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ORIGINAL ARTICLE

25-Hydroxycholecalciferol Response to Single Oral Cholecalciferol Loading in the Normal Weight, Overweight, and Obese

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ABSTRACT

Objective: The aim of the study is to evaluate the response of 25- hydroxycholecalciferol (25OHD) to a single oral administration of cholecalciferol in the normal weight, overweight, and obese individuals.

Place and duration of study: The study is conducted in Pak International medical College Hayatabad and the duration of study was from March 2021 to March 2022

Material and Method: We have examined 60 healthy women from the age groups of 24-68 years(mean+ SD, 51.2+ 9.6) with a body mass index in kg/m^2 ranging from19.2 to 43.2 (mean + SD 28.2+5.9). Female individuals are divided into 3 groups based on their body mass index, 1st group is having normal female individuals having BMI less than 25 kg/m^2 (n=22), 2nd group having BMI of 25.1-29.9 kg/m^2(n=23)and 3rd group having BMI greater than 30Kg/m^2(n=15). Every participants is taken a single oral dose of cholecalciferol(300,000 IU) and their Venous blood samples are taken to measure the concentration levels of 25OHD, 1,25(OH)2D, parathyroid levels, calcium and phosphorus levels. The results are categorized in the form of mean, standard deviation, p-values, least square means with 95% confidence intervals (CI) in each group of individuals at 8th and 31st days of cholecalciferol administration.

Results: The total body fat of normal weight group is significantly lesser than that overweight group of individuals, which is lesser than that of group of obese individuals. At the beseline detection of serum level of 25 OHD all the women have detectable serum levels of 25OHD. In the obese group of individuals there will be a lesser levels of 25 OHD observed than normal group of individuals and the difference is approximately equal in the case of overweight group of individuals. The obese group of individuals also have approximately lesser levels of 1,25(OH)2D than the normal group of individuals but have increasing levels of parathyroid hormones. After administration of cholecalferol the levels of parathyroid hormone is observed significantly lesser at day 8 than baseline in the normal weight of individuals not in other groups, which approximately increasing over time at day 31 in all the groups of individuals. There is a positive correlation found between the concentrations of 25OHD and 1, 25(OH)2D while there is a negative correlation found between the levels of 25 OHD and parathyroid hormone at all time points.

Conclusion: Serum levels of 25 OHD become decreases in obese individuals is due to their increase body volume. The levels of decline of 25 OHD in obese is due to their larger body size and slower release of vitamin D from their body fat.

Keywords: Adipose tissues, Obesity, Vitamin D, Cholecalciferol, Overweight, Calcium.

INTRODUCTION

Vitamin D is an essential component to ensure the intestinal absorption of calcium in humans. It is also taking part in a lot of metabolic processes in human body based on many pathological and pathological processes including immune system[1,2] processing, cardiovascular[3], endocrine[4,5] or oncological disorders[6,7]. Cholecalciferol (vitamin D3) taken in any form is metabolized in liver. The form of 25 OHD provides the substrate to 1,25 dihydroxyvitamin D having a systemic effects in the body of humans. 25 OHD vitamin d3 form is considered to be the most reliable form of calcium in human body. Many studies suggested the idea that 25 OHD and levels of parathyroid hormones in the body is inversely proportional to each other, higher levels of serum 25OHD cause decrease levels of parathyroid hormone.25 OHD levels higher than 30 ng/ml[8] is considered to be the range which is effective in lowering the incidence of colon cancer, juvenile diabetes and other disorders[9].

The quantity of adipose tissues plays a vital role in the distribution of vitamin D inside the human body. It is evident in various past studies that serum levels of 25 OHD is inversely proportional with obesity[10-17] however the deposition of vitamin D in adipose tissues is release in circulation when requires to a body in still under study considerations and a point to debate.

