Students' Corner

Obesity induced Magnesium deficiency can be treated by Vitamin D supplementation

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Abstract

Objective: To determine the effect of vitamin D injection on Serum Magnesium concentration in obese and non obese women.

Method: This Interventional study was performed on 82 women (17-50 years) which were randomly selected from general population of Tabriz city. They were assigned into two experimental groups. Obese group with stage 1 and 2 obesity and non obese group with normal weight. Weight was measured to the nearest 0.1 kg using a calibrated Seca scale. Height was measured using a cotton ruler which was pasted on the wall. Body mass index was calculated based on weight and height results. Biochemical parameters were measured before and after injection of 600000 IU doses of vitamin D. Serum Magnesium was measured calorimetrically and Serum 25 hydroxy vitamin D was estimated by Chemiluminescence Immuno Assay method (CLIA).

Results: Baseline concentrations of serum Magnesium and 25 hydroxy vitamin D in obese individuals was lower than non obese individuals, the former being significant. Twenty seven percent of obese women versus 15% of non obese women were Magnesium deficient. Vitamin D injection caused a significant increase in serum Magnesium concentration in obese subjects but not in non obese subjects. There was also a significant increase of serum 25 hydroxy vitamin D in both groups. Mean elevation in serum Magnesium level among women who had Magnesium deficiency was higher than women with Magnesium adequacy ($P<0.05$).

Conclusion: Low serum Magnesium concentration in obese individuals can be modified by vitamin D injection (JPMA 59:258; 2009).

Introduction

Magnesium a divalent ion, is widespread throughout the mammalian organism.[1] The physiological role of Magnesium is achieved through its ability to form chelates with important intracellular ligands especially ATP.[2] Magnesium is therefore essential for the synthesis of nucleic acids and proteins, for intermediary metabolism and for specific actions in different organs such as neuromuscular and cardiovascular system.[3] Magnesium deficiency can be divided to primary and secondary deficiency. Primary Magnesium deficiency is entirely due to reduced dietary intake and secondary Magnesium deficiency is a result of increased gastrointestinal or renal loss of Magnesium.[4,5]

Recent studies linked obesity with low serum magnesium. Obesity is characterized by a high risk for glucose intolerance, cardiovascular disease, dyslipidaemia and insulin resistance.[6] It is speculated that one of the causes for the aforementioned disorders in obese individuals, is Magnesium deficiency.[6-10] Several studies have identified low serum Magnesium in obesity. Huerta et al[7] and Song et al[11] found a negative correlation between serum magnesium and BMI in healthy children and adults($P<0.05$). In some of studies low serum and intracellular Magnesium has been reported in obesity.[12,13]

On the other hand, if Magnesium deficiency is detected, it should be treated because non treated Hypomagnesemia can lead to chronic disease as atherosclerosis, myocardial infarction, hypertension and renal calculi.[5] Although no hormone or factor has been described that regulates Magnesium absorption ,the effect of vitamin D on serum Magnesium concentration has been confirmed in some of studies.[14] In this study, the active metabolite of vitamin D,1,25 (OH)2 -vitamin D, increased intestinal absorption of Magnesium in physiologically normal human subjects.[14] In another study by Heaton and his colleagues[15] vitamin D enhanced intestinal absorption of both Magnesium and calcium, however these results were not confirmed by some other studies.

Wilz et al[16] found no relationship between plasma 1,25 (OH)2-viatmin D and net intestinal Magnesium absorption.

Table 1: Profile of obese and none obese woman in the study.

Characteristic	obese (n=43)	none obese (n=43)	P
Age(years)	32.54 ± 7.7	31.38 ± 6.8	0.470
Weight(kg)	81.07 ± 10.1	58.19 ± 6.4	0.000
Height (cm)	157.45±5	160.23 ±5	0.036
BMI[a] (kg/m2) 32.92 ± 2	22.63± 3.1	0.000	
Dietary energy (Kcal/day)	2080.57 ±697	2236.65±575	0.298
Dietary Carbohydrate(%)	57.13 ± 12.87	61.70 ± 10.22	0.078
Dietary protein(%)	14.59± 3.6	14.17± 3.3	0.591
Dietary Fat(%)	28.20 ±11.42	24.17 ±10.01	0.091
Dietary Vitamin D(IU b/d)	8.08 ±10	12.83 ± 19	0.165
Dietary Magnesium (mg/d)	122.43±17	144.66±17.48	0.373
Dietary calcium intake(mg/d)	601.4±53	525±34	0.219

a: Body Mass Index, b: IU International Unit (1IU of vitamin D: 0.025 microgram)

