

THE EFFECT OF VITAMIN D3 SUPPLEMENTATION PER ORAL AND SUN EXPOSURE ON THE EMPLOYEES OF PROF. DR. R SOEHARSO ORTHOPEDIC HOSPITAL OF SURAKARTA WITH VITAMIN D INSUFFICIENCY OR DEFICIENCY

Pamudji Utomo¹, Mujaddid Idulhaq¹, Agus Wahyudi², Muhammad Abdulhamid², Muhammad Qathar RF Tulandi²

¹Department of Orthopaedic and Traumatology Faculty of Medicine , Universitas Sebelas Maret
RSUD Dr. Moewardi – RSO Prof. DR.R Soeharso, Surakarta

²Resident of Department of Orthopaedic and Traumatology Faculty of Medicine, Universitas Sebelas Maret
RSUD Dr. Moewardi- RSO Prof. DR. R. Soeharso, Surakarta

Email: a_yoedi@yahoo.co.id

ABSTRACT

Background : Vitamin D insufficiency affects almost 50% of the population worldwide. About 1 billion people worldwide from all ethnicities and age groups, have a vitamin D deficiency. This pandemic of hypovitaminosis D closely related to lifestyle (such as less of outdoor activities) and environmental (such as air pollution) factors that reduce exposure to sunlight, which is required for ultraviolet-B (UVB)-induced vitamin D production in the skin. High prevalence of vitamin D insufficiency is an important public health issue because hypovitaminosis D is an independent risk factor for total mortality in the general population. Last studies suggest that we may need more vitamin D to prevent chronic disease. As few foods contain vitamin D, guidelines recommended supplementation at suggested daily intake and tolerable upper limit levels. It is also suggested to take a measurement of the 25-hydroxyvitamin D level serum as the initial diagnostic test in patients at risk for deficiency. Treatment with either vitamin D2 or vitamin D3 is recommended for deficient patients.

Method : This study was an experimental study with one group design pretest and posttest. Target population was employee of Prof dr R Soeharso Orthopaedic hospital with deficiency or insufficiency of vitamin D level. Total of 40 subjects has been measured serum 25-hydroxyvitamin D level. The result found that 1 sample is normal and excluded from the study, and 39 others are included in the study. All of them have been treated with vitamin D3 supplement 50.000 IU per week for eight weeks then measured serum 25-hydroxyvitamin D level post treatment. All the result was analyzed with Wilcoxon test respectively

Results : All samples undergoing treatment with vitamin D3 supplement had a significant improvement on the result of Vitamin D level. Wilcoxon rank test shows the value of $p = <0.001$ ($p <0.05$) which means that there is a significant improvement of vitamin D serum levels before and after treatment.

Conclusion : Normalization of hypovitaminosis D level with cholecalciferol (D3) treatment significantly reduces the severity of fatigue symptoms in person who has complain about fatigue conditions.

Keywords : Vitamin D level, Vitamin D3 Supplement.

ABSTRAK

Pendahuluan: Kekurangan vitamin D mempengaruhi hampir 50% populasi di seluruh dunia. Sekitar 1 miliar orang di seluruh dunia dari semua etnis dan kelompok umur, mengalami kekurangan vitamin D. Pandemi hipovitaminosis D ini terkait erat dengan gaya hidup (seperti kurangnya aktivitas di luar ruangan) dan faktor lingkungan (seperti polusi udara) yang mengurangi paparan sinar matahari, yang diperlukan untuk produksi

vitamin D yang diinduksi ultraviolet-B (UVB) di kulit. Prevalensi tinggi kekurangan vitamin D merupakan masalah kesehatan masyarakat yang penting karena hipovitaminosis D merupakan faktor risiko independen untuk keseluruhan kematian pada populasi umum. Studi terakhir menunjukkan bahwa kita mungkin membutuhkan lebih banyak vitamin D untuk mencegah penyakit kronis. Karena sedikit makanan yang mengandung vitamin D, suatu pedoman merekomendasikan suplementasi pada asupan harian yang disarankan dan tingkat batas atas yang dapat ditoleransi. Juga disarankan untuk melakukan pengukuran serum level 25-hidroksivitamin D sebagai tes diagnostik awal pada pasien yang berisiko mengalami defisiensi. Perawatan dengan vitamin D2 atau vitamin D3 direkomendasikan untuk pasien yang kekurangan.