MATERIAL AND METHODS

This Study is conducted in the Park International Medical College Hayatabad Peshawar and The duration of study was from March 2021 to March 2022.We have examined 60 healthy women from the age groups of 24-68 years(mean+ SD, 51.2+ 9.6) with a body mass index in kg/m^2 ranging from19.2 to 43.2 (mean + SD 28.2+5.9).

Inclusion criteria of women in this study is age not less than 20 years , no endocinological or intestinal disorder, not taking medication which interferes with the metabolism of vitamin D or calcium. Our exclusion criteria of women in this study are intestinal malabsorption, intake of vitamin D in any shape , kidney or liver disorders and prior history of surgery.

Montomoli et al.prepared the instrumental questionnare, having 15 number of questions based on the usage of food and beverages commonly ingested in the 1 week of time period in healthy women, collected data based on baseline and daily calcium intake in healthy women. Sun exposure is calculated as per the suggestion of Glanz et al. based on average time in week days spend in sunlight without using sunscreens.

Female individuals are divided into 3 groups based on their body mass index, 1st group is having normal female individuals having BMI less than 25 kg/m^2 (n=22), 2nd group having BMI of 25.1-29.9 kg/m^2(n=23)and 3rd group having BMI greater than 30Kg/m^2(n=15).

Every participant is taken a single oral dose of cholecalciferol(300,000 IU) in any diluted solution or in bread slice during lunch. Venous blood samples are taken from all subjects to measure the concentration levels of 25OHD, 1,25(OH)2D, parathyroid levels, calcium and phosphorus levels, also their fasting blood levels were collected at morning time between 7-9 AM before cholecalciferol loading. Participants are observed at the time interval of 8th and 31st day of cholcalciferol administration.

Serum levels of calcium and phosphorus are measured by using colorimetric assay. Parathyroid hormone levels are measured by using the method of immunoassay.

The results are categorized in the form of mean, standard deviation, p-values, least square means with 95% confidence intervals (CI) in each group of individuals at 8th and 31st days of cholecalciferol administration. Quantitative data of participants are

tested by using ANOVA technique followed by Bonferroni's multiple comparisons and baseline characteristics are measured by using chi-square test. Baseline trends in all parameters are estimated by using Pearson's correlation coefficient and then their p-value are calculated to estimate their significance levels. Significance level is set at 5%.Research participants fat mass is measured by using DEXA Technique(Dual energy X-ray absorptiometry).

RESULT

In Table 1, we are spotting the lifestyle parameters of 3 different groups we are Examining in this research study. In the whole sample population, the sample we are examining in the normal group of individuals is n=22 having mean age in years is 50.1, while in overweight and obese groups these are n=23 (51.2 years) and n=15(53.1 years). In the whole consideration of groups the normal range of mass in fat ranges from 11.8 to 54.6 kg, when all the groups are examined as per the body mass index the total body fat of normal weight group is significantly lesser than that overweight group of individuals, which is lesser than that of group of obese individuals.

At the baseline detection of serum level of 25 OHD all the women have detectable serum levels of 25OHD, but 97.2% of them have decrease levels than 75nmol/L, which is considered as a minimum levels of 25 OHD, Only 3 women in the overweight group have levels greater than 75 nmol/L.In the obese group of individuals there will be a lesser levels of 25 OHD observed than normal group of individuals and the difference is approximately equal in the case of overweight group of individuals. The obese group of individuals also have approximately lesser levels of 1,25(OH)2D than the normal group of individuals but have increasing levels of parathyroid hormones.

The daily intake of calcium and exposure to sun in all the group of individuals are approximately same and donot differ statistically in all the groups of individuals.

In Table 2, we are noticing the levels of 25OHD, PTH, and 1, 25(OH)2D after cholecalciferol administration, the sample individuals levels of 25 OHD is significantly increasing after cholecalciferol administration and become increasingly higher at the 8 day. The levels of 25 OHD at the day 8 and 31 after cholecalciferol administration is significantly higher in the normal weight of group of inviduals that the overweight and obese group of individuals. After peaking at day 8, the levels of 25 OHD drops down over time at day 31 observed in all age groups.

