# Serum 25(OH)D and Lipid Levels in Chinese Obese and Normal Weight Males before and after Oral Vitamin D Supplementation<sup>\*</sup>

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### Abstract

**Objective** To study the effect of oral vitamin D (VD) supplementation on VD status and serum lipid in Chinese obese and healthy normal-weight men.

**Methods** Twenty-one obese men with their body mass index (BMI)>28 kg/m<sup>2</sup> served as an obese group and 22 healthy normal-weight men with their BMI<24 kg/m<sup>2</sup> served as a control group in this study. After they were given 50 000 IU of oral VD, once a week for 8 weeks, the serum 25-hydroxyvitamin D [25(OH)D] concentration was measured with an enzyme-immunoassay kit.

**Results** After oral VD supplementation, the serum 25(OH)D concentration significantly increased from 46.1±9.1 nmol/L to 116.7±20.3 nmol/L in the obese subjects (P<0.01) and from 52.8±17.8 nmol/L to 181.3±30.2 nmol/L in the control ones (P=0.13). The serum high-density lipoprotein cholesterol (HDL-C) level was reduced within the normal reference range in the obese group. However, no significant change was observed in the level of other serum lipids (triglycerides, total cholesterol, and low-density lipoprotein cholesterol) in either of the two groups.

**Conclusion** The effect of high-dose oral VD supplementation is weaker on VD status in the obese group than in the control group. High-dose oral VD supplementation has no side effect on serum lipid level in obese and control groups.

Key words: Vitamin D; Obesity; Serum 25(OH)D; Serum lipid

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# INTRODUCTION

t has been reported that vitamin D (VD) can increase the skeletal function and reduce the incidence of diseases, such as diabetes, cancer, cardiovascular diseases, and bacterial infections<sup>[1]</sup>. For these reasons, the cut-point for plasma or serum 25-hydroxy vitamin-D [25(OH)D], a reliable biomarker for assessment of VD status, is recommended to be raised from 25 nmol/L (10 ng/mL) to 50 nmol/L or more<sup>[1-3]</sup>. Consequently, VD deficiency is revealed to be pandemic throughout the world<sup>[1,4-5]</sup>. Obesity, one of the most serious public health problems in the 21st century<sup>[6]</sup>, has

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been linked to VD deficiency<sup>[7-11]</sup>, which likely increases the prevalence of obesity-related chronic diseases. Several mechanisms have been proposed to explain the low VD level in obese people, including sequestration of VD and 25(OH)D by fat tissues<sup>[9,12]</sup>, and body size<sup>[13]</sup>. On the other hand, abnormal fasting serum or plasma lipid level is one of the most prominent symptoms resulting from obesity<sup>[14]</sup>, and the effect of VD supplementation on lipid profiles remains controversial<sup>[15]</sup>. In this study, the effect of high-dose oral VD supplementation on serum 25(OH)D and lipid levels was looked into in obese and normal weight Chinese male adults.

### MATERIALS AND METHODS

### Subjects and Human Trial Protocol

The study was approved by the Ethics Committee of Shenzhen Center for Chronic Disease Control. Male subjects aged 20-69 years were recruited from a community of Shenzhen City. After providing informed consent, 21 volunteers with their body mass index (BMI) ranging 18.5-24 kg/m<sup>2</sup> served as a control group while 22 obese people with their BMI>28 kg/m<sup>2[16]</sup> served as an obese group. Their fasting serum glucose and 2-h postprandial blood glucose were <7.0 mmol/L and <11.1 mmol/L, respectively. Liver and kidney functions were assessed according to their serum levels of alkaline phosphatase (ALP), aspartate aminotransferase (AST), and creatinine. Those who did not match the above inclusion criteria or were diagnosed with organic diseases were excluded from the study. Data about VD-containing food intake, health status and history, and other lifestyle factors were collected using questionnaire.

