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DEMOGRAPHIC VARIABLES AND EFFECT OF VITAMINS DEFICIENCY IN MENOPAUSAL WOMEN

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Abstract

The effect of calcium and vitamin D alone and combined on applicable variables in menopausal women participants with initial serum 25OHD levels lower 60nmol/L. Participants were assigned randomly to two groups. Group I received one week of calcium 1000mg, followed by seven weeks with additional vitamin D 1000mg i.e. every day, group II received seven weeks of vitamin D 1000 i.e. every day, followed by one week with additional calcium 1000 mg. We determined serum calcium, PTH, phosphate, CTX, ALP and 25OHD at baseline and after one and eight weeks in group I and after seven and eight weeks in group II. There was no correlation modification in ALP from either calcium or vitamin D. Calcium produced significant increment of serum 25OHD also mostly suppressed serum CTX that could not easily be accounted for PTH suppression. Vitamin D produced no remarkable modification in any variables except increment of serum 25OHD. The calcium suppressive effect on serum CTX was threefold higher compared to vitamin D, though their suppressive effect on serum PTH was similar. Vitamin D and calcium caused higher and more remarkable effects on all variables than either treatment alone. This conclude that calcium may increased serum 25OHD by prolonging its half-life and it may have an inhibitory effect on resorption of bone independent or addition to its PTH suppression.

Keywords: *Menopause, calcium, hyperparathyroidism, Parathyroid hormone.*

Introduction

Menopause is literally the terminate of menstruation, however an extensive definition including 'the indefinite cessation of menstrual cycles followed the mislaying activity of ovarian follicles'. The transitional phase climacteric is the first symptom of ovarian senescence till its fulfilled installation. Between different changes in endocrines that the continuing loss of function of ovaries and leads to menopause, the main important is the reduction of ovarian steroids circulating levels (Stein et al, 1996). Menopause is correlated with higher prevalence of metabolic syndrome, cardiovascular disorder, obesity and osteoporosis. Gain of weight is found between the women midlife and has been described to both menopause transition and chronological aging. Recently data from a higher population dependent cohort in the United States fortify the idea that gain of weight is not only relates to the transition of menopause also the mass of fat increased quickly in this phase Bates (2003). There are three reasons for the correlation among hip fracture and deficiency of vitamin D. the first one is that deficiency of vitamin D can leads to weakness of muscle and increased the falling risk, the second one is that it can reduce the bone quality by mineral content reduction and the third reason is caused secondary hyperparathyroidism (Sahota et al, 1999) that increased the turnover of bone however it reduced mass of bone and accelerates the process of osteoporosis. The vitamin D seminal trial with calcium in fracture of hip prevention assigned their success to the reversal of secondary hyperparathyroidism but developed strength of muscle and the consequent decrease in falls likely made a remarkable contribution as well (Melton et al,1997). The dose dependent power of vitamin D with calcium to stop fractures of osteoporosis, there is still uncertain about the interpose level of serum 25- hydroxyvitamin D (25OHD) about the serum concentration of target 25OHD and the optimal dose to attain the target Garnero et al, 2000. In this dispute, surprisingly small attention has been made to supplementation of calcium role, despite the common recognition that the convincing proof of prevention of fracture with vitamin D derived from studies in that it was joined with calcium (Heaney, 2003). So therefore, this study was to designed the establishment of suppressive effect of calcium and vitamin D, combined and alone on serum parathyroid hormone (PTH) and on resorption of bone marker c-terminal telopeptide (CTX) in menopausal participants with deficiency of vitamin D as defined by serum concentration of 25OHD below 60 nmol/L, that is threshold lower which we see a increase in turnover marker of bone.

Materials and methods

One hundred and fifty women aged among 50 and 70 years who had a serum 25OHD level lower than the 60 nmol/L on continuous screening ordered by their common practitioners were invited to participate in this study. Fifty declined and 25 were excluded because of renal function impairment, diabetes, hypercalcemia, malignancy and estrogen treatment. Twenty five participants who were living independently with no chronic illness gave informed consent and commenced the study however five dropped out, leaving forty five who had completed the study. One of these, with an initial serum 25OHD of 59 nmol/L, had a level of 65 nmol/L on starting the actual trial but the balances were still lower 60 nmol/L on starting.