After administration of cholecalferol the levels of parathyroid hormone is observed significantly lesser at day 8 than baseline in the normal weight of individuals not in other groups, which approximately increasing over time at day 31 in all the groups of individuals.

Participants' 1.25 dihydroxy vitamin D levels are significantly higher at days 8 and 31 in all groups of individuals than baseline.

There is a positive correlation found between the concentrations of 25OHD and 1, 25(OH)2D, as the levels of both increasing at day 8 after cholecalciferol administration except at day 31, while there is a negative correlation found between the levels of 25 OHD and parathyroid hormone at all time points.

Table 1: Lifestyle values of 3 different group examined values shown in mean and standard deviation.

Parameters	Normal weight (a) (n = 22)	Overweight (b) (n = 23)	Obese (c) (n = 15)
Age (years)	50.1(9.4)	51.2(11.8)	53.1(5.4)
Body mass index (kg/m2)	22.2(1.9)	28.5(2.7)	36.3(4.5)
Parathyroid hormone (pmol/L)	65.1(26.1)	70.1(26.4)	99.1(41.1)
25OHD (nmol/L)	44.2(21.1)	49.1(22.4)	29.4(15.3)
1,25(OH)2D (pmol/L)	102.7(39.2)	75.4(32.8)	67.9(27.8)S
Calcium (nmol/L)	2.4(0.3)	2.3(0.2)	2.3(0.3)
Phosphorus (nmol/L)	1.3(0.3)	1.2(0.3)	1.3(0.3)
Mass in fat (kg)	17.1(4.1)	26.4(5.1)	38.5(9.1)
Calcium intake (daily >1gm/day)	11(52)	11(52)	10(66)
Sun exposure	1: 3 (16) 2: 11 (56) 3: 6 (32)	1: 0 (0) 2: 14 (68) 3: 7 (35)	1: 2 (15) 2: 9 (65) 3: 3 (25)

Body mass index (BMI in kg/m2), PTH Normal range is 16–68 pmol/L), 25OHD vitamin D (sufficiency > 50 nmol/L), 1,25 (OH)2D 1,25 dihydroxyvitamin D (normal range 43-148 pmol/L)

Table 2: Least squares means (95 % confidence interval), Mean and standard deviation at baseline at 8th and 31st day after Vitamin D administration in the 3 different groups

		Observed means (SD)			Least squares means (95 % CI with Bonferroni adjustment)		
		Normal	Overweight	Obese	Overweight vs normal	Obese vs normal	Obese vs overweight
25 hydroxy vitamin D	Baseline	44.6(21.00)	48.7(22.3)	29.6(15.3)	---	---	---
	8 day	135.2(26.20) p = 0.0003	107.8(22.82) p < 0.0002	89.08(28.) p= 0.0012	-29.03(-44.02;-12.15) p = 0.0262	-43.93(-63.52;-28.12) p = 0.0001	-17.72(-35.02;+0.69) p=1.1
	31 day	124.2(27.1) p = 0.0004	95.3(29.03) p < 0.0002	83.22(22.03) p= 0.0012	-30.12(-58.20;-2.42) p=0.0301	-41.12(-71.23;-11.01) p=0.0016	-12.01(-42.23;+19.23) p=2.0
1.25 dihydroxy vitamin D (pmol/L)	Baseline	104.04(41.03)	77.50(34.2)	69.20(29.02)	-----	-----	------
	8 day	186.3(79.02) p = 0.0014	154.20(49.03) p = 0.0003	133.70(39.03) p = 0.0012	-17.01(-72.83;+40.01) p=2.0	-30.10(-92.56;+33.02) p=1.0	-13.01(-72.83;+45.19) p=2.2
	31 day	180.02(65.80) p=0.003	168.40(79.02) p=0.002	135.20(65.03) p=0.0008	+0.72(-80.31;+81.52) p=2.0	-31.52(-119.42;+55.92) p=2.2	-32.19(-115.92;53.12) p=1.5
Parathyroid hormone (pmol/L)	Baseline	65.85(26.30)	69.08(26.62)	99.05(41.67)	------	------	------
	8 day	52.40(17.82) P=0.030	58.33(21.80) p=0.072	86.82(24.73) p=0.52	+4.9(-16.12;+25.23) p=1.3	+22.22(-0.69;+48.12) p=0.0592	19.01(-5.12;+41.92) p=2.2
	31 day	60.07(19.50) p=0.81	62.82(24.45) p=0.22	88.62(33.04) p=0.62	+0.22(-25.52;+25.12) p=1.5	=16.12(-13.01;+45.32) p=0.9	+16.01(-12.52;+43.67) p=1.2