The baseline information and blood samples were collected at the end of week 0 in June 2011. The subjects in the two groups swallowed a capsule containing natural VD<sub>3</sub> at the dose of 50 000 IU (1.25 mg) (Bio-Tech Pharmacal, Inc. Cat no.: 7184-01, USA) with meals once a week for 8 weeks. During the intervention period, the subjects were required to maintain their daily lifestyle and nutritional habits. Sun exposure time between 10:00-15:00 and any complaint about possible VD toxicity were assessed via telephone interview every other day. At the end of week 8, the concerned indices were reevaluated.

After the VD intervention, 6 volunteers from each group were followed up for more than 14 weeks, during which the changes in fasting serum 25(OH)D level were monitored.

# Anthropometric Parameter Assay and Laboratory Analysis

Anthropometric parameters, including height, body weight, skin fold, waist circumference, and hip circumference, were measured as previously described<sup>[17]</sup>. Blood pressure was measured with a mercury sphygmomanometer by a skilled nurse. Body compositions, including fat mass, fat free mass, total body water, were detected using the SBP7 body composition analyzer (ImpediMed, Australia) at a 10 s interval and repeated 5 times by spectroscopy.

Overnight fasting (>10 h) blood samples were collected at 7:30-9:30 a.m. for laboratory analysis. Serum 25(OH)D levels in all samples from VD external quality assessment scheme (DEQAS) on a microplate reader (Multiskan FC, Thermo Fisher Scientific Inc., USA), were measured in duplicate by enzyme-immunoassay (IDS Ltd., Cat no.: AC-57F1, UK). Both intra- and inter-assay coefficients of 25(OH)D assay were <8%. Serum levels of triglycerides (TG), total cholesterol (TC), low-density (LDL-C), lipoprotein cholesterol high-density lipoprotein cholesterol (HDL-C), creatinine, ALP, and AST were analyzed with an automatic biochemical analyzer (OLYMBUS AU400, Japan). Blood profiles including hemoglobin were measured with an blood analyzer (XS-800i, automatic Sysmex Corporation, Japan). Calcium in whole blood was detected by atomic absorption spectrometry (BH5100, Bohui Innovation Technology Co., Ltd, Beijing, China).

# Statistical Analysis

Data were analyzed by paired-or independentsamples t test. Non-parametric variables were analyzed by Mann-Whitney U test (MWU). Relation between serum 25(OH)D level and other indices was analyzed by Pearson and partial correlation analysis. P<0.05 was considered statistically significant.

# RESULTS

# Effect of Biometric Profiles and Lifestyle on VD Status

After VD intervention, one obese man was excluded because of his significant lifestyle change and 4.7% BMI decrease. Ultimately, 21 subjects in each group were included for data analysis. The BMI remained constant (*P*>0.21). The value of biometric

parameters at baseline was higher in the obese group than in the control group (Table 1).

| Table 1. Biometric Profiles of Adult | Males |
|--------------------------------------|-------|
| (mean±SD) <sup>1</sup>               |       |

| Indices                            | Normal     | Obesity    |
|------------------------------------|------------|------------|
| Age, y                             | 34.3±8.0   | 44.7±8.8   |
| Body mass index, kg/m <sup>2</sup> | 21.9±1.2   | 30.3±1.7   |
| Triceps skinfold, mm               | 10.7±2.5   | 20.5±4.7   |
| Subscapular skinfold, mm           | 17.7±4.5   | 34.9±7.0   |
| Abdominal skinfold, mm             | 21.8±6.8   | 36.5±7.0   |
| Waist circumference, cm            | 80.0±4.7   | 104.7±5.3  |
| Waist-hip ratio                    | 0.84±0.05  | 0.98±0.03  |
| Total body water, %                | 66.3±3.2   | 58.8±2.7   |
| Fat mass, %                        | 9.4±4.4    | 19.6±3.8   |
| SBP, mmHg                          | 110.4±10.3 | 131.3±13.9 |
| DBP, mmHg                          | 70.8±7.2   | 91.1±9.2   |

**Note.** <sup>1</sup>: All indices were significantly different between the two groups (*P*<0.01). SBP: systolic blood pressure; DBP: diastolic blood pressure.