Gray TK et al[17] also reported that intravenous injection of 1,25 (OH)2-viatmin D had no significant effect on intestinal Magnesium absorption. No interventional study examining the effect of intramuscular injection of vitamin D in treatment of Magnesium deficiency in obesity was found in literature search. The aim of this interventional study was to determine the effect of vitamin D supplementation on serum Magnesium concentration in obese and non obese women.

Subjects and Methods

This study was carried out in northwestern region of Tabriz- Iran ,with the approval of the Tabriz University of Medical Science Ethics Committee and the consent of the volunteers. The study was performed during winter (January through March, 2007) on 82 reproductive age women (17-50 years), 40 of them had normal BMI (18.5-24.9 kg/m^2) and 42 had stage 1 and stage 2 obesity (BMI: 30-34.9 and 35-39.9 kg/m^2 respectively). Women with a history of Hepatic or Renal Disorders, Cardiovascular disease, Diabetes and Hypertension were excluded from the study. None of subjects was taking vitamin D and calcium supplements, anticonvulsant medications, Hormone Replacements such as estrogen, oral contraceptives (OCP), loop diuretics or corticosteroids. Fasting blood samples were collected in the morning and stored at -70 0C until assay. Each subject received a dose of 6000000 IU of vitamin D intramuscularly and after 2 weeks blood samples were collected again to determine the effect of vitamin D injection on serum Magnesium level.

Serum Magnesium was measured colorimetrically (Darman Kave , Res). CV of this test was 6%. Our reference range for serum Magnesium was 1.5-2.1 meq/l and Magnesium deficiency was identified as serum magnesium lower than 1.5meq/l.[18] Serum 25 hydroxy vitamin D was measured using a Chemiluminescence Immuno Assay method or CLIA (Diasorin, Still water, MN).[19] Sensitivity of this assay was 7.0 ng/ml. Mean inter and intra assay coefficient of variation (CV) were 13.2 and 10.8 respectively.

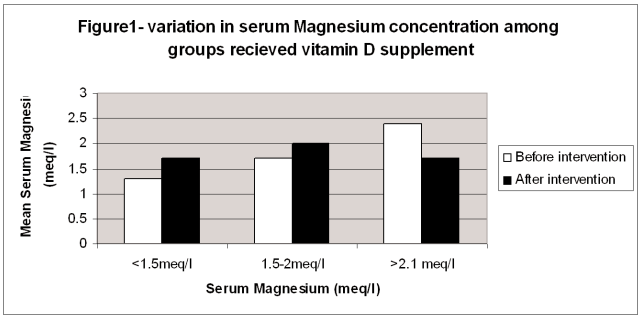

Figure: Variation of serum Magnesium levels among the groups received Vitamin D supplement.

Table 2: Comparison of biochemical characteristic between obese and none obese women.

Characteristic	Before intervention			after intervention		
	Obese	non obese	p	obese	non obese	p
Magnesium[a] (meq/l)	1.7±0.2	1.9± 0.5	0.030	2.04± 0.7	1.88 ± 0.5	0.077
25OHD[b] (ng/ml)	15.98±7.7	17.48 ± 10.45	0.596	24.6± 10.8	30.87±10	0.042

a: P value < 0.05 for Before and after intervention comparisons of serum Magnesium only in obese women (Paired t-test).
b: P value < 0.01 for Before and after intervention comparisons of serum 25OHD in both groups (Paired t-test).

Weight was measured to the nearest 0.1 kg using a calibrated Seca scale while subjects had light clothes and no shoes. Height was measured using a cotton ruler which was pasted to the wall. Body mass index was calculated based on weight and height BMI: Weight (kg)/Height (m^2). Demographic characteristic of participants were measured using an interview questionnaire. A 3-day diet record was obtained from participants. Average daily nutrient intakes were calculated by Nutritionist III software. It should be noted that all of participants had been educated to have their usual diet during 15 days follow up period.

