Klinik Araştırma

Effects of Vitamin D Supplementation on Cardiac Functions

Vitamin D Takviyesinin Kardiyak Fonksiyonlar Üzerine Etkileri

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ABSTRACT

Background and Objectives: *In this study we aimed to investigate the effects of vitamin D supplementation on cardiac functions in stage III-IV systolic heart failure patients with concomitant vitamin D deficiency.*

Patients and Methods: *This prospective study was carried out in 33 stage III or IV systolic heart failure patients (13 women, mean of 66.82 ± 10, 41 years, ranging from 35 to 86) with vitamin D deficiency. Serum 25-hydroxyvitamin D levels less than 20 ng/mL were accepted as vitamin D deficiency. All patients' left ventricular ejection fraction, interventricular septum and posterior wall thickness at baseline and after vitamin D supplementation were measured with Area-Length method. In addition, all patients' serum albumin, calcium, phosphