Vitamin D supplementation in tuberculosis patients: A cross-sectional study

D.K. Sari & N.K. Arrasyid
Faculty of Medicine, Universitas Sumatera Utara, North Sumatera, Indonesia

R.L. Kusumawati
Epidemiology Graduate Programme, Faculty of Medicine, Prince of Songkla University, Hat Yai, Thailand

Y.S. Harahap
Teladan Community Health Service, North Sumatera, Indonesia

ABSTRACT: Previous studies have not been able to show with certainty the effect of vitamin D supplementation in tuberculosis patients. The objective of this study is to determine whether vitamin D supplementation to patients with tuberculosis could influence 25-hydroxy-vitamin D (25(OH)D) and calcium serum levels. Results: after 28 days, the vitamin D supplementation showed significant increase of 25(OH)D serum level at the end point ($p = 0.001$), but not for the calcium serum level ($p = 0.3$). Conclusions: supplementation with 1,000 IU vitamin D per day increased the 25(OH)D serum level but there was no association with the calcium serum level. These results suggest a.

Keywords: Calcium, Tuberculosis, Vitamin D

1 INTRODUCTION

Vitamin D supports the induction of pleiotropic antimicrobial responses in tuberculosis patient, resulting from an immunomodulatory effect (Coussens et al., 2012). Vitamin D supplementation accelerates sputum smear conversion and enhanced tuberculosis treatment (Martineau et al., 2011; Siempos et al., 2008).

Vitamin D is also known to be essential to Mycobacterium tuberculosis containment and killing through the activation of 25-hydroxyvitamin D (25(OH)D) receptors, present in all immune cells (Liu et al., 2006).

Deficiency in vitamin D is found in healthy people, especially women in tropical countries (Sari et al., 2017a, 2017b). Low sunlight exposure, vitamin D intake, physical activity, and vitamin D receptor gene polymorphism are risk factors for vitamin D deficiency (Sari et al., 2017c). However, low 25(OH)D serum level does not affect calcium serum level (Sari et al., 2017d).

Calcium signalling in tuberculosis infection plays a significant role in the pathogenesis of tuberculosis (Sharma, 2017). Calcium is also known to be a ubiquitous second messenger, which can control multiple processes and is included in cellular activities like division, motility, stress response, and signalling. However, Ca is thought to be a regulative molecule regarding tuberculosis infection but its binding relation with proteins which are influenced by Ca concentrations in host pathogen (Chan, 2017).

We therefore conducted a clinical trial to determine the effect of 1,000 IU vitamin D for 28 days on the 25(OH)D and calcium serum levels.
2 METHODS

The objective of this study is to determine the effect of 1,000 IU per day vitamin D supplementation for 28 days on the 25(OH)D and calcium serum levels in tuberculosis patients who lived in three community health centre areas in Medan City, North Sumatera, Indonesia between June and September 2017. This is a randomised control trial involving 48 patients: 24 tuberculosis patients for vitamin D supplementation, and a placebo group.

The subjects of this study consisted of tuberculosis patients from community health centres with a higher tuberculosis prevalence, in Medan, North Sumatera, Indonesia. The 32 men and women studied had various occupations, and were sampled purposively. The inclusion criteria were tuberculosis patients in the age range of 18–60 years. Exclusion criteria were subjects with a history of diabetes mellitus, myocardial infarction, and renal or liver dysfunction. In addition to those exclusion criteria, subjects who were pregnant and lactating were also excluded.

We measured 25(OH)D serum concentration by Chemiluminescent Immunoassay (CLIA) technology (Diasorin, Stillwater, MN). Measures were between 4.0 and 150 ng/mL. The lowest value was 4.0 ng/mL, which is based on an inter-assay precision of 3.90% CV. Reference ranges were <20 ng/mL, categorised as deficiency, 20–30 ng/mL (insufficiency), and 30–100 ng/mL (sufficiency) (Holick, 2007). To convert ng/mL to nmol/L, multiply by 2.496. Calcium serum was measured by ADVIA Bayer Assayed Chemistry Controls, with principal procedure: calcium ions form a violet complex with o-cresolphthalein complexone in an alkaline medium. The reaction is measured at 545/658 nm, and normal concentration of calcium was 8.3–10.6 mg/dL.

