Study of the Safe Dosage of Ergocalciferol

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Vitamin D2 or ergocalciferol can replace vitamin D3, but its dosage must be a higher international unit: one unit of vitamin D3 is equal to 4 units of vitamin D2. A proper interval of administration should take 200,000 IU per day. The 123 cases enrolled for study, every case had blood levels of 25 (OH) D and blood calcium checked before intake of vitamin D2 followed by a second check after 2 months. The means of before-intake group was 31.92 ng/ml and after-intake group was 48.62 ng/ml; the pair sample mean was 0.001. We found the level of 25 (OH) D was greater than 70 ng/ml (max = 90), 3.2 percent. Twelve cases showed no response, 9.6 percent. No cases of hypercalcemia or allergic phenomenon were noted. Before the study, we tried a random dosage of 200,000 IU per week and found the pair mean showed nothing significant (p = 0.052). In practice, the dosage of 200,000 IU of vitamin D2 is suitable for treatment of vitamin D deficiency, but for long-term treatment, dosage should be adjusted by monitoring the levels of 25 (OH) D from time to time.

Keywords: *Ergocalciferol, Vitamin D2*

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For medication to be safe and effective, this requires knowledge and understanding of how the medication enters the body. Erroneous medicating due to the wrong drug, the wrong dose, wrong timing of administration and wrong route of administration accounts for 1.3 million injuries each year in the United States (FDA 2009)[1].

Dose and time of medication is important in its administration. Ergocalciferol or vitamin D2 application acts in the same manner as other drugs. A right understanding will avoid unwanted effects and give dramatic treatment.

The metabolism pathway for vitamin D2 is rather complicated. Ergosterol or vitamin D2 has a plant precursor e.g. mushroom, which changes after exposure to ultraviolet B to vitamin or ergocalciferol. Human intake of ergocalciferol is metabolized in the liver into 25-hydroxy vitamin D2 or calcidiol or 25 (OH) D2 acting as prohormone and then turns into an active form of vitamin D or 1, 25 (OH) 2D at the kidney, which acts as a hormone.

In medicine, a calcidiol or 25 (OH) D (we measure both vitamin D3 and D2 or called total vitamin D) blood test is used to determine how much vitamin D is in the body. The blood concentration of calcidiol is considered as the best indicator of vitamin D status. There is no consensus of normal value of 25 (OH) D, but most experts recognized 30-80 nanogram per milliliter as a normal level[2]. Cannel suggested the 25 (OH) D level is 40-70 ng/ml to maintain year round; however, if there is underlying disease the cover level will be 55-70 ng/ml[4].

The human skin can synthesize the precursor of vitamin D, the 7-dehydrocholesterol after exposure to ultraviolet B, and change it to vitamin D3 with liver metabolized to 25 (OH) D3 or calcifediol and renal metabolism turns into active form, 1.25 (OH) 2D3. Normal distribution in human circulation shows that vitamin D3 outnumbers vitamin D2. In blood tests, we measure both vitamin D called total vitamin D.

Vitamin D2 is inferior to vitamin D3[5] such as low binding power to vitamin D binding protein; the free form excretes through the kidney quickly, the potency of vitamin D2 is less than D3 about 1:9.5; shelf live is shorter than D3 and four units of D2 equal to one unit of D3.

Vitamin D3 is not available in some counties. Therefore, management of vitamin D2 is necessary. This study shows how to use vitamin D2 application.

Material and Method

Vitamin D2 20,000 IU is available in the market so was selected for the study. After consideration, see graph Fig. 1[6], the level of 25 (OH) D2 dropped quickly

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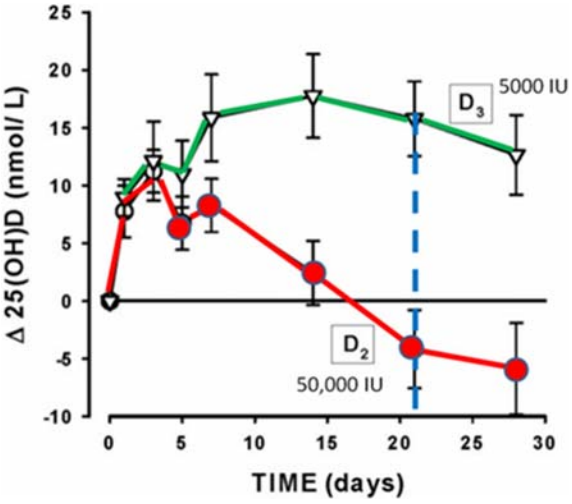

Fig. 1 The change of 25 (OH) D level after single dose of vitamin D3, D2[6].

Table 1. A group of 20,000 IU of vitamin D2 per week

	n	Min	Max	Mean	SD
Baseline	9	18.5	26.5	21.93	3.31
3 month	9	19.8	28.6	23.86	3.11

Table 2. The result of vitamin D2: a group of daily intake of 20,000 IU

	Min	Max	Mean	SD
Before intake	6.14	59.69	31.92	13.01
After intake	16.28	90.00	48.62	14.81

Before beginning the study, the suitable doses were random: we created two groups: one group takes vitamin D2 20,000 IU per week (10 cases) and other group takes 20,000 IU per day (123 cases).