Data was reported as mean ± SD. To compare Serum Magnesium and 25 hydroxy vitamin D before and after injection and between groups, paired t-test, independent

sample t-test and one way ANOVA (analysis of variance) were used. P value less than 0.05 was considered significant.

Results

The demographic characteristics of subjects are shown in Table 1. The mean age of obese and non obese women were 32.54 ±7.79 and 31.38 ± 6.68 years respectively. There was no significant differences between dietary energy and macronutrients intake between obese and non obese women. Dietary vitamin D and Magnesium intake was higher in non-obese women than in obese women (Vitamin D: 12.83 ± 19 vs 8.08 ±10 IU/d) (Magnesium: 144.66±17.48 vs 122.43±17mg/d) and Dietary calcium intake was slightly higher in obese women although these differences in both vitamin D and calcium intake were not statistically significant. Twenty seven percent of obese women versus 15% of non obese women were Magnesium deficient. Table 2 summarizes the biochemical characteristic of participants. There was no significant difference in serum 25 hydroxy vitamin D between obese and non-obese subjects. Mean serum Magnesium in obese women was significantly lower than non obese women ($P<0.05$).

After vitamin D injection there was a significant increase in serum Magnesium concentration in obese individuals ($P<0.05$) but serum Magnesium concentration in non obese individuals before and after intervention was not significantly different. Serum 25 hydroxy vitamin D has increased significantly in both obese and non-obese subjects ($p<0.01$).

Mean elevation in serum Magnesium level after vitamin D injection among women who had Magnesium deficiency (Serum Magnesium <1.5meq/l) was ±0.37 meq/l whereas women with Magnesium adequacy (Serum Magnesium 1.5-2 meq/l) showed ±0.26 meq/l elevation in serum Magnesium. Women with Serum Magnesium higher than 2.1 meq/l showed ±0.86 meq/l decrease in serum Magnesium ($P<0.01$) (Figure 1).

Discussion

In the present Interventional study, we found a significant increase in serum magnesium concentration in obese individuals after vitamin D supplementation ($p<0.05$). There was no significant difference in serum Magnesium concentration in non obese individuals before and after intervention. Baseline concentration of serum magnesium in obese subjects was significantly lower than non obese subjects ($p = 0.005$). Some of other previously published studies have also reported lower serum Magnesium concentration in obese individuals.[7,11]

Some of the factors that can cause low serum magnesium in obesity, are lower dietary intake of Magnesium,[7] reduced Magnesium intestinal absorption because of high fat or calcium intake,[20] and high inflammatory factors in obesity.[21]

The effect of vitamin D on serum Magnesium is controversial. Some of studies reported increasing in serum Magnesium concentration in response to vitamin D supplementation. Schmulen et al[22] found that vitamin D increases intestinal absorption of Magnesium in normal human subjects and in patients with chronic renal failure.

On the other hand, Wilz et al[16] could not find any relationship between plasma 1,25 (OH)2vitamin D concentration and net intestinal Magnesium absorption. Wiltz et al[16] also found that Magnesium is absorbed by persons with no detectable plasma 1,25 (OH)2 vitamin D and in contrast to calcium absorption, no significant correlation exists between plasma 1,25 (OH)2 vitamin D and Magnesium absorption.

In addition to intestinal Magnesium absorption renal excretion is also another important key in regulating Magnesium homeostasis. The kidney is the critical organ regulating serum magnesium concentration. The 1,25 (OH)2 D- dependent calcium binding proteins, Calbindin -D 9K and Calbindin -D 28K in the kidney, are localized in the distal tubule where a significant portion of calcium and Magnesium is reabsorbed[23] Calbindin -D 9K has a relatively high affinity for Magnesium[24] suggesting a role for these binding proteins in renal Magnesium control. Dai LJ et al[25] in their study demonstrated that 1,25 (OH)2 vitamin D increases magnesium entry rates in distal tubule cells and the response is concentration dependent. This means that the higher Magnesium reaches to distal tubule, the higher is renal Magnesium excretion.

In our study increase in serum Magnesium concentration in response to vitamin D supplementation in obese women, but not in non obese women, can also be explained by this mechanism. Lower baseline concentration of serum Magnesium in obese subjects can induce higher renal Magnesium retention after vitamin D supplementation.