Methods

The designed study was an inter and intra participants comparison. The subjects were randomized into two groups by a computer dependent random number generator. Group I received one week of 1000 mg of calcium as the carbonate followed by seven weeks of continuous calcium with added vitamin D 1000 i.e. Second group received the same in reversible order like 1000 i.e. in vitamin D everyday alone for seven weeks followed by one week of continuous vitamin D with added calcium 1000 mg every day. Participants were asked to take the supplements at 9 pm. Serum samples were collected at 9 am after the overnight fasting after one and eighth week in group I and after seven and eight weeks in group II. The variables measured were serum calcium, PTX, CTX, phosphate, ALP and 25OHD. Total serum phosphate and serum were measured spectrophotometrically by using the reagents metallochromogen arsenazo III and ammonium molybdate respectively. Serum 25OHD was measured by enzyme immune assay and PTH measured by an automated enzyme-labeled chemiluminescent assay. Then the serum ALP was measured using the substrate of pNPP.

Results

Demographics and Baseline Values

The median values and ranges of baseline are applicable to measured variables are presented in table-1. All values were within the reference ranges except for the below levels of 25OHD and the increased presumed because of insufficiency of vitamin D. There was one participant with an unknown higher ALP at 145 U/L however there was no remarkable modification in ALP at this study period and this variable will not be further considered.

Table 1: Mean values and ranges of relevant measured variables at baseline in menopausal women

Variables	Mean	Range
Age	61	55 to 68
Height (m)	1.60	1.53 – 1.69
Weight (kg)	65	47 - 106
BMI (kg/m2)	25.6	19.1 – 38.2
tCa (mmol/L)	2.35	2.19 – 2.68
PO4 (mmol/L)	1.14	0.65–1.45
ALP (IU/L)	82	30 – 110
CTX (ng/L)	450	<400
PTH (pmol/L)	4.3	0.8 – 5.5
25OHD	45.3	29.0-64.0

Table-2: Mean values (SD) of all measured variables at first, second, and third visits by group

	V1	V2	V3
tCa (mmol/L)			
GI	2.35 (0.091)	2.46 (0.098)**	2.42 (0.063)
GII	2.33 (0.10)	2.37 (0.081)	2.42 (0.132
t	1.02	2.17	–0.3
p	0.31	0.045	0.68
PO4 (mmol/L)			
GI	1.10 (0.060)	1.25 (0.10)***	1.08 (0.11)**
GII	1.10 (0.12)	1.17 (0.14)	1.21 (0.11)
t	0.06	1.53	2.55
p	0.95	0.13	0.019
CTX (ng/L)			
GI	411 (192)	278 (148)***	230 (122)
GII	433(136)	411 (128)	311 (111)***
t	0.28	2.17	1.56
p	0.74	0.045	0.13
25OHD			
GI	49.10 (9.3)	70.7 (13.6)***	75.5 (16.7)
GII	48.4 (10.6)	90.5 (21.6)***	91.3(24.2)
t	0.12	2.5	1.4
p	0.89	0.16	0.14
PTH			
GI	5.63(2.27)	4.18 (2.56)	3.91 (1.40)
GII	6.39 (3.37)	5.63 (2.96)	4.75 (1.81)
t	0.62	0.36	0.16
p	0.53	0.71	0.16

*** P\0.001, ** P\0.01, * P\0.05

Table-3: Changes in measured variables after treatment with calcium (first or second) for 1 week or with vitamin D (first or second) for 7 weeks (means SE)

Variables	Modification after one week of calcium	Modification after 7 weeks of vitamin D	Variation among calcium and vitamin D	
			t	p
tCa (mmol/L)	0.060 (0.019)**	0.00 (0.022)	2.1	<0.11
PO4 (mmol/L)	0.087 (0.026)**	20.030 (0.036)	2.6	<0.01
CTX (ng/L)	19.69 (0.48)	20.61 (2.25)	0.02	0.97
PTH (pmol/L)	8.56 (4.5)*	24.2 (5.7)***	2.02	<0.11
25OHD	2113 (18.0)***	232.3 (18.2)	4.0	<0.001