DISCUSSION

In Our sample population 25 OHD levels are deficient in indiduals having higher BMI. This observation is consistent with previous studies showing negative correlation between 25 OHD and BMI[18], this negative relationship based of various hypothesis i.e. limited exposure to sun[19] , increasing vitamin D uptake in adipose tissues[20] and more volume dilution[21]. These Hypothetical perceptions in the back studies showing the lesser levels of 254 OHD in obese group of individuals. Drincic et al. in this studies conducted previously explains that body weight and body fat is negatively associated with levelsm of 25 OHD.As per researchers the dose response curve in the obese and non-obese individuals in the back studies, examined that the dilution of vitamin D may be different in fat tissues and extracellular fluids.

In the study that we have conducted shows that the levels of 25 OHD after cholecalciferol administration is greater in normal weight group of individuals than in overweight and obese groups. This finding is consistent with previous studies based on the concentrations of dilutions of vitamin D in body tissues.

After achieving the peak levels of 25 OHD, drops down more slowly in obese group of individuals than other groups suggesting the negative relationship between body fat and decrease 25 OHD levels after peaking, this assumption is supporting the concept of cholecalciferol accumulation in the subcutaneous fat tissues of obese individuals. Didriksen et al. in his study explains the subcutaneous tissues store large amount of cholecalciferol in its long term oral administration[22].

Levels of 1,25(OH)2D found to be lower in overweight and obese females than in normal weight females.We found position correlation between time points of 25OHD and 1,25(OH)2D in this study.

We have found a nehative association between PTH and 1,25(OH)2D at all time points,exclaim that the increase in serum 1,25(OH)2D levels in human body pose a decrease levels of parathyroid hormones and vice versa.25 OHD levels decreasing the levels of parathyroid hormone secretion by binding with vitamins D receptors further it has been noticed that increase in body fat may increase parathyroid levels in obese individuals which is independent with the concentration of metabolites of vitamin D.As this study conducted having a sample population of female individuals so the results of this study is not implemented for male gender of individuals. This study donot considered white or brown race of individuals so the result may be different for the vitamin D metabolism of specific race-based individuals.

CONCLUSION

In conclusion, 25 OHD effect to single oral dose of cholecalciferol is different in relation with body mass index in obese and normal weight individuals according to this study. Serum levels of 25 OHD become decreases in obese individuals is due to their increase body volume. The levels of decline of 25 OHD in obese is due to their larger body size and slower release of vitamin D from their body fat.

REFERENCES

1 Höck AD (2014) Vitamin D3 deficiency results in dysfunctions of immunity with severe fatigue and depression in a variety of diseases. In Vivo 28(1):133–145

2 Lucas RM, Gorman S, Geldenhuys S, Hart PH (2014) Vitamin D and immunity. F1000 Prime Rep. 1;6:118

3 Zittermann A (2014) Vitamin D and cardiovascular disease. Anticancer Res 34(9):4641–4648

4 Romagnoli E, Pepe J, Piemonte S, Cipriani C, Minisola S (2013) Management of endocrine disease: value and limitations of assessing vitamin D nutritional status and advised levels of vitamin D supplementation. Eur J Endocrinol 169(4):R59–R69

