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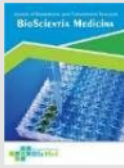
Submission date: 20-May-2021 02:51PM (UTC+0700)

Submission ID: 1590169835

File name: 4_count_of_HIVAIDS_Patients_Receiving_Antiretroviral_Therapy.pdf (535.14K)

Word count: 1826

Character count: 8883



The Effect of Vitamin D Supplementation on the Increase in CD4 count of HIV/AIDS Patients Receiving Antiretroviral Therapy

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ARTICLE INFO

Keywords:

Vitamin D
Calcitriol
CD4 Count
HIV
Antiretroviral Drugs

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All authors have reviewed and approved the final version of the manuscript.

<https://doi.org/10.32539/bsm.v5i1.186>

ABSTRACT

Introduction. Vitamin D plays a role in health overall, but hypovitaminosis D still occurs throughout the world. HIV/AIDS patients are prone to suffer from hypovitaminosis D because of the infection itself and the side effects of antiretroviral therapy. Various effort have been tried to improve the immune status of HIV/AIDS patients, one of them is by adding vitamin D. Vitamin D acts as an antiinflammatory so that it can prevent apoptosis of CD4 T cells and increase CD4 cell count.

Methods. This is a randomized control trial add on a study that aims to determine the effect of vitamin D to increase in CD4 counts of HIV / AIDS patients who have received antiretroviral drugs. Subjects were HIV / AIDS patients who had received antiretroviral drugs. A total of 20 subjects were divided randomly into two groups; one group received vitamin D (calcitriol 0.5 mcg per day) for eight weeks, and the other group that received a placebo. Each group was measured of CD4 cell count before and after treatment. **Results.** There was a significant increase in the CD4 cell count of the vitamin D group ($p = 0.046$), but not in the CD4 cell count of both groups ($p = 0.985$). The comparison of mean CD4 cell counts between groups before treatment was not significantly different ($p = 0.057$), but after treatment, it became significantly different ($p = 0.040$). **Conclusion.** Vitamin D has been successful in increasing CD4 cell count in the vitamin D group, and it is recommended to give HIV / AIDS patients to increase CD4 cell count.

1. Introduction

Vitamin D deficiency is still common worldwide. The prevalence of hypovitaminosis D in HIV patients in Europe, Australia, and America ranges from 45-87%.¹ In HIV infection, there is an abnormality of the 1 α hydroxylase enzyme in the kidney so that it cannot convert calcidiol to its active form, calcitriol.² Antiretroviral therapy (ART) worsens hypovitaminosis D because it affects vitamin metabolism D.^{2,3} Haug's (1994) study found that HIV-deficient vitamin D patients had significantly low CD4 cell counts.⁴ Ross (2011) study of HIV patients on ART who failed to achieve CD4 recovery suggested high vitamin D levels were associated with more remarkable CD4 T cell recovery after using ART.⁵

Bang (2012) gave calcitriol together with cholecalciferol in HIV patients, did not get a significant change in T lymphocyte levels. However, there was a significant relationship with an increase in calcitriol levels with an increase in activated CD4 T lymphocytes.⁶ Kakalia (2011), giving vitamin D increases serum calcidiol levels but does not increase CD4 counts. This study aims to determine whether the addition of vitamin D affects increasing the CD4 counts of HIV/AIDS infection patients who have received ART at dr. Mohammad Hoesin Palembang.

2. Methods

This is a prospective, double-blind, randomized

clinical trial (RCT) conducted at the VCT Polyclinic Dr Mohammad Hoesin (RSMH) Palembang from December 2019 to May 2020. The research subjects were HIV / AIDS patients who came to the VCT Polyclinic of RSMH Palembang, male or female, aged 18-60 years, who had received antiretroviral drugs—checking the CD4 count by an accredited laboratory, using the fluorescent flow cytometry method. Research ethics from the Ethical Committee Faculty of Medicine, Universitas Sriwijaya. The data were processed with SPSS version 25.0 for

windows.

3. Results

The subjects of the treatment group were ten people, and the placebo group was ten people. The CD4 count of the vitamin D group increased higher than the placebo group. The mean CD4 cell count of the vitamin D group increased by 10.7% (38.8 cells/mm³ from 361.3 cells/mm³), while the placebo group increased by 7.1% (39.7 cells/mm³ from 559.4 cells/mm³).

