Journal of Steroid Biochemistry and Molecular Biology 180 (2018) 23–28

Contents lists available at ScienceDirect

Journal of Steroid Biochemistry and Molecular Biology

journal homepage: www.elsevier.com/locate/jsbmb

Efficacy of different modes of vitamin D supplementation strategies in Saudi adolescents

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ARTICLE INFO

Keywords:
Vitamin D deficiency
Fortified milk
School children

ABSTRACT

Vitamin D deficiency is rampant in the Middle East, even in children and adolescents. This study was designed to investigate the effects of different vitamin D repletion strategies commonly used on serum vitamin D levels of Saudi adolescents. Study design: A 6-month multi-center, controlled, clinical study, involving 34 schools in the central region of Riyadh, Saudi Arabia. Different strategies of vitamin D supplementation were tested (200 ml fortified milk of different brands or vitamin D tablet (1,000IU). Anthropometrics were taken and fasting blood samples withdrawn at baseline and after intervention for the quantification of serum glucose, lipid profile and 25(OH) vitamin D. A significant increase in 25(OH)D level was observed in subjects supplemented with vitamin D tablet, milk brand 2 and milk brand 4, whereas subjects supplied with fortified milk brands 1 and 3 respectively, exhibited a significant decrease in 25(OH)D levels. Analysis of covariance showed that after adjusting for baseline 25(OH)D, age, gender and BMI, the mean 25(OH)D levels of children who were taking vitamin D tablet (9.1 ± 0.8 nmol/l) and milk brand 4 were significantly higher (7.3 ± 1.1 nmol/l) than children taking milk brand 2 (1.6 ± 1.0 nmol/l). Subjects supplied with milk brands 1 and 2 exhibited a significant increase in total cholesterol level, while it dropped significantly in subjects taking milk brand 3, while no changes were observed in other groups. Different strategies in vitamin D supplementation used in this clinical study elicited varying degrees of improvement in serum 25(OH)D level. The observed outcomes were dependent on the strategy and gender in the Saudi adolescent population, with oral tablet supplementation being favored in boys.

1. Introduction

Vitamin D deficiency is a global public health concern affecting people of all ages and sexes [1–5]. Extensive research has been carried out on the pleiotropic effects of vitamin D on human health in the recent decade due to the pandemic of vitamin D deficiency. Of particular interest is the extra-skeletal effects of vitamin D in the development of chronic, non-communicable (mostly metabolic) diseases in both children and adults [2,6].

Humans acquire vitamin D through two sources: one through endogenous production in the skin via sunlight exposure [7,8] and through diets such as natural vitamin D-fortified food sources (fish oil, liver, sun-exposed mushrooms, etc.) [9,10] and oral supplementations [11,12].

The Kingdom of Saudi Arabia (KSA) is drenched with sufficient sunlight throughout the year so, hypothetically, should not have issues regarding vitamin D deficiency. But this is not the case, as recent and previous studies consistently point out to a very high prevalence of vitamin D deficiency [13–15]. This is mainly attributed to indoor lifestyle, avoidance of sunlight to prevent from scorching heat effects on

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https://doi.org/10.1016/j.jsbmb.2018.02.002
Received 30 October 2017; Received in revised form 28 January 2018; Accepted 1 February 2018
Available online 09 February 2018
0960-0760/

Table 1
Mean differences in Baseline Characteristics among Vitamin D Tablet versus Milk Brands.

Parameters	Vitamin D tablet	Milk Brand 1	Milk Brand 2	Milk Brand 3	Milk Brand 4
N	272	177	154	113	168
F/M	168/104	118/59	86/68	40/73	103/65
Age (years) #	15.0 (4.0)	14.0 (2.0)^{AC}	15.0 (3.0)	11.0 (1.0)^{ABC}	13.0 (2.0)^{ACD}
BMI (m/kg^2)	24.1 ± 6.7	22.2 ± 5.3^{A}	23.7 ± 5.6	18.4 ± 4.4^{ABC}	23.6 ± 5.3^{D}
BMI (Z-Score)	0.22 ± 1.11	−0.11 ± 0.89^{A}	0.14 ± 0.93	−0.74 ± 0.74^{ABC}	0.13 ± 0.88^{D}
WHR	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1^{B}	0.9 ± 0.1^{AB}	0.8 ± 0.1^{D}
Systolic BP (mmHg)	117.8 ± 14.3	114.7 ± 13.6	118.0 ± 11.6	108.1 ± 12.0^{ABC}	116.0 ± 15.7^{D}
Diastolic BP (mmHg)	73.2 ± 11.8	67.3 ± 10.1^{AC}	73.4 ± 16.3	68.9 ± 12.1^{AC}	71.8 ± 10.5^{B}
Total Cholesterol (mmol/l)	4.9 ± 0.9	4.6 ± 0.7^{AD}	4.8 ± 0.8	5.0 ± 0.6	4.7 ± 0.7^{AD}
HDL-Cholesterol (mmol/l)	1.3 ± 0.4	1.3 ± 0.3	1.2 ± 0.3	1.4 ± 0.5 ^{BC}	1.3 ± 0.4^{D}
Glucose (mmol/l)	5.1 ± 0.6	5.0 ± 0.6	5.2 ± 0.8^{BD}	4.9 ± 0.5	5.2 ± 0.6^{BD}
Triglycerides (mmol/l)	1.2 ± 0.5	1.1 ± 0.4	1.1 ± 0.4	0.9 ± 0.3^{A}	1.2 ± 0.5^{CD}
25(OH)Vitamin D (nmol/l)	37.2 ± 16.8	37.9 ± 17.2	34.7 ± 14.5	44.9 ± 19.7^{ABC}	33.1 ± 14.8^{D}

