

Oral Vitamin D versus Injectable Vitamin D in Treating Obese Women with Vitamin D Deficiency

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ABSTRACT

Background: Vitamin D deficiency is a widespread problem especially in females. The presence of different vitamin D preparations (oral, parenteral) with no definite evidence about the most appropriate method for vitamin D deficiency treatment aroused the need for more studies about the most effective route. **Aim:** To evaluate the oral vitamin D preparation compared to intramuscular (IM) vitamin D preparation in correcting vitamin D deficiency in affected women. **Subjects and methods:** This is an interventional research performed on obese female patients diagnosed with vitamin D deficiency in the 2019–2022 timeframe for outpatient clinics at Zagazig University Hospitals. Eighty females were included in the study. They were allocated randomly into 2 equal groups (40 females per group); oral group and injection groups, based on their preference. Pre and post intervention assessment was done by assessing the level of serum vitamin D.

Results: There was statistically insignificant difference among studied groups concerning vitamin D level before therapy, while there was significant difference between them after therapy, where oral group had significantly higher level. Within each group, there was significant increase in vitamin D level after therapy. There was statistically significant positive correlation between percent of increase in vitamin D and both age and body mass index (BMI) of patients in the oral group, but no significant correlation was detected in injectable group between age and percent of change.

Conclusion: Treatment for vitamin D insufficiency works well when administered intramuscularly and orally but oral group showed more improvement.

Keywords: Vitamin D deficiency, Oral preparations, Injectable preparations.

INTRODUCTION

Vitamin D is a lipophilic vitamin essential for bone mineralization process. The most important factor as a primary contributor to vitamin D formation is sunlight exposure ⁽¹⁾.

Vitamin D deficiency is a widespread problem that affects many people around the world. Vitamin D deficiency represents a common problem for Egyptian people. This problem is commonly detected in people who are not exposed to adequate sun exposure and those with sedentary kind of life, unhealthy eating patterns and inadequate calcium consumption in their diets ⁽²⁾. In addition, there are many risk factors for vitamin D deficiency such as variances in the seasons, aging, increase weight, dark skin pigmentation and morbidities of malabsorption ^(3,4).

For all-cause mortality, vitamin D deficiency and insufficiency are frequently risk factors. Most evidence indicates that they are connected to conditions affecting other organ systems, muscle health, and bones ⁽⁵⁾.

Many cross-sectional studies have illustrated that low serum 25(OH) D levels are inversely correlated with obesity. Most parameters of obesity specially (BMI) are assumed to be inversely correlated with plasma 25(OH) D and 1,25(OH)₂D levels. A previous study stated that obese people had lower levels of plasma 25(OH)D and 1,25(OH)₂D than people with normal weight ⁽⁶⁾.

The Endocrine Society advises treating all vitamin D deficient adult populations with 50,000 IU of vitamin D3 once a week for two months in order to boost the level of vitamin D above (30 ng/mL). A maintenance therapy of 1500–2000 IU/d should be given after this treatment ⁽⁷⁾. There are various vitamin D preparations; oral and injectable. There is no sufficient evidence about the effectiveness of one of them over the other type. This debate aroused the need for more studies about the most effective route especially in obese women. This intervention study was conducted to evaluate the outcomes of oral vitamin D preparation versus intramuscular (IM) vitamin D preparations in correcting vitamin D deficiency in affected obese women.

SUBJECTS AND METHODS

- **Study design:** Interventional study
- **Study Setting:** The investigation was carried out in 2021 at outpatient clinics of Zagazig University Hospitals.
- **Population:** Women visiting the outpatient clinics of the University Hospitals in Zagazig.

Inclusion criteria:

Adult females in childbearing period (18-50 years old) with a body mass index greater than 30 kg/m² and a serum 25 OH D level less than 10 ng/ml.

Exclusion criteria: Women who were pregnant or nursing were not included in the study since their dietary demands were different.