Metode penelitian : Penelitian ini merupakan penelitian eksperimental dengan rancangan one group pretest and posttest. Populasi sasaran adalah pegawai RS Ortopedi Prof dr R Soeharso yang mengalami defisiensi atau defisiensi vitamin D. Sebanyak 40 subjek telah diukur kadar serum 25-hidroksivitamin D. Hasil penelitian didapatkan 1 sampel normal dan dikeluarkan dari penelitian, dan 39 lainnya termasuk dalam penelitian. Semuanya telah diobati dengan suplement vitamin D3 50.000 IU/ minggu selama delapan minggu kemudian diukur kadar serum 25-hidroksivitamin D pasca pengobatan. Semua hasil dianalisa dengan uji Wilcoxon.

Hasil: Semua sampel yang menjalani pengobatan dengan suplementasi vitamin D3 mengalami peningkatan yang signifikan terhadap hasil kadar Vitamin D. Uji Wilcoxon rank menunjukkan nilai $p = <0,001$ ($p <0,05$) yang berarti terdapat peningkatan yang signifikan pada serum vitamin D pada tingkat sebelum dan sesudah pemberian suplemen vitamin D.z

Kesimpulan: Normalisasi kadar hipovitaminosis D dengan pengobatan cholecalciferol (D3) secara signifikan mengurangi keparahan gejala kelelahan pada orang yang mengalami kondisi kelelahan.

Kata kunci: level Vitamin D, Suplemen Vitamin D3

BACKGROUND

Vitamin D can be called “*sunshine vitamin*”. High vitamin D serum level are essential for normal skeletal mineralization and growth. Vitamin D is obtained from dietary sources and photochemical transformation of 7-dehydrocholesterol (provitamin D3) to precholecalciferol (previtamin D3) in the skin, which is converted to either vitamin D3 (cholecalciferol) or inert photoproducts^(1,2,3)

Hypovitaminosis D level has been correlated with an increased risk of type 1 diabetes mellitus, cardiovascular disease, certain cancers, cognitive decline, depression, pregnancy complications, autoimmunity, allergy, and even frailty^(4,5,6). Indonesia is sun-drenched country throughout the year. Until now, the studies about prevalence vitamin D deficiency are very rare related to sun exposure

and food intake especially those specifically aimed at workers who are inside indoors and outdoors.

Fatigue is a common complaint of 33% patients presenting in the ambulatory primary care offices in the US. The prevalence of fatigue in the US workforce has been estimated as 37.9% in a 2-week period.⁽⁷⁾ Although fatigue is meant as a state of inability to maintain or sustain a force, nevertheless it is interchangeably used by the patients to describe a state of tiredness or “low energy.” It has significant negative impact on social life, family life, and work performance.⁽⁸⁾ In otherwise healthy individuals, fatigue can be a manifestation of low vitamin D levels and its impact on reduced maximum functioning of skeletal muscles via vitamin D receptors.⁽⁹⁾ Whether correction of low vitamin D alleviates

fatigue in such individuals is still unknown.

Almost all of employee of Prof. DR. R Soeharso hospital complain about in fatigue during their work. They often felt tired after arriving home from hospital. And this impairs their work performance and can affect mood during their work. Therefore, it is necessary to do research on the vitamin D3 levels of Prof. Dr. R Soeharso Orthopedic Hospital Surakarta employees, to find out how many cases of vitamin D3 deficiency or insufficiency of them. Based on this problem, we take a random sampling of Prof. Dr. R Soeharso Orthopedic Hospital Surakarta employee about 41 samples based on slovin formula. All of samples have been measured of their vitamin D serum level and categorized into deficiency, insufficiency, or sufficiency of Vitamin D. From 41 persons of

random sampling were collected. Two patients excluded because were not qualified. All of samples are treated by vitamin D3 supplementation 50.000 IU/ week for eight weeks, and have 15 minutes sun exposure for two weeks. Then evaluated for their vitamin D serum level post treatment. The data was then analyzed with IBM® SPSS® Statistics Ver. 23.

RESULT

All 39 samples have low vitamin D serum level in which sample with deficiency vitamin D (25(OH) D level in blood is less than 20 ng/mL) are 34 samples and insufficiency vitamin D (25(OH) D level in blood is in range 21-29 ng/mL) are 5 samples. And the characteristic of them is presented in the table below.

Table 1. Distribution of Prof. Dr. R Soeharso Orthopedic Hospital of Surakarta employees with vitamin D insufficiency or deficiency.

Characteristics	Result (n=39)
Sex	
Male	8 (20,5%)
Female	31 (79,5%)
Age	42,85 ±9,56
Height	158,72 ±6,32
Body Weight	61,38 ±9,66
BMI	24,29 ±3,16

Based on the table 39 samples were collected. Thirty one samples (79,5%) were female and eight others (20,5%) were male. The age of employee are in the productive age range 42,85 ±9,56, the height 158,72 ±6,32 cm, body wight 61,38 ±9,66 kg, and nutritional status of the employee based on body mass index range 24,29 ±3,16.

