

# The Effect of Vitamin D as Supplementary Treatment in Patients with Moderately Advanced Pulmonary Tuberculous Lesion

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## ABSTRACT

**Aim:** to compare the vitamin D group of pulmonary tuberculosis patients with a placebo group in terms of clinical improvement, nutritional status, sputum conversion, and radiological improvement.

**Methods:** sixty seven tuberculosis patient visiting the Pulmonary Clinic, of Cipto Mangunkusumo Hospital, Jakarta, from January 1<sup>st</sup> to August 31<sup>st</sup>, 2001 were included in this study. The subjects were randomised to receive vitamin D (0.25 mg/day) or placebo in a double blind method, during the 6<sup>th</sup> initial week of Tb treatment.

The rate of sputum conversion, complete blood counts, blood chemistry as well as radiologic examination were evaluated.

**Results:** there were more male patients than females (39:28), 78.7% were in the productive age group, 71.6% had low nutritional status, 62.4% with low education level, and 67.2% with low income. One hundred percent of the vitamin D group and only 76.7% of the placebo group had sputum conversion. This difference is statistically significant ( $p=0.002$ ).

**Conclusion:** the sputum conversion had no correlation with the hemoglobin level, blood clotting time, calcium level, lymphocyte count, age, sex, and nutritional status. There were more subjects with radiological improvement in the vitamin D group.

**Key words:** vitamin D, tuberculosis, sputum conversion, nutritional status.

## INTRODUCTION

Tuberculosis is a global health problem, especially with the emerging epidemic of HIV/AIDS. Indonesia has the third highest case numbers after China and India. The obstacles for treating pulmonary tuberculosis are low cure

rate, drug resistance, and long therapy time leading to high cost and high number of treatment discontinuation. Thus, alternatives to the treatment are needed. One of such is adding vitamin D to the standard regimen. This is based on the knowledge of characteristics of vitamin D, the immune response in tuberculosis patients, and a research on low vitamin D levels in tuberculosis patients. Hence, it was expected that the addition of vitamin D to the regimen will shorten cure time.

This research was aimed to compare a vitamin D group and a placebo group, in terms of clinical improvement, nutritional status, sputum conversion and radiological improvement. The effects of hemoglobin level, lymphocyte count, blood clotting time, age, nutritional status, and sex on sputum conversion were also observed.

## METHODS

Subjects were 67 new cases of pulmonary tuberculosis patients with moderately advanced lesion, positive acid fast bacilli, age range 15-59 years old. All patients were not on corticosteroids/immunosuppressive treatment, did not suffer from AIDS, renal failure, diabetes mellitus, liver cirrhosis, malignancies, measles, leprosy, or severe nutritional deficiency. The subjects were randomized in a double-blind and allocated into vitamin D and placebo group. The vitamin D tablets and the placebo were manufactured in the same shape and size. The dosage of the vitamin D was 0.25 mg/day, given in the initial six weeks of antituberculosis drugs therapy.

Measurements of hemoglobin, hematocrite, leukocyte, thrombocyte levels, blood clotting time, ureum, creatinine, blood sugar, SGOT/SGPT levels, and differential count were done. Radiological examinations (PA thorax) were conducted at the beginning and on the sixth month of therapy. Every two weeks patients came for examinations which consisted of physical examination, body weight measurement, and history

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taking of any complaints. Acid fast bacilli were examined three times, at the beginning, and on the 6<sup>th</sup> and 8<sup>th</sup> weeks. If the acid fast bacilli remain positive, it would be examined again on the tenth week. If the result remain positive, sputum culture, IFN $\gamma$  and TNF $\alpha$  were examined on the twelfth week.

Data were analyzed using chi square test (Fisher test). The results were considered significant if  $p < 0.05$ .

## RESULTS

Out of 67 randomized subjects, 34 patients received anti-tuberculosis drugs and vitamin D, while 33 subjects received anti-tuberculosis drugs and placebo. The regimen given was in accordance with the DOTS program, first category: 2RHZE/4RH.

The data showed that 79.9% complained of cough while 20.1% complained of hemoptysis. All of these complaints disappeared on the sixth week of therapy, with an improved appetite. There were more male patients than females (39:28). About 78.7% were in the productive age group, 67.2% had low income, 62.4% had low education level, and 71.6% were in low nutritional status.