Non-fasting blood was investigated for 25 (OH) D by Cobas® 6000 analyzer, Roche Diagnostics at Siriraj Hospital.

The vitamin D levels were checked every month for safety including blood calcium.

Results

The means before and after treatment are 21.93, 23.86 nanogram per milliliter, respectively.

The pair mean test, $p = 0.052$. The statistic is different between the two means, but the level of 25 (OH) D is not equal to the normal level of 25 (OH) D. Thus, the study in this group was cancelled.

Intake of vitamin D2 for 2 months found no hypercalcemia. This study had 4 cases or 3.2 percent which contained levels of 25 (OH) D above 70 ng/ml (maximum = 90 ng/ml). In addition, 12 cases or 9.6 percent showed blood levels of 25 (OH) D, below 30 ng/ml. The mean of 25 (OH) D of pretest and post treatment showed a significant difference, $p = 0.001$. The response of vitamin D2 is wide therapeutic length; some cases did not respond while others had high levels of 25 (OH) D. The therapeutic length of 25 (OH) D is controversial but the recommended level is 30-80 ng/ml[3].

Some experts adjusted doses to 50-80 ng/ml[4]. Doses of vitamin D are dependant on underlying status of patient; recommended dose is high for cancer, multiple sclerosis, rheumatoid; however, it should not exceed 150 ng/ml. The best way to adjust the dose needed is 25 (OH) D and blood calcium check-up from time to time. Vitamin D2 administration needs a long time, several years, especially for prevention. For the prevention of hypercalcemia, calcium intake must be limited, not more than 800 mg/day.

Summary

Ergocalciferol can be replace calciferol of vitamin D3. The dose is higher than vitamin D3, the power of vitamin D3 is stronger four times than vitamin D2[5,6]. Ergocalciferol has short metabolization, so the blood levels of 25 (OH) D turn down quickly. Dosage adjustment and duration of this type vitamin D require monitoring and blood checks of 25 (OH) D.

Potential conflicts of interest

None.

References

1. Food and Drug Administration, U.S. Department of Health and Human Service. Drugs@FDA glossary of terms [Internet]. 2015 [cited 2015 Mar 31]. Avaliable from: http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#M
2. 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.
3. Cannel JJ, Hollis BW. Use of vitamin D in clinical practice. Altern Med Rev 2008; 13: 6-20.
4. Houghton LA, Vieth R. The case against ergocalciferol (vitamin D2) as a vitamin supplement. Am J Clin Nutr 2006; 84: 694-7.

5. Tripkovic L, Lambert H, Hart K, Smith CP, Bucca G, Penson S, et al. Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis. Am J Clin Nutr 2012; 95: 1357-64.
6. Armas LA, Hollis BW, Heaney RP. Vitamin D2 is much less effective than vitamin D3 in humans. J Clin Endocrinol Metab 2004; 89: 5387-91.

รายงานการศึกษาวิตามิน ดีสอง

ณรงค์ บุณยะรัตเวช

ศึกษาขนาดของวิตามินดีสอง 200,000 อินเทอร์แนชชะเนิลยูนิตในคนไทยจำนวน 123 รายที่ตรวจพบระดับวิตามินดี 25 (OH) D เฉลี่ย 31.92 นาโนกรัมต่อมิลลิลิตร ให้ยาวิตามินดีสองขนาด 200,000 อินเทอร์แนชชะเนิลยูนิตต่อวันนาน 60 วัน พบว่าระดับวิตามินดีในเลือดเฉลี่ยเป็น 48.62 นาโนกรัมต่อมิลลิลิตร (p = 0.001) ซึ่งเป็นค่าปกติที่ยอมรับได้ (30-80 ng/ml) แต่มี 9.6 เปอร์เซ็นต์ ที่ระดับวิตามิน ดี ไม่ขึ้นเกินค่าปกติ และ 3.2 เปอร์เซ็นต์มีค่ามากกว่า 70 นาโนกรัมต่อมิลลิลิตร ทุกรายไม่มีภาวะแคลเซียมในเลือดสูง การตรวจวัด 25 (OH) D เป็นสิ่งจำเป็นเพื่อป้องกันการได้รับวิตามินมากหรือน้อยไป

ก่อนทำการศึกษาได้ลองสุ่มตัวอย่างในการให้วิตามินขนาดเดียวกันนี้แต่ช่วงเวลาห่างกัน 7 วัน จำนวน 10 รายพบว่าค่าเฉลี่ย (Mean) ก่อนและหลังได้ยามีค่า 21.93 และ 23.86 ตามลำดับ ค่า p = 0.052 ถือว่าผลที่ได้ไม่พอใจ

โดยสรุปวิตามินดี สอง ขนาด 200,000 ยูนิตสามารถให้ได้ทุกวันถ้าให้ระยะยาวจำเป็นต้องปรับขนาดยา โดยใช้การตรวจวัดหาระดับ 25 (OH) D เป็นตัวช่วยในการปรับระดับให้เหมาะสม