The Age of samples under 50 years are 30 persons (76%) and 9 others are over than 50 years (24%). Based on the places of their work divided into in the office and out of office is 18 samples (46%) compare to 21 samples (54%). And they travelled to work 28 (72%) samples were riding motorcycle and 11 (28 %) samples were riding car. Then

laboratory finding from general check up all of hospital employee were

normal all of samples include routine blood test, liver and renal function test.

There is no difference vitamin D level measurement condition between under 50 and over 50 years, all of them have insufficiency and deficiency of vitamin D level by comparison 34 samples (87%) have deficiency of vitamin D level and 5 samples (13%) have sufficiency of vitamin D level.

Due to pretest data was abnormal

distributed, then data analysis were done with non parametrical Wilcoxon rank test to know about the effects of vitamin D3 supplementation per oral on the employees of Prof. Dr. R Soeharso Orthopedic Hospital of Surakarta with vitamin D insufficiency or deficiency respectively. The result showed significancy of the effect vitamin D supplementation per oral for who had vitamin D insufficiency or deficiency with p value= $<0,001$ ($p<0,05$)

Table 2. Wilcoxon rank test result

Variable	Pretest	Posttest	p-value
Vitamin D level measurement	13,85 $\pm 5,09$	49,71 $\pm 11,27$	$<0,001$

Due to pandemic of covid-19, some of employees checked for the their immunity by evaluating their NLR ratio especially for them where their work place has the closed contact with the patient. 16 persons of 39 persons have evaluated their NLR ratio post having vitamin D supplements. All of them had NLR ratio < 3.13 (normal reference ranges value) and no one of them got wheter IgM or IgG covid 19 reactive from rapid test.

The other complaints we evaluated before treatment were fatigue, which had negative effect on their life and work performance. We evaluated post treatment that all of them had a better condition especially correlated with their fatigue rate during their work performance.

DISCUSSION

The important finding of this study reveal that low level vitamin D serum almost found in all

samples employee of Prof. Dr. R Soeharso Orthopedic Hospital of Surakarta. It can be associated with lack of physical activity and sun exposure. Vitamin D suppelementaion is one of the way to treat vitamin D deficiency or insufficiency case.

Either both vitamin D2 or vitamin D3 can be used for vitamin D supplementation, although there is controversy regarding vitamin D3 vs vitamin D2 for achieving and maintaining higher serum 25(OH)D levels. Although a recent metaanalysis showed that vitaminD3 is more effective on raising serum 25(OH)D concentrations than is vitamin D2. ^(10,11) Several prospective studies have found them to be equally effective in raising and

maintaining serum 25(OH)D levels in children and adults. The RDA (recommended daily allowance) for vitamin D and tolerable upper-limit levels vary in different age groups and in certain condition. ^(11,12,13) Although vitamin D intake is recommended that RDAs of 600 to 800 IU daily should meet the requirements to optimize bone health in most of the population, higher vitamin D intakes (1000-2000 IU) are needed to reach and maintain 25(OH)D levels greater than 30 ng/mL. ^(11,12) It is known that for every 100 IU of vitamin D ingested, the blood level of 25(OH)D raises to approximately 0.6 to 1 ng/mL. ⁽¹³⁾

When the serum 25(OH)D level is less than 15 ng/mL, 100 IU of vitamin D will increase the 25(OH)D level by as much as 2 to 3 ng/mL. ^(13,14) Consistent with our findings, Holick report that an effective strategy to treat vitamin D deficiency and insufficiency in children and adults is to give them 50,000 IU of ergocalciferol once in a week for 6 to 8 weeks, respectively.

Fatigue is the end result of the underlying muscle fatigue, which is more general encountered than muscle weakness. ⁽¹⁵⁾ Hypovitaminosis D is also associated with inappropriate activation of the renin-angiotensin system, which fails to inhibit abnormal cell proliferation. ^(16,17)

Our findings provide a proof of evidence that normalization of low vitamin D levels in patients with fatigue conditions, significantly improves their condition by reducing the fatigue. Based on oral regimens therapeutic of cholecalciferol the 50,000 IU in a week for 8 weeks regimen combine with sun exposure for 15 minutes along two weeks have shown the efficiency of treatment, without adverse events, or toxicity.