Sample:

- **Sample size:** 80 participants (40 per group) with a 95% confidence level, and an 80% test power based on the study of **Tellioglu et al.** (8).
- **Sample technique:** Systematic random sample technique was used.
- **Duration:** Three months.

Operational design:

✓ **Study design:**

Females included in this study (80 females) were allocated randomly into 2 equal groups (40 females per group); oral group and parenteral group, based on whether they will receive oral vitamin D or injectable vitamin D preparations. Each female in both groups was interviewed at the beginning of the research.

First session: We illustrated the study goal for the participants. Sociodemographic data were collected, and a blood sample was obtained for measuring serum 25-hydroxyvitaminD [25(OH)D] concentration level at baseline.

Then the participants were divided into two groups: oral and parenteral.

Oral cholecalciferol 50,000 IU was given as part of the oral treatment once a week for one month and then once a month for two months. For three months, the parenteral group received monthly injections of 200 000 IU of vitamin D.

Follow up: The participants were followed every 2 weeks to motivate them and monitor their compliance to treatment and give them the medication of the next 2 weeks.

Final visit: For determining the blood 25-hydroxyvitamin D concentration [25(OH)D], 3 months after the start of treatment.

✓ **Administrative design and Ethical issues:**

The study protocol was approved by the Institutional Review Board (IRB) of the Department of Medicine at Zagazig University. Confidentiality was upheld, as well as ethical issues. All study participants gave their informed consent before participating after being fully informed. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The analysis was conducted using SPSS 26.0. Normally distributed quantitative data were presented as mean and standard deviation (SD) and independent t-test was used to compare them between the 2 groups and paired t-test was

used to compare between before and after treatment in the same group. Non-normally distributed quantitative data were presented as median and interquartile range (IQR) and were compared by Mann-Whitney U test. Qualitative data were presented as frequency and percentage and were compared by the chi-square test. Person correlation was used to correlate vitamin D level with both age and BMI. P-values were considered statistically significant if they were less than 0.05.

RESULTS

Table (1) illustrates that there were statistically insignificant differences among studied groups in terms of age, BMI, residence and social class ensuring matching of the studied groups.

Table (1) Comparison between the studied groups regarding demographic data:

Parameter	Oral group N=40(%)	Parenteral group N=40(%)	P
Age (year): Mean ±SD	36.6 ± 8.01	33.38 ± 8.2	0.079
Residence:			
Rural	4 (10%)	6 (15%)	0.628
Semiurban	28 (70%)	24 (60%)	
Urban	8 (20%)	10 (25%)	
BMI (kg/m²): Mean ±SD	33.39 ± 1.65	33.28 ± 2.02	0.781
Social class:			
Low	11 (27.5%)	6 (15%)	0.172
Middle	29 (72.5%)	34 (85%)	

BMI: body mass index

There was statistically insignificant difference among studied groups in terms of vitamin D level before therapy while there was significant difference between them after therapy where oral group had significantly higher level. Within each group, there was significant increase in vitamin D level after therapy (Table 2).

Table (2) Comparison between the studied groups regarding vitamin D before and after therapy

Parameter	Oral group N= 40	Parenteral group (N= 40)	P value
Before	8.44 ± 2.08	8.35 ± 2.16	0.785
After	26.65 ± 1.54	21.02 ± 1.49	<0.001**
P	<0.001**	<0.001**	-----

** : Highly significant

Regarding percent of increase in level of vitamin D, median increase in oral group was significantly higher than within IM group (209.44%, IQR from 185.01 to 275.07% versus 148.38%, IQR; 120.8 to 210.57% respectively) (Figure 1).

