Turkish Journal of Medical Sciences

Volume 41 | Number 1 Article 5

1-1-2011

The optimal dose of vitamin D in growing girls during academic years: a randomized trial

MEHRDAD SHAKINBA

SAMANE TEFAGH

ZAHRA NAFEI

TÜBİTAK

Original Article

Turk J Med Sci
2011; 41 (1): 33-37
© TÜBİTAK
E-mail: medsci@tubitak.gov.tr
doi:10.3906/sag-1006-884

The optimal dose of vitamin D in growing girls during academic years: a randomized trial

Mehrdad SHAKINBA, Samane TEFAGH, Zahra NAFEI

Aim: Prevalence of vitamin D deficiency is remarkable during childhood and adolescence throughout the world. Sufficient intake of vitamin D contributes to a number of health outcomes. The aim of this study was to specify the optimal dose of vitamin D in growing girls in a Muslim country during an academic year.

Materials and methods: This randomized clinical trial study was carried out in Yazd in the center of Iran in 2007;120 junior high school girls (aged 12-15 years) were randomly divided into 4 groups. Sixty students in groups I and II were treated for vitamin D deficiency with 300,000 IU vitamin D3 and then randomly received 50,000 U/monthly or 100,000IU/3 months vitamin D3; 60 other students in groups III and IV received 50,000 IU/3 months and 100,000/3 months from the beginning of the academic year. Medication continued for the entire academic year; 1 month after the last dose, serum 25(OH)D levels were measured.

Results: The mean level of 25 (OH) D was 29.7 ± 4.60 ng/mL in group I and 30 ± 5.61 ng/mL in group II. Mean serum levels of 25 (OH) D were 15.2 ± 6 ng/mL and 23 ± 6.8 ng/mL for groups III and IV, respectively.

Conclusion: Neither doses of about 800 IU/day nor 1000 IU/day are sufficient to maintain 25(OH)D in optimal level (> 20 ng/mL) for all, but after the treatment of deficiency, intakes of about 1000 IU/day or 2000 IU/day of vitamin D maintained optimal level in all of the students.

Key words: Vitamin D, girl, bolus therapy, 25OH vitamin D

Introduction

Vitamin D is an essential hormone for growth and development of bones in children and strong skeletal structure in adults (1). In vitamin D deficiency, only 10%-15% of calcium of normal diet is absorbed. This amount increases to 40% in the presence of adequate vitamin D (2,3). Moreover, epidemiologic studies show vitamin D deficiency increases the risk of important diseases like malignancy, cardiovascular disease, hypertension, stroke, diabetes, multiple sclerosis, rheumatoid arthritis, and inflammatory bowel disease (4). Many studies in recent years have demonstrated that vitamin D deficiency could exist in children and young adults without any obvious sign or symptoms (5-12). Girls particularly are more prone to vitamin D deficiency because of their less exposure to the sun and also their limited outdoor activities (5). Since about 35% of bone mass is acquired during 4 years around puberty (13) it seems rational to pay special attention to this age group. Diagnosis, treatment, and prevention of vitamin D deficiency in adolescents could, therefore, be very important for their future health (14). In Iran, primary evaluation demonstrated a high percentage of vitamin D deficiency in different age groups and in various locations especially in winter (15-19).

Received: 14.06.2010 – Accepted: 04.08.2010
Department of Pediatrics, Shahid Sadoghi Medical University, Avicenna street, Yazd - IRAN
Correspondence: *Mehrdad SHAKIBA, Department of Pediatrics, Shahid Sadoghi Medical University, Avicenna street, Yazd - IRAN*
E-mail: shakiba@ssu.ac.ir

There are different ways to receive sufficient vitamin D: either enough exposure to sunshine or consumption of supplements separately or in combination with fortified foods. Considering the importance of puberty, in some countries (e.g. France and Argentina) in which foods are not fortified, vitamin D supplements are offered to the girls in bolus doses every few months (18,20-22). Currently recommended intakes of vitamin D are 200-400 IU/day for young adults. These recommendations are not sufficient to reach the optimal 25(OH)D concentration in most of the population. For the majority of endpoints, an advantageous serum concentration of 25(OH)D is 30 ng/mL (4). The recommended dose of vitamin D for serum 25(OH)D level of 30 ng/mL in 50% of subjects is 1000 IU/day and for 88% of them is 4000 IU/day (23,24).

Results of several studies supported that intake of vitamin D 4000-10000 IU/day for adults and 2000 IU/day for children over the age of 1 is safe and sufficient (23,25).