Table 1. Characteristics of subjects before the study

Characteristics	Vitamin D Amounts (%)	Placebo Quantities	Average ± SD	Median (Min-Max)	P*
Gender					
• Male	9 (45)	5 (25)			
• Female	1 (5)	5 (15)			
Age (years)					
• 18 – 24	2 (10)	-	34.35 ± 1.90		0.304
• 25 – 49	8 (40)	9 (45)			
• ≥ 50	-	1 (5)			
BMI (kg/m²)					
• < 23	7 (35)	8 (40)		21.35 (16.5-32.9)	0.016
• ≥ 23	3 (15)	2 (10)			
Sun Exposure per day					
• < 30 minutes	8 (40)	8 (40)			
• ≥ 30 minutes	2 (10)	2 (10)			
Length of ART					
• < 6 month	6 (30)	2 (10)			
• ≥ 6 month	4 (20)	8 (40)			
Efavirenz					
• Yes	10 (50)	9 (45)			
• No	0	1 (5)			
Number of CD4 (cells / mm ³)				460.3 ± 234.8	0.051
Vit D levels (ng / mL)				18.5 ± 5.7	0.882
Vit D levels (ng / mL)	18.07 ± 5.3	19.10 ± 6.2			0.698**

* Saphiro-Wilk normality test. If the p value > 0.05 means that the data is normally distributed

** Independent sample T test. Meaningful if the p value <0.05

Table 2. Changes in CD4 count after treatment

Category	Difference in CD4	p*	CD4 count before		CD4 count after		p**
			Average	p*	Average	p*	
Vit D	38.8 ± 52.9	0.985	361.3 ± 148.3	0.057	400.1 ± 175.3	0.049	0.046
Placebo	39.7 ± 137.7		558.4 ± 269.5		599.1 ± 223.3		0.386

* Independent sample T test. Meaningful if the p value <0.05

** Paired T test. Meaningful if the p value <0.05

4. Discussion

The difference in CD4 difference is not significant because in HIV patients who have a relatively good immune function and experience hypovitaminosis D, giving vitamin D does not increase CD4 counts even though vitamin D levels have improved as a result of supplementation.^{7,8} The subjects of this study had immune function still relatively good seen from the average CD4 count of more than 350 cells/mm³ so that vitamin D did not cause a significant increase in CD4 counts.

The CD4 count of the vitamin D group increased higher than the placebo group. The mean CD4 cell count of the vitamin D group increased by 10.7% (38.8 cells/mm³ from 361.3 cells/mm³), while the placebo group increased by 7.1% (39.7 cells/mm³ from 559.4 cells/mm³), but this difference was not statistically significant ($p = 0.985$). Administration of vitamin D increased CD4 cell counts higher in the group with lower CD4 counts. This result is different from the results of other studies which state that if the initial CD4 count is low, the ability to restore will be more difficult⁹.

The addition of 25 (OH) D 10 ng / mL in HIV patients on ART by Abraham (2018) managed to increase blood levels of 25(OH)D and 1.25(OH)₂D and was associated with the rate of increase in CD4 counts. A high baseline CD4 count correlates with a slower rate of increase.¹⁰ This statement is consistent with the results of this study in which the placebo group's higher CD4 cell count increased more slowly than the vitamin D group.

The effect of adding vitamin D was tested using a paired T-test. In the vitamin D group, the mean CD4 count before the addition of vitamin D was 361.3+185.2 cells/mm³ increased to 400.1 + 185.2 cells/mm³ ($p = 0.046$), while in the placebo group the p-value was = 0.386. In the independent sample T-test, the mean comparison of baseline CD4 counts was not significantly different ($p = 0.057$), after treatment, it was significantly different ($p = 0.04$). This suggests that the addition of vitamin D succeeded in increasing CD4 counts because vitamin D increased the expression of

CD38 which competes with gp120 in binding to CD4 receptors so that CD4 T cells are not infected with HIV.^{8,11} Vitamin D increases Foxp3 expression which is required for T-reg cell transcription.¹² FoxP3 inhibits NFAT activity in the HIV transcription process. Foxp3 inhibits the wild-type HIV-1 LTR reporter by binding to NFAT. Thus CD4 T cells do not undergo apoptosis.¹³

5. Conclusion

The supplementation of vitamin D significantly increased CD4 counts in the vitamin D group, but this addition did not increase the CD4 counts in either group.

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