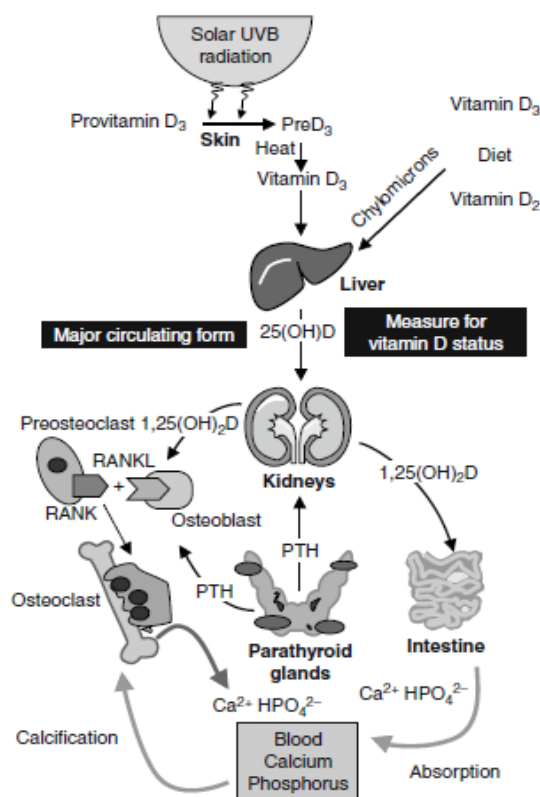


Fig. 1 Schematic representation of cutaneous production of vitamin D₃ (cholecalciferol) and its metabolism and regulation for calcium and bone metabolism. (Source from : Review Article “Drugs Aging 2007; 24 (12): 1017-1029”)

CONCLUSION

Vitamin D deficiency is a common underdiagnosed condition that has received increasing attention in the world. Vitamin D supplementation per oral can be one of choice to increase vitamin D serum level. Besides need more cost and some person may get the complication of supplement consumption. Other ways need to increase vitamin D serum level have to compare are sun exposure and

increasing physical activities that no need more cost and almost no complications.

Normalization of hypovitaminosis D level with cholecalciferol (D3) treatment significantly reduces the severity of fatigue symptoms in person who has complain about fatigue conditions.

Authors Contribution

All authors contributed equally to this work.

Financial Support and Sponsorship

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors declare that the study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

REFERENCES

1. Loomis F. Skin-pigment regulation of vitamin D biosynthesis in man. *Science* 1967, 157: 501-506.
2. Holick M.F., McCollum Award lecture, 1994. Vitamin D—new horizons for the 21st century. *Am. J. Clin. Nutr.* 1994, 60: 619-630.
3. Reichel H., Koefler P., Norman A.W. The role of the vitamin D endocrine system in health and disease. *N. Engl. J. Med.* 1989, 320: 986-991.
4. Smit E, Crespo CJ, Michael Y, et al. The effect of vitamin D and frailty on mortality among non-institutionalized US older adults. *Eur J Clin Nutr.* 2012;66(9):1024-1028.
5. Holick MF. Nutrition: D-iabetes and D-eath D-efying vitamin D. *Nat Rev Endocrinol.* 2012;8(7):388-390.
6. Hossein-nezhad A, Holick MF. Optimize dietary intake of vitamin D: an epigenetic perspective. *Curr Opin Clin Nutr Metab Care.* 2012;15(6):567-579.
7. Ricci JA, Chee E, Lorandean AL, Berger J. Fatigue in the U.S. workforce: Prevalence and implications for lost productive work time. *J Occup Environ Med.* 2007;49:1-10.
8. Rosenthal TC, Majeroni BA, Pretorius R, Malik K. Fatigue: An overview. *Am Fam Physician.* 2008;78:1173-9.
9. Holick MF. Resurrection of vitamin D deficiency in rickets. *J Clin Invest.* 2006;116:2062-72.
10. Bjorkman M, Sorva A, Tilvis R. Responses of parathyroid hormone to vitamin D supplementation: a systematic review of clinical trials. *Arch Gerontol Geriatr.* 2009;48(2): 60-166
11. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and revention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011;96(7):1911-1930.
12. Ross AC, Manson JE, Abrams SA, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *J Clin Endocrinol Metab.* 2011;96(1):53-58.
13. Holick M.F. Vitamin D deficiency. *N Eng J Med.* 2007;357(3):266-281
14. 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(1):204-210.
15. Brown RH, JR, Amato AA, Mendell JR. Muscular dystrophies and other muscle diseases. In: Fauci AS, Braunwald E, Kasper DL, editors. *Harrison's Principles of Internal Medicine.* New York: McGraw Hill Medical; 2008. pp. 2678-95.
16. Resnick LM, Müller FB, Laragh JH. Calcium-regulating hormones in essential hypertension. Relation to plasma renin activity and sodium metabolism. *Ann Intern Med.* 1986;105:649-54.
17. Li YC, Kong J, Wei M, Chen ZF, Liu SQ, Cao LP. 1, 25-Dihydroxyvitamin D (3) is a negative endocrine regulator of the renin-angiotensin system. *J Clin Invest.* 2002;110:229-38.