results of the quantitative test of the VDRL test tend to correlate with disease activity so that it is very helpful in screening, the titer rises when the disease is active (failed to treatment or is infected) and falls when treatment is sufficient. The existence of syphilis therapy has a significant impact on the activity of the HIV virus, this is evidenced by the gap in CD4 levels before and after syphilis therapy is given. Weakened immune response can even lead to false-negative results in HIV diagnostic tests that detect anti-HIV antibodies can affect the results of the VDRL test (Li Y, Zhao JK, Wang M, Han ZG, Cai WP, Zheng BJ, et al., 2010)

CONCLUSION

In HIV patients, syphilis infection can increase HIV viral load and decrease CD4 levels. The success of syphilis therapy can prevent an increase in viral load resulting in a decrease in CD4 levels. Syphilis patients with HIV/AIDS infection who are successfully treated for syphilis and undergoing ARV therapy will help increase the patient's CD4 levels. Based on the results of the study, it can be concluded that the administration of syphilis therapy is proven to be able to increase CD4 levels. This increase was obtained based on the results of calculations before and after syphilis therapy. The increase in CD4 levels in HIV patients through syphilis therapy was also followed by a decrease in VDRL. Based on the test results, it is known that there is a significant difference before and after being given therapy where the VDRL decreases every time it is tested starting from from 1^{st} titer to 4^{th} titer with the average obtained (1^{st} titer = 11.04), (2^{nd} titer = 4.72), (3^{rd} titer = 4.08) and (4^{th} titer = 1.84). Maintaining CD4 levels to remain high or close to normal is important in HIV/AIDS patients because the higher the CD4 count, the lower the risk of fatigue in HIV/AIDS patients. Syphilis therapy has been shown to be able to increase CD4 levels in syphilis patients with HIV and reduce VDRL levels.

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