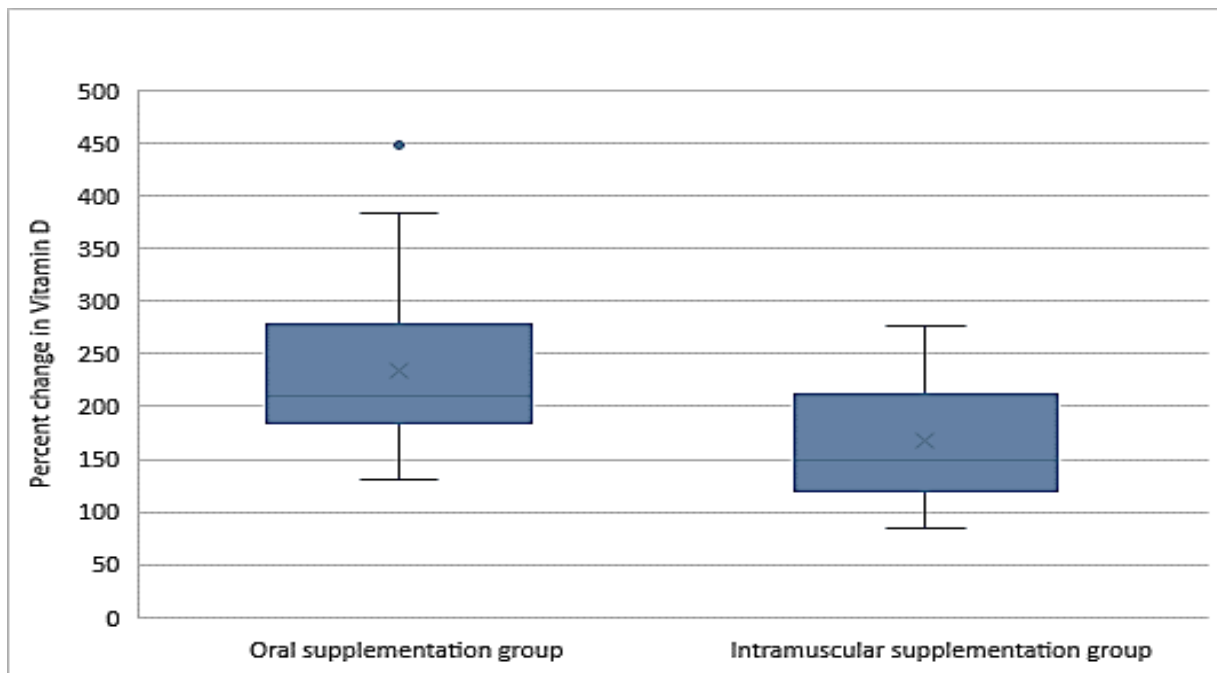


Figure (1): Boxplot showing comparison between groups regarding percent increase in vitamin D (p<0.001).

There was significant difference between both groups regarding the frequency of patients who achieved higher level of vitamin D, as in oral group all the patients achieved higher level compared to 75% only in the parenteral group (Table 3).

Table (3) Comparison between the studied groups regarding vitamin D status after treatment

Vitamin D level After intervention		Oral group	Parenteral group	P-value
<20 ng/ml	N	0	10	<0.001*
	%	0.0%	25.0%	
≥20 ng/ml	N	40	30	
	%	100.0%	75.0%	

There was a strong positive relationship between the percentage increase in vitamin D after therapy and age and BMI in oral group and significant positive correlation between percent increase in vitamin D after therapy and BMI in parenteral group (Table 4).

Table (4) Correlation between percent increase in vitamin D after therapy and age and BMI:

Parameter	Oral group		Parenteral group	
	r	P	r	p
Age (year)	0.318	0.04*	0.09	0.579
BMI	0.322	0.03*	0.349	0.027*

Person correlation *: Significant.

DISCUSSION

Obesity is frequently associated with vitamin D insufficiency risk and this may be explained by lower absorption of circulating 25-hydroxyvitamin D (25OHD). Low vitamin D level may also encourage adipogenesis, which could lead to further increases in adiposity⁽⁹⁾.