Studies have investigated the required daily dose of vitamin D for adults (26,27); however, further studies are needed to evaluate the best dose of vitamin D for optimal 25(OH)D concentrations in healthy growing children and adolescents.

In view of the high prevalence of vitamin D deficiency among girls in Yazd (28) this study was designed to determine the adequate amount of vitamin D to maintain a level more than 20 ng/mL through academic years. Yazd is one the sunniest provinces in the country and the Middle East, and, therefore, this study could reveal the minimum requirement of vitamin D in other areas with less sunshine than our region.

Methods

This study was conducted as a randomised clinical trial on the female students at junior high school (aged 12-15 years) in Yazd during autumn and winter 2007. A total sample size of 120 subjects was calculated based on a previous study (20), considering CI = 95%, study power of 80%, SD1 = 4.4 ng/mL, SD2 = 4.6 ng/mL and minimal clinical differences (d = 3.3 ng/mL) with loss to follow up of 20%. The students were all healthy without any history of endocrine, bone, liver, kidney, gastrointestinal, and metabolic diseases. None of the students had been consuming any vitamin D supplements. Students were chosen randomly and after an explanatory session to describe the details of experiment to the parents and students, their consents were taken. Students were then arbitrarily divided into 4 groups: 60 in group I and II who treated as vitamin D deficiency with 300,000 vitamin D3 and then randomly received 50,000 IU each month (about 2000 IU/day) or 100,000 IU/3 months (about 1000 IU/day), 30 in group III received 50,000 IU/3 months (400 IU/day), and 30 in group IV received 100,000 IU/3 months (about 1000/day). A questionnaire was filled face to face for each student. Height, weight, and the stage of their puberty (Tanner stage) were then assessed. Vitamin D3 was given as a pearl (50,000 units, Alhavi Company Iran) to groups. The second and complementary doses (identical to dose one) were given at the intervals up to the end of the academic year. An information pack on side effects of vitamin D along with a questionnaire was provided for participants to fill if any of side effects occurred within 2 weeks of taking doses. After 2 weeks all the questionnaires were collected. One month after taking the final dose, a 3-5 mL blood sample was taken and assessed for 25(OH)D. The blood samples were transferred to the laboratory where they were centrifuged and frozen at -20 °C. Chemiluminescence immunoassay (DiaSorin, LIAISON® 25 OH Vitamin D assay) was used to measure 25(OH)D (as a main indicator of vitamin D). SPSS was used to analyse the data where statistical descriptive and analytic tests like mean (SD), t-test, and Mann-Whitney were applied. $P < 0.05$ was considered as the significant level of differences.

Results

One hundred and twenty students were enrolled in this study. Two students in group I and 7 students in group II were eliminated because of their changing school or not using the right dose. In the 2 groups who were treated first as deficient**,** the mean levels of 25(OH)D were 29.7 ± 4.60 ng/mL in the 50,000 IU group and 30 ± 5.61 ng/mL in the 100,000 IU group. There were no significant differences in serum level means (P value = 0.75 t-test). The range of serum 25(OH)D level in the 1000 IU/day group was 20.34-

36.23 ng/mL and while it was 20.43-47.88 in the 2000 IU/day group. All the students who received vitamin D had serum level of > 20 ng/mL. Serum 25(OH)D levels in 53.5% of 2000 IU/day group and 43.5% of 1000 IU/day group were > 30 ng/mL. The Table shows the vitamin levels at the end of the academic year.

In the other 2 groups mean serum levels of 25(OH)D were 15.2 ± 6 ng/mL and 23 ± 6.8 ng/mL for groups III and IV, respectively. Differences between means in groups III and IV were significant (PV = 0.0000). The range of serum 25(OH)D level in group III was 7-27 ng/mL while it was 13.4-37.5 in group IV. Neither dosage produced serum levels of 25(OH)D above 20 ng/mL in all cases, but in group IV all had levels of 25(OH) more than 12 ng/mL and 55% more than 20 ng/mL. In group III only 13% had levels of 25(OH) more than 20 ng/mL. All these doses were safe for all of the students although some complained about headaches and nausea for which none of them needed any medical care.

Discussion

In this study we evaluated the effect of 4 oral vitamin D bolus doses on 25(OH)D level in junior high school girls in Yazd (with its geographical location of 30°N). The required serum 25(OH)D level is the point which avoids serum parathyroid hormone (PTH) elevation. Several studies estimated this point to be between 8 and 35 ng/mL, but for most of the population, 25(OH)D level of 20 ng/mL or even higher is considered appropriate (29).

Intake of vitamin D 1600 IU/day to maintain serum 25(OH)D concentrations > 32 ng/mL in 97.5% of the 20- to 40-year-old adults was suggested by Cashman et al. (26), but Heaney et al. recommended 5000 IU/day for this purpose ([2]5). Although the exact optimal consumption dose of daily vitamin D is not determined, 2000 units/day has been suggested to be safe for adolescents (31). In a study carried out in French adolescents aged 10-15 years, 100,000 units of vitamin D every 3 months during winter were able to raise their serum level of vitamin D above 20 ng/mL with decreasing parathyroid hormone levels. This study is similar to our study regarding the duration and the age of participants (30). In our study, after 9 months, 36% of students who received vitamin D 2000 IU/day had serum 25(OH)D concentrations > 32 ng/mL. It seems that a greater requirement of vitamin D in adolescent girls or severe initial deficiencies in this region could be reasons for these differences.

Conclusion

Results of this study show that in the area with high prevalence of vitamin D deficiency (more than 50%), the recommended dose of neither 400 IU/day nor 800 IU/day is sufficient to maintain optimal level in all. However, after treatment of deficiency with 300,000 IU of vitamin D, both doses of 1000 or 2000 IU/day would maintain serum 25(OH)D concentrations > 20 ng/mL in all of the samples during academic years. If we consider level more than 30 ng/mL as the ideal level our study revealed higher doses than what we use should be recommend.

Table. The distribution of 25 OH vitamin D among treated groups at the end of the academic year.

100,000 unit/ 3 months Group IV (n: 30)	50,000 unit/ 3 months Group III (n: 30)	300,000 IU + 100, 1000/ 3 months Group II (n: 23)	300,000 IU + 50,000/months Group I (n: 28)	Groups Level 25OH-VITD
0%	13.5%	zero	zero	Severe deficiency (25(OH)D<10)
45%	%73	zero –	zero	Deficiency 25(OH)D=10-20
35.5%	10.8%	57% –	47%	Adequate 25(OH)D=20-30
19.5%	2.7%	43% –	53%	Ideal 25(OH)D=30-100

Acknowledgment

The authors wish to thank the students and parents who took part in this study. We also would like to thank F. Shamsi for her contribution in the statistics part of our manuscript. This article is based on a research conducted by Dr S. Tefagh, as her dissertation for medical degree, which was supervised by Dr Shakiba.