5 Muscogiuri G, Mitri J, Mathieu C, Badenhoop K, Tamer G, Orio F, Mezza T, Vieth R, Colao A, Pittas A (2014) Mechanisms in endocrinology: vitamin D as a potential contributor in endocrine health and disease. Eur J Endocrinol 171(3):R101–R110

6 Shui I, Giovannucci E (2014) Vitamin D status and cancer incidence and mortality. Adv Exp Med Biol 810:33–51

7 Ordóñez Mena JM, Brenner H (2014) Vitamin D and cancer: an overview on epidemiological studies. Adv Exp Med Biol 810:17– 32

8 Sai AJ, Walters RW, Fang X, Gallagher JC (2011) Relationship between vitamin D, parathyroid hormone, and bone health. J Clin Endocrinol Metab 96(3):E436–E446

9 Gandini S, Boniol M, Haukka J, Byrnes G, Cox B, Sneyd MJ, Mullie P, Autier P (2011) Meta-analysis of observational studies of serum 25-hydroxyvitamin D levels and colorectal, breast and prostate cancer and colorectal adenoma. Int J Cancer 128(6): 1414–1424

10 Peterson CA, Tosh AK, Belenchia AM (2014) Vitamin D insufficiency and insulin resistance in obese adolescents. Ther Adv Endocrinol Metab 5(6):166–189

11 Cipriani C, Pepe J, Piemonte S, Colangelo L, Cilli M, Minisola S (2014) Vitamin D and its relationship with obesity and muscle. Int J Endocrinol 2014:841248. doi:10.1155/2014/ 841248

12 Gulseth HL, Gjelstad IM, Birkeland KI, Drevon CA (2013) Vitamin D and the metabolic syndrome. Curr Vasc Pharmacol 11(6):968–984

13 Vanlint S (2013) Vitamin D and obesity. Nutrients 5(3):949–956

14 Blum M, Dallal GE, Dawson-Hughes B (2008) Body size and serum 25 hydroxy vitamin D response to oral supplements in healthy older adults. J Am Coll Nutr 27(2):274–279

15 Lee P, Greenfield JR, Seibel MJ, Eisman JA, Center JR (2009) Adequacy of vitamin D replacement in severe deficiency is dependent on body mass index. Am J Med 122(11):1056–1060

16 Tepper S, Shahar DR, Geva D, Ish-Shalom S (2014) Predictors of serum 25(OH)D increase following bimonthly supplementation with 100,000 IU vitamin D in healthy, men aged 25-65 years. J Steroid Biochem Mol Biol 144 Pt A:163–166

17 Ekwaru JP, Zwicker JD, Holick MF, Giovannucci E, Veugelers PJ (2014) The importance of body weight for the dose response relationship of oral vitamin D supplementation and serum 25-hydroxyvitamin D in healthy volunteers. PLoS One 9(11):e111265

18 Saneei P, Salehi-Abargouei A, Esmaillzadeh A (2013) Serum 25-hydroxyvitamin D levels in relation to body mass index: a systematic review and meta-analysis. Obes Rev 14(5):393–404

19 Holick MF (2004) Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. Am J Clin Nutr 80(6 Suppl):1678S–1688S

20 Foo LH, Teo PS, Abdullah NF, Aziz ME, Hills AP (2013) Relationship between anthropometric and dual energy X-ray absorptiometry measures to assess total and regional adiposity in Malaysian adolescents. Asia Pac J Clin Nutr 22(3):348–356

21 Drincic AT, Armas LA, Van Diest EE, Heaney RP (2012) Volumetric dilution, rather than sequestration best explains the low vitamin D status of obesity. Obesity 20(7):1444–1448

22 Didriksen A, Burild A, Jakobsen J, Fuskevåg OM, Jorde R (2015) Vitamin D3 increases in abdominal subcutaneous fat tissue after supplementation with vitamin D3. Eur J Endocrinol 172(3):235– 241