Effects of Vitamin D and calcium

The mean value of the measured variables at the first, second and third meeting in the two groups are showed in table-2. At second meet, group I showed remarkable increment of serum phosphate, 25OHD and calcium. There was a little, non-significant fall of PTH however a main significant fall of CTX. In group II there was no significant modification in any variables except for a increase in serum 25OHD. At third meet, the only main modification was a significant fall in serum CTX in group II after the calcium to vitamin D addition. Comparison of total values in the two groups at every meet, the only remarkable variation in group I than II and the phosphate at meet was significantly increased in group II than I. The mean changes in the measured variables after one week of supplementation of calcium and seven weeks of supplementation of vitamin D in all participants (Table-3) Seven days of calcium leads to little but significant increase in total serum phosphate and calcium, a remarkable rise in 25OHD and a very significant fall in CTX, the fall in PTH was not significant. Seven weeks of vitamin D had no significant effect on any variables except for the final and initial values of the measured

variables with the significance of the modification within the participants, they represents the total effect of first week of calcium combined with 7 to 8 weeks of vitamin D. The combined therapy produced significant rise of serum calcium and 25OHD and significant suppression of CTX and PTH.

Discussion

This study is as far as know, the first one in which vitamin D and calcium have been compared individually and together in the similar individuals. The logic of this study was that calcium was known to employ its effect on bone resorption and PTH within 12 hours, whereas it is known that conventional dosage of vitamin D takes many weeks for the equilibrium 25OHD level production (Chapuy et al, 1992). The study that allowed one week of calcium compared directly with 7 or 8 weeks of vitamin D in the same participants, we did not predict any variation among the effects of 7 and 8^{th} weeks of vitamin D on serum 25OHD (Meunier, 1998). The two points of specific interest are the remarkable positive effect of calcium alone on serum 25OHD and the notably higher negative effect of calcium than vitamin D on CTX of serum (Tang et al, 2007, Bischoff-Ferrari et al, 2009). The data also represents that the combination of vitamin D and calcium is commonly powerful than either alone especially in suppression of PTH. None of these results can easily be assigned to the little power of the study. The previous studies of the vitamin D effect without or with calcium on serum PTH was fall significantly at 12% and. When the participants were given vitamin D with calcium, the mean fall of PTH was significantly 30%. These observations are not only qualitatively however also quantitatively same to our results in which the combined therapy leads fall in PTH twice than treatment alone (Lips, 2004; Malabanan et al, 1998; Dawson Hughes, 2004). The rise in 25OHD from 50 to 70 nmol/L after seven days of calcium alone of group I. Though this was not seen that calcium was added to the group II vitamin D and it is potentially chief and offered an another explanation for reduced serum level of 25OHD, that are globally attributed to lower point of vitamin D (Bischoff-Ferrari et al,2006). the deficiency of calcium and vitamin D lower serum 25OHD by shortening its half-life about 25 days. We suggested that supplementation of calcium may inhibits the 25OHD metabolism to account for our results. Some previous studies reported that deficiencies D in Western countries are accounted for its shortened half-life not just decreased. The other interest aspect of this study is that the serum CTX suppression by calcium was not only much higher than suppression of vitamin D but emerged to all proportion to its PTH suppression (Heaney,

2000). This determined that calcium may have a directly suppressive effect on resorption of bone atleast in postmenopausal women either by osteoclasts suppression or by acting directly by physiochemical equilibrium among the calcium phosphate in the tissue fluids and the bone mineral. This was agreed with Jesudason (2002) who has attention to the higher interface among tissue fluids and bone mineral at resting surface and had bone formation regulation and resorption cannot sufficiently explained the tight calcium homeostasis regulation (Thomas et al., 2008; Meyer et al, 2002). The fact is that the variables accomplished to peak in the early morning and night fall after the feeding at day in case the fast is continued (Patel et al, 2001). The extra calcium effect is to reduce the serum PTH to much the similar degree at all time points, so the modification in fasting is illustrative of the rest (Schlemmer and Hassager, 1999). The major effect of evening load of calcium on bone markers with slight changes in the day (Scopacasa et al, 1998). The clinical proofs also suggested that the requirement for both vitamin D and calcium (Boonen et al, 2007; Brown et al, 2009). The fracture of osteoporotics mainly linked to hip fractures that were not prevented by vitamin D alone. Mostly the preventive trails of fractures are included in the combination of calcium and vitamin D in recent meta-analysis used (Eastell et al, 2005).

Conclusion

This study concludes that the combination of calcium and vitamin D is highly effective at bone resorption suppression than either the treatment of alone and effect of calcium does not definitely operate only or mostly by suppression of PTH. The significant changes in ALP lack might be because of lack of power however is probably due to well-known time lag among the effect of antiresorptive treatment on resorption of bone and formation of bone.

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