References

1. Holick MF. Vitamin D deficiency. N Engl J Med 2007; 357: 266-81.
2. Holick MF. Vitamin D: The underappreciated D-lightful hormone that is important for skeletal and cellular health. Curr Opin Endocrinol Diabetes 2002; 9: 87-98.
3. Heaney RP, Dowell MS, Hale CA, Bendich A. Calcium absorption varies within the reference range for serum 25-hydroxyvitamin D. J Am Coll Nutr 2003; 22: 142-6.
4. Cannell JJ, Hollis BW. Use of vitamin D in clinical practice. Altern Med Rev 2008; 13: 6-20.
5. El-Hajj Fuleihan G, Nabulsi M, Choucair M, Salamoun M, Hajj Shahine C, Kizirian A et al. Hypovitaminosis D in healthy schoolchildren. Pediatrics 2001; 107: E53.
6. Du X, Greenfield H, Fraser DR, Ge K, Trube A, Wang Y. Vitamin D deficiency and associated factors in adolescent girls in Beijing. Am J Clin Nutr 2001; 74: 494-500.
7. Guillemant J, Taupin P, Le HT, Taright N, Allemandou A, Pérès G et al. Vitamin D status during puberty in French healthy male adolescents. Osteoporos Int 1999; 10: 222-5.
8. Rovner AJ, O'Brien KO. Hypovitaminosis D among healthy children in the United States: a review of the current evidence. Arch Pediatr Adolesc Med 2008; 162: 513-9.
9. Gordon CM, DePeter KC, Feldman HA, Grace E, Emans SJ. Prevalence of vitamin D deficiency among healthy adolescents. Arch Pediatr Adolesc Med 2004; 158: 531-7.
10. Lehtonen-Veromaa MK, Möttönen TT, Nuotio IO, Irjala KM, Leino AE, Viikari JS. Vitamin D and attainment of peak bone mass among peripubertal Finnish girls: a 3-y prospective study. Am J Clin Nutr 2002; 76: 1446-53.
11. Outila TA, Kärkkäinen MU, Lamberg-Allardt CJ. Vitamin D status affects serum parathyroid hormone concentrations during winter in female adolescents: associations with forearm bone mineral density. Am J Clin Nutr 2001; 74: 206-10.
12. Looker AC, Dawson-Hughes B, Calvo MS, Gunter EW, Sahyoun NR. Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal subpopulations from NHANES III . Bone 2002; 30: 771-7.
13. Das G, Crocombe S, McGrath M, Berry JL, Mughal MZ. Hypovitaminosis D among healthy adolescent girls attending an inner city school. Arch Dis Child 2006; 91: 569-72.
14. Huh SY, Gordon CM. Vitamin D deficiency in children and adolescents: epidemiology, impact and treatment. Rev Endocr Metab Disord 2008; 9: 161-70.
15. Moussavi M, Heidarpour R, Aminorroaya A, Pournaghshband Z, Amini M. Prevalence of vitamin D deficiency in Isfahani high school students in 2004. Horm Res 2005; 64: 144-8.
16. Hashemipour S, Larijani B, Adibi H, Javadi E, Sedaghat M, Pajouhi M et al. Vitamin D deficiency and causative factors in the population of Tehran. BMC Public Health 2004; 25; 4: 38
17. Maghbooli Z, Hossein-Nezhad A, Shafaei AR, Karimi F, Madani FS, Larijani B. Vitamin D status in mothers and their newborns in Iran. BMC Pregnancy Childbirth 2007; 12; 7: 1.
18. Dahifar H, Faraji A, Yassobi S, Ghorbani A. Asymptomatic rickets in adolescent girls. Indian J Pediatr 2007; 74: 571-5.
19. Rabbani A, Alavian SM, Motlagh ME, Ashtiani MT, Ardalan G, Salavati A et al. Vitamin D Insufficiency among Children and Adolescents Living in Tehran, Iran. J Trop Pediatr 2009; 55: 189-91.
20. Maalouf J, Nabulsi M, Vieth R, Kimball S, El-Rassi R, Mahfoud Z et al. Short- and long-term safety of weekly high-dose vitamin D3 supplementation in school children. J Clin Endocrinol Metab 2008; 93: 2693-701.
21. Tau C, Ciriani V, Scaiola E, Acuña M. Twice single doses of 100,000 IU of vitamin D in winter is adequate and safe for prevention of vitamin D deficiency in healthy children from Ushuaia, Tierra Del Fuego, Argentina. J Steroid Biochem Mol Biol 2007; 103: 651-4.
22. Duhamel JF, Zeghoud F, Sempé M, Boudailliez B, Odièvre M, Laurans M et al. Prevention of vitamin D deficiency in adolescents and pre-adolescents. An interventional multicenter study on the biological effect of repeated doses of 100,000 IU of vitamin D3. Arch Pediatr 2000; 7: 148-53.
23. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr 2006; 84: 18-28.
24. Vieth R, Chan PC, MacFarlane GD. Efficacy and safety of vitamin D3 intake exceeding the lowest observed adverse effect level. Am J Clin Nutr 2001; 73: 288-94.
25. Heaney RP, Davies KM, Chen TC, Holick MF, Barger-Lux MJ. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. Am J Clin Nutr. 2003; 77: 204-10.
26. Cashman KD, Hill TR, Lucey AJ, Taylor N, Seamans KM, Muldowney S et al. Estimation of the dietary requirement for vitamin D in healthy adults. Am J Clin Nutr 2008; 88: 1535-42.

27. Cannell JJ, Hollis BW, Zasloff M, Heaney RP. Diagnosis and treatment of vitamin D deficiency 2008; 9: 107-18.

28. Shakiba M, Nafei Z, Lotfi MH, Shajari A. Prevalence of Vitamin D Deficiency among Female Students in Secondary Guidance School in Yazd City, Acta Medica Iranica 2009; 47: 209-14.

29. Lips P. Which circulating level of 25-hydroxyvitamin D is appropriate? J Steroid Biochem Mol Biol 2004; 89-90: 611-4.

30. Duhamel JF, Zeghoud F, Sempé M, Boudailliez B, Odièvre M, Laurans M et al. Prevention of vitamin D deficiency in adolescents and pre-adolescents. An interventional multi center study on the biological effect of repeated doses of 100,000 IU of vitamin D3. Arch Pediatr 2000; 7: 148-53.

31. Maalouf J, Nabulsi M, Vieth R, Kimball S, El-Rassi R, Mahfoud Z et al. Short- and long-term safety of weekly high-dose vitamin D3 supplementation in school children. J Clin Endocrinol Metab 2008; 93: 2693-701.