**Table 1. Mean and Standard Deviation for Variables Age, Hb, LED, Calcium, Lymphocyte and Nutritional status in the Vitamin D Group Compared to Placebo Group**

Variable	Vitamin D x ± SD	Placebo x ± SD	p
Age (years)	29.85±11.08	32.55±11.6	0.26
LED (mm/hour)	31.41±5.89	36.67±6.12	0.27
Calcium	9.73±1.28	9.4±0.92	0.236
BMI week I	16.87±2.06	17.68±2.54	0.154
BMI week VI	17.88±1.79	18.77±2.47	0.096
Hemoglobin	12.45±1.53	12.45±1.81	0.986
Total	2671.27±826.06	2959.82±957.62	0.278
Lymphocyte			

**Table 2. Conversion Rate in the Vitamin D and Placebo Groups**

Group	Conversion		Total
	Yes	No	
Vitamin D	34	0	34
Placebo	25	8	33
	59	8	67

Note :  $p = 0.002$

The mean values of these variables: age, blood clotting time, calcium and hemoglobin levels, initial and sixth week therapy nutritional status, and total lymphocyte count, were not significantly different, between vitamin D and placebo groups.

Table 2 showed sixth week sputum conversion in 34 subjects of the vitamin D group (100%) and in 25 subjects of the placebo group (76.7%), which was

statistically significant ( $p = 0.002$ ). Out of 8 patients with no sputum conversion on the sixth month, 7 exhibited sputum conversion on the 8<sup>th</sup> week. One did not have sputum conversion until the 12<sup>th</sup> week, yet the culture result was negative. The results of IFN $\gamma$  and TNF $\alpha$  were not present.

The mean values of age, hemoglobin level, blood clotting time, calcium level, total lymphocyte count, and nutritional status in the groups with and without sputum conversion were not statistically significant, as shown in table 3 and 4.

**Table 3. Mean and Standard Deviation for Variables Calcium, Hb, LED, Total Lymphocyte and Patient's Age in the Conversion and No Conversion Groups**

Variable	Conversion	No Conversion	p
Calcium	9.32±0.86	9.61±1.15	0.52
Hemoglobin	12.36±2.0	12.46±1.65	0.88
LED	60.49±35.74	59.5±29.28	0.88
Total lymphocyte	32.40±826.06	29.34±904.69	0.07
Age	31.25±11.35	31.17±11.43	0.98

**Table 4. The Correlation between Sputum Conversion and Calcium, Total Lymphocyte, Hb, LED, Nutritional status and Sex in the Placebo Group**

Variable	Conversion		p
	Yes	No	
Calcium			
< 9 mg/ul	8	1	0.27
> 9 mg/ul	17	7	
Lymphocyte			
< 1500	20	7	0.678
> 1500	5	1	
Hemoglobin			
Anemia	9	3	0.627
Normal	16	5	
LED			
< 30 ml/hour	9	2	0.645
> 30 ml/hour	16	6	
Nutritional status			
Overweight	2	0	0.71
Normal	10	4	
Underweight	13	4	
Sex			
Male	14	5	0.554
Female	11	3	

## DISCUSSION

The results of this study are similar to the WHO national survey: the percentage of males were higher than females, 78.7% of subjects were in productive age group. This might having occurred as productive males higher mobility, thus the possibility of contact with tuberculosis patients is higher. In addition, a study in India stated that females were more resistant to tuberculosis due to higher vitamin D response.

In this study, there were 71.6% subjects with low nutritional status. This is also in accordance with the WHO survey and related with low income (67.2%) and low educational level (62.4%).

Nutritional status amelioration was observed on the sixth and eighth weeks. In this study the nutritional status progress was not significant. Therefore, it might be useful to re-observe the nutritional status on the sixth month. There were 34.3% subjects with anemia, probably due to hemoptysis (23.9%) and nutritional status.

It is anticipated that the addition of vitamin D might cause hypercalcemia. Therefore the measurement of calcium level in this study was done, not to depict the vitamin D level, but as thorough therapy observation.

The raised vitamin D level was not in accordance with the raised calcium level. This could not explain the correlation between vitamin D level and calcium homeostasis abnormality.

The measurement of blood clotting time does not always support the diagnosis of tuberculosis and cannot be used to observe the progress of treatment.

In this study, sputum conversion had no correlation with sex, age, blood clotting time, calcium level, nutritional status, hemoglobin level and lymphocyte count.

One subject had no sputum conversion until the twelfth week, while sputum culture was negative. This might be due to dead bacilli phenomena, as the patient's clinical condition and radiological examination were improving. Unfortunately the results of IFN and TNF examination were not available at that time.

The evaluation of radiological examination on the sixth week was done in 36 people (53.73%), as 19.4% stopped treatment, 17.9% had moved to a different address and did not come to the sixth month examination, one subject died, one was pregnant, and 6% were not x-rayed. The x-ray images showed improvement in 87.5% of the vitamin D group and in 65% of the placebo group. The same x-ray images were found in 35% of the placebo group and 12.5% of the vitamin D group. One subject in the placebo group had radiological improvement, yet no sputum conversion.

## CONCLUSION

The addition of vitamin D in the therapy of moderate advanced pulmonary tuberculosis had been proven to show a significant difference in sputum conversion compared with placebo. The percentage of radiological improvement was also higher in the vitamin D group.

Sputum conversion was not influenced by nutritional status, hemoglobin level, calcium level, lymphocyte count, age, or sex.

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