Note: Data presented as Mean ± SD for continuous variables and frequencies for categorical variables; # denotes non-Gaussian variables presented as Median (IQR); A denotes significance compared to vitamin D tablet; B denotes significance compared to milk brand 1; C denotes significance compared to milk brand 2; D denotes significance compared to milk brand 3.

skin and women covering the entire body with dark veils for cultural and religious reasons [16].

For most countries including KSA, fortified foods is an efficient means to provide the needed vitamin D [17–19]. However, fortified foods in the Middle East, particularly dairy products, have never been tested as to whether their claimed vitamin D content is effective in at least raising vitamin D status of those consuming such products. Hence, the main objective of this interventional study was to evaluate whether intake of locally available vitamin D fortified milk results in the restoration of physiological vitamin D levels in Saudi adolescents.

2. Materials and methods

A total of 889 apparently healthy Saudi adolescents aged 11–17 years were randomly enrolled from 34-different schools in Riyadh city during the months of November-May 2014–2015. Written informed consents from parents as well as assent from children and adolescents were obtained prior to inclusion in the study. Ethical approval was obtained from the Ethics Committee of the College of Science Research Center, King Saud University, Riyadh, KSA.

2.1. Exclusion criteria

Subjects with chronic conditions such as asthma, type 1 diabetes mellitus, hypertension, history of cardiac, kidney or liver disease, use of medications known to affect body weight (such as glucocorticoids), afflicted by psychiatric conditions, and those taking calcium, vitamin D, or multivitamin supplements were excluded from the study.

2.2. Study implementation

A previously approved questionnaire [20] that included demographic information and medical history were provided to all participants and completed with the assistance of their parents. Subjects were randomly allocated into five [5] groups of supplementations. Each day for six months, all the subjects in group 1 were given vitamin D tablet (1000 IU) (VitaD1000®, Synergy Pharma, Dubai, UAE) and the other four groups were given four different brands of locally available fortified milk, 200 ml/tetra pack, respectively.

2.3. Anthropometry and blood collections

Subjects were requested to visit their respective schools after an overnight fast (≥10 h). Physical examination was carried out by the attending physician to determine whether the participants met the inclusion criteria. Weight (kg) and height (cm) were recorded using an international standard scale (Digital Pearson Scale, ADAM Equipment Inc., USA) and body mass index (BMI) was calculated as kg/m^2.

Systolic and diastolic blood pressure (mmHg) was measured using a calibrated, mercurial sphygmomanometer and was measured twice, with a 15-minute interval and the mean of the two readings was recorded. Fasting blood samples were collected and transferred to a non-heparinized tube for centrifugation. All measurements were repeated after the 6-months intervention. Collected serum samples were transferred to pre-labeled plain tubes, placed on ice, and delivered to the Biomarkers Research Program (BRP) laboratory in King Saud University, Riyadh, KSA, for storage at −20 C.

2.4. Sample analyses

Fasting glucose and lipid profile were measured using a chemical analyzer (Konelab, Espoo, Finland). Serum 25(OH)D was measured with a Roche Elecsys modular analytics Cobas e411 using an electrochemiluminescence immunoassay (Roche Diagnostics, GmbH, Mannheim, Germany) and commercially available IDS kits (IDS Ltd, Boldon Colliery, Tyne & Wear, UK). BRP laboratory is participating in the Vitamin D External Quality Assessment Scheme (DEQAS), and Quality Assurance (QA) standards are maintained by ISO 9000 and 17,025. The QA department audits the BRP laboratory at regular intervals.

2.5. Data analyses

Data were analyzed using SPSS (version 16.5 Chicago, IL, USA). Mean and standard deviations were used to represent data for normal variables, while the median and interquartile range was used to report non-normal variables. Normality was assessed using the Kolmogorov-Smirnov test. Analysis of Variance (ANOVA) and paired sample t-test were used to assess mean differences, while GLM univariate analysis was used to control for age, BMI, gender and baseline vitamin D. P-value < 0.05 was considered statistically significant.

3. Results

The median age, number of male and female, BMI, 25(OH)D levels, along with other biochemical parameters of the subjects are illustrated in Table 1. These subjects were randomized into five-groups; one group received vitamin D tablet (1000 IU) (VitaD1000®) (Synergy Pharma, Dubai, UAE) and other four groups received different brands of 200 ml of fortified milk. ANOVA was used to identify the difference in baseline characteristics among treatments. Significant differences were observed in age, BMI, systolic BP, and vitamin D levels. No significant