Continuous variables were expressed as continuous variables as means ± standard deviations (SDs). Categorical variables were expressed as percentage proportions, using chi-squared to express significant differences between two groups, and the Fischer test if the data did not meet the criteria. Values of \( p < 0.05 \) were considered statistically significant. We used the SPSS program (version 11.5; SPSS Inc., Chicago, IL) to perform the analysis.

This study was carried out after ethical approval was obtained from the Health Research Ethics Committee of Sumatera Utara University Medical School (No. 264/TGL/KEPK FK USU-RSUP HAM/2017) and all participants gave written informed consent to the study procedures.

3 RESULTS

3.1 Characteristics of subjects

Table 1 shows the characteristics of the two groups, one receiving vitamin D supplementation and the other a placebo; there were no significant differences between the two groups.

Table 2 shows the difference before and after intervention in the intervention group. After supplementation, there was a significant increase in vitamin D intake, while there was no significant difference in any of the nutrient intakes in the control group.

Table 1. Demographic and lifestyle characteristics of subjects before intervention.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intervention (D) group</th>
<th>Control (C) group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 24)</td>
<td>(n = 24)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>37 ± 2.5</td>
<td>33.8 ± 9.1</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>19.8 ± 3.9</td>
<td>20.3 ± 3.1</td>
</tr>
<tr>
<td>Serum 25(OH)D (ng/mL)</td>
<td>19.7 ± 6.6</td>
<td>19.3 ± 4.6</td>
</tr>
<tr>
<td>Serum calcium (mg/dL)</td>
<td>9.0 ± 0.5</td>
<td>9.1 ± 0.5</td>
</tr>
</tbody>
</table>
Table 3 shows the difference before and after intervention in both groups. After supplementation, there was a significant increase in vitamin D intake, while there was no significant difference in any of the nutrient intakes in the control group.

4 DISCUSSION

Vitamin D helps the body to effectively absorb calcium; there is an interaction between vitamin and mineral. Calcium is known to be a ubiquitous second messenger that can control multiple processes, has a role in tuberculosis infection, and a significant role in pathogenesis.

Calcitriol, the active metabolite of vitamin D, induces innate antimicrobial responses and suppresses proinflammatory cytokine responses in vitro (Martineau, 2007). This microbial activity is mediated via induction of reactive nitrogen intermediates, reactive oxygen intermediates, antimicrobial peptides, and autophagy (Hewison, 2011). These studies report similar findings to previous studies of tuberculosis patients that found vitamin D deficiency (Martineau et al., 2011; Salahuddin et al., 2013). However, after vitamin D supplementation, baseline patients categorised in deficiency, resulting in greater weight gain and a more rapid radiographic clearing of disease, as compared to the placebo (Salahuddin et al., 2013; Sari et al., 2017d). The previous study showed that high dose of vitamin D (which in that study was 600,000 IU vitamin D intramuscular) accelerated clinical, radiographic improvement in all tuberculosis patients and increased host immune activation, but the study lasted 12 weeks (Salahuddin et al., 2013). In this study, the length was 28 days (4 weeks), and the tuberculosis patients received 1,000 IU oral vitamin D supplementation per day. However, this study also showed an increase of 25(OH)D serum level at the end point.

Hypercalcaemia found in tuberculosis patient; the previous study confirmed that serum calcium is raised in tuberculosis, but the effect may be reduced by a low calcium intake and a low parathyroid hormone level. Although the calcium and vitamin D metabolism appeared to be altered in tuberculosis, no direct relationship between serum calcium and 1,25(OH)2D, was found (Chan, 2017). Our study reported normal calcium serum levels and no significant difference before and after vitamin D supplementation. But we found that serum
Our study had limitations. We did not assess parathyroid hormone, nor other clinical tuberculosis parameters such as chest X-ray or blood examination (C-reactive protein).

5 CONCLUSION

From the study results, it can be concluded that in tuberculosis patients there were vitamin D deficiency and insufficiency, but the calcium serum level was normal. No association was found between 25(OH)D and calcium serum level.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge that the present research is supported by the Ministry of Research and Technology and the Higher Education Republic of Indonesia, Research and Community Service, Universitas Sumatera Utara. The support is under the research grant TALENTA of the year 2017 Contract Number 212/UN5.2.3.1/PPM/KP-TALENTA USU/2017.

REFERENCES