No significant difference was found in the dietary VD intake between the 2 groups (MWU, P=0.96) averaging 250.9±555.7 IU/d (6.27±13.9 µg/d). The main dietary VD sources for the subjects were oily fish, yolk, animal liver and meat, and mushroom, but none of the subjects consumed VD-fortified food. This might not be unusual because almost no food in China is fortified with VD. During the VD intervention, all the subjects maintained their normal dietary habits, and the food frequency questionnaire confirmed that they did not increase

the intake of VD rich food. The sun exposure time with summer clothing between 10:00-15:00 did not differ between the two groups (MWU, P=0.34), and averaged 0.47±0.55 h/d. During the study, none of the subjects felt uncomfortable or had symptoms of VD toxicity.

### Serum 25(OH)D Response to VD Intervention

The changes in serum 25(OH)D level before and after VD intervention are shown in Figure 1. Before the oral VD supplementation, the baseline 25(OH)D level was not significantly different between the control group and the obese group (52.8±17.8 nmol/L vs 46.1±9.1 nmol/L, P=0.13). Eight weeks after VD supplementation, the serum 25(OH)D level significantly increased to 181.3±30.2 nmol/L and 116.7±20.3 nmol/L, respectively, and the final 25(OH)D level was higher in the control group than in the obese group (P<0.01, Figure 1A). The VD deficiency (<50 nmol/L), insufficiency (50-75 nmol/L), and sufficiency (75-250 nmol/L)<sup>[3,18-20]</sup> before VD supplementation was 47.6%, 42.9%, and 9.5%, respectively, for the control group and 71.4%, 28.6%, and 0%, respectively, for the obese group. After VD intervention, all subjects in the control group were VD sufficient and 90.5% of subjects in the obese group were VD sufficient. Neither severe VD deficiency (<25 nmol/L) nor VD excess (>250 nmol/L) was detected in any of the subjects before or after VD intervention. The data about the 6 subjects who were followed up for more than 14 weeks are shown in Figure 1B. Consistently, a significant difference was observed in serum 25(OH)D level between the two groups at week 8. The serum 25(OH)D level decreased to 75-80 nmol/L 10 weeks after the final VD supplementation.



**Figure 1.** Changes in fasting serum 25(OH)D level within a group and between the two groups before and after VD supplementation. Data are expressed as mean±SEM. (A) within a group or between groups, date labeled with different letters differ (P<0.05); (B) <sup>\*</sup>indicates the data in the obese group differing from those in the normal group (P<0.05).

# Relationship of Serum 25(OH)D Level and Obesity

The serum 25(OH)D level was reversely related with the fat mass (r=-0.358, P=0.020), but not with the BMI (r=-0.145, P=0.361) before VD intervention. The serum levels were reversely correlated with both variables after VD intervention (fat mass: r=-0.693, P<0.001; BMI: r=-0.760, P<0.001). When controlling for the three variables of age, dietary VD intake, and sun exposure in partial correlation analysis, these significant correlation still existed (Figure 2).

### Effect of VD Supplementation on Serum Lipid and Other Biochemical Indices

The serum levels of TG, TC, LDL-C, and HDL-C were significantly different between the two groups before or after VD supplementation (P<0.05, Figure 3). The serum HDL-C level decreased from 1.25±0.20 mmol/L to 1.16±0.18 mmol/L (P=0.04) whereas it remained above the reference value (1.04 mmol/L) in the obese group after VD supplementation (P=0.04).