In this study, effectiveness of different routes for supplementing vitamin D for obese patients with vitamin D deficiency was evaluated. Within each group (the group which received oral vitamin D supplements, and the group which received IM supplements) there was highly statistically significant improvement in vitamin D levels after treatment in both groups when compared with its level before treatment.

This outcome is consistent with several studies that evaluated vitamin D levels before and after oral or intramuscular vitamin D supplementation. **Wylon et al.**⁽¹⁰⁾ stated that in contrast to the group under control, the mean 25(OH)D blood levels rose considerably following oral cholecalciferol ingestion. The mean 25(OH)D blood concentration peaked in those receiving 100,000 IU of cholecalciferol intramuscular at 28 ng/ml after 4 weeks, as opposed to 13.08 ng/ml in the placebo group.

According to research by **Brar et al.**⁽¹¹⁾ in 20 obese patients with vitamin D insufficiency, oral vitamin D therapy dramatically raised 25OHD levels.

In this research among the groups under study, there was a statistically significant difference when comparing vitamin D after treatment results with highest values in oral treatment group with all the cases in the oral group achieved a level more than 20 versus 75% in the parenteral group. These results were compatible with **Tellioglu et al.**⁽⁸⁾ who stated that IM group mean serum 25(OH)D levels significantly rose at the sixth week (32.72 9.0 ng/ml) compared to baseline (11.76 7.6 ng/ml) following vitamin D therapy. The values in the oral group were 47.57 12.7 and 14.87 6.9 ng/ml, respectively. In comparison to the IM group, there was a noticeable increase in the oral group by the sixth week. However, it went up in the IM group in the twelfth week. However,

because the kinetics of a single oral and intramuscular dose of VD3 (600,000 IU) were compared in this study, the longer the follow-up period, the better the results were for the IM group. Similarly, **Shahrivari et al.** ⁽¹²⁾ reported that after treatment, oral method's vitamin D level was higher than injectable method's. Additionally, oral treatment had a stronger impact on the serum 25(OH) D3 level in obese people.

Moreover, **Zabihyeganeh et al.** ⁽¹³⁾ found that serum 25 (OH) D levels were equivalent at the end of the 6-month intervention but were noticeably higher in the oral group than the injection group at month 3.

Gupta et al. ⁽¹⁴⁾ found that the difference between the oral and injection groups' mean serum 25OHD levels at baseline was not statistically significant. The oral cholecalciferol group's serum 25OHD level rose at 6 weeks before declining at 12 weeks. At 12 weeks, the oral cholecalciferol group had greater mean serum 25OHD levels than the IM group.

When **Rahafard et al.** ⁽¹⁵⁾ compared between the two groups, they found that the oral therapy group had somewhat greater vitamin D levels at weeks 3 and 4 following treatment, and a statistically significant difference was identified between the two groups.

Romagnoli et al. ⁽¹⁶⁾ investigation involved 32 senior ladies who had taken 300,000 IU of VD2 and VD3 via PO and IM methods. In response to the oral administration of VD3, levels of 25-OHD increased as early as day 3 and persisted until day 30, at which point they began to fall. The levels increased steadily with IM dosage and weren't sufficient for VD3 until day 60.

Kearns et al. ⁽¹⁷⁾ carefully examined 30 papers and discovered that peak levels are reached with oral bolus dosage in 7 to 30 days. These findings might also imply that maintenance doses of oral vitamin D, given after the first boost in vitamin D brought on by the oral route, are a better way to maintain this elevation.

On the other hand, **Mondal et al.** ⁽¹⁸⁾ stated that vitamin D oral dose and 600000 IU intramuscular single dose effects were compared in the study. The results of the investigation showed that there was no appreciable difference in the two regimens' efficacy based on the biochemical and radiological markers.

CONCLUSION

It can be concluded that treatment for vitamin D insufficiency works well when administered intramuscularly and orally but oral group showed more improvement.

- **No conflict of interest between authors.**
- **Funding:** Nil.

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