The blood calcium level and serum levels of creatinine, ALP and AST were measured before and after the experiment for monitoring the VD toxicity (Table 2). No significant difference was found in VD toxicity between groups or within group either before or after VD intervention (P>0.05). However, the serum AST level in the obese group was significantly higher at the endpiont than that at the baseline (P=0.03). The mean blood calcium level tended to increase in both groups after VD supplementation (0.05<P<0.06) and was still lower than the reference limit (1.55 mmol/L). The baseline hemoglobin level was significantly higher in the obese group than in the control group, which is consistent with the reported findings<sup>[21]</sup>.

### DISCUSSION

Obesity is usually correlated with the higher prevalence of hypovitaminosis or the lower circulating 25(OH)D level<sup>[22-24]</sup>. In the present study, though the prevalence of VD deficiency was higher in the obese group than in the control group (71.4% vs 47.6%), no significant difference was observed in the mean baseline circulating 25(OH)D level between the two groups, which might be partly due to the sampling strategy and relatively small size of population. Moreover, the lower mean baseline serum



**Figure 2.** Correlation between serum 25(OH)D and fat mass (A, C) or BMI (B, D) before (A, B) and after (C, D) VD intervention. The control variables are age, dietary VD intakes, and sun exposure.

25 (OH)D level in the two groups, Chinese criteria for obesity, and lifestyle should be considered to attenuate their difference. BMI>30 kg/m<sup>2</sup> is commonly accepted as a criterion for obesity in Western countries, nevertheless Asian populations develop negative health consequences at a lower BMI than Caucasians. Japanese guidelines define obesity as the BMI>25 kg/m<sup>2[25]</sup> while the Chinese population</sup> with their BMI>28 are considered obese<sup>[26]</sup>. The mean BMI in the obese group was about 30 kg/m<sup>2</sup>, lower than that in Western populations<sup>[22-24]</sup>. The skin VD production rate and gastrointestinal VD absorption decline with age<sup>[27-28]</sup>, but the difference in age between the two groups in this study was not large enough to significantly impact the baseline serum 25(OH)D, which is consistent with the reported findings<sup>[29]</sup>. The weekly high-dose VD supplementation for 8 weeks resulted in 100% of VD sufficiency in the control group, but one-tenth of subjects in the obese group remained VD insufficient, demonstrating that the VD bioavailability decreases in obese populations as previously reported<sup>[9]</sup>.

The rate for low total VD from skin synthesis and oral intake to convert into 25(OH)D is significantly higher than that for high total VD from skin synthesis and oral intake. VD is mainly stored in body fat<sup>[30]</sup>. It is likely that a larger fat tissue mass stores more VD and 25(OH)D, thus resulting in less circulating 25(OH)D<sup>[8]</sup>. In this study, the fat mass was negatively correlated with the serum 25(OH)D level both before and after VD supplementation (Figure 2A and 2C). Thus, obese men, especially those residing in high latitude, should pay more attention to their VD nutrition. When the high-dose VD supplementation

**Table 2.** Changes in Biochemical Indices between the Two Groups (mean±SD)<sup>1</sup>

| Indices <sup>2</sup> — | Ва                      | Baseline                |                         | Endpoint                |           |
|------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-----------|
|                        | Normal                  | Obese                   | Normal                  | Obese                   | Values    |
| Blood calcium, mmol/L  | 1.40±0.17               | 1.42±0.16               | 1.50±0.18               | 1.50±0.17               | 1.55-2.10 |
| Creatinine, µmol/L     | 91.9±12.3               | 90.8±9.3                | 93.3±11.7               | 89.9±9.4                | 74-110    |
| ALP, IU/L              | 72.7±16.0               | 69.0±21.3               | 77.2±18.3               | 71.4±25.9               | 30-120    |
| AST, IU/L              | 23.8±5.9 <sup>a</sup>   | 24.5±4.8 <sup>a</sup>   | 25.1±5.7 <sup>a,b</sup> | 27.1±6.9 <sup>b,c</sup> | 0-35      |
| Hemoglobin, g/L        | 143.5±24.0 <sup>°</sup> | 158.5±18.9 <sup>b</sup> | n.d.                    | n.d.                    | 120-160   |

**Note.** <sup>1</sup>: between the two groups, data that do not share the same superscript letter are different (a, b, c), *P*<0.05, and data that share the same superscript letter of without superscript letters are not different, *P*>0.05. <sup>2</sup>: ALP: alkaline phosphatase; AST: aspartate aminotransferase; n.d.: not detected.



**Figure 3.** Serum levels of TG (A), TC (B), LDL-C (C), and HDL-C (D) in the two groups before and after VD supplementation. Data are expressed as mean $\pm$ SD. Between groups, <sup>\*</sup>indicates *P*<0.05, and within the same group, data labeled with different letters (a, b) differ, *P*<0.05.

was terminated, the serum 25(OH)D level began to decrease in the two groups. Ten weeks after the last administration of VD capsule, the curve tended to flatten out between 75-80 nmol/L and the serum 25(OH)D level remained above 75 nmol/L for about 70-80 d, which are consistent with the reported findings<sup>[31]</sup>. Thus, a duration of 70-80 d for the high-dose VD clearance and a hidden mechanism for retaining a relatively stable serum/plasma 25(OH)D level are a reasonable speculation based on the above analyses. No significant difference during this period was observed in the serum 25(OH)D level between the two groups in this study, which may be due to the 25(OH)D production derived from the VD released from fat tissues in obese subjects<sup>[30]</sup> and the above mentioned unknown mechanism. So when the VD nutrition is assessed in obese individuals, the potential replenishment from fat tissues should not be neglected.

Dyslipidemia is a well-described independent risk factor for cardiovascular disease in obese individuals<sup>[14]</sup>. Though the VD bioavailability decreased in obese individuals in the present study, the effect of VD on lipid profiles is not always consistently reported with varied study protocols and subjects<sup>[32]</sup>. In this study, the effect of large dose VD supplementation on serum lipid profile (TG, TC, LDL-C, and HDL-C) was assessed, expecting that the incidence of dyslipidemia was higher in the obese group than in the control group and VD supplementation had no significant effect on the lipid profiles in the latter. It was reported that the serum TG, TC, and LDL-C levels were not affected by the improved VD status in obese individuals<sup>[33-34]</sup>. In this study, however, the HDL-C level significantly decreased in the obese group, which is consistent with the findings of previous studies<sup>[35-36]</sup>. This interesting phenomenon and its mechanisms call for further randomized controlled trials and laboratory experiments.

The oral "loading dose" of VD at 50 000 IU once a week for 8 weeks is a commonly applied strategy for severe VD deficiency or VD deficiency in adults<sup>[3,37]</sup>, and has been used in previous human trials without any observed side effects<sup>[1,38]</sup>. Of the 42 subjects included in the present study, none suffered from severe VD deficiency, 59.5% had VD deficiency and 35.7% had VD insufficiency, suggesting that the present VD supplementation protocol is safe for Chinese men.

While direct measurement is not available because of technical and practical difficulties,

telephone interview and food frequency questionnaire are the alternatives to collect sunshine exposure time and dietary VD intake data<sup>[39-40]</sup>. With a number of disadvantages, these methods yet cost less. Despite the variations in dietary pattern, food fortification, dietary supplements, age, and sex, the general dietary VD intake in adult males throughout the world is estimated to be 75-324 IU/d (1.88-8.11 µg/d)<sup>[41]</sup>, which is far less than the recommended 600 IU/d to achieve the 50 nmol/L target level of circulating 25(OH)D<sup>[2]</sup>. The VD intake in our subjects was also insufficient, and longer sun exposure time or appropriate VD supplement is recommended to improve their VD status in order to maintain health.

In conclusion, high-dose VD supplementation at 50 000 IU, once a week for 8 weeks, improves the VD status in Chinese males with almost no effect on serum lipid profile except for the reduction of HDL-C in obese individuals. The serum 25(OH)D level is lower in obese males than in normal-weight males after the 8 weeks' high-dose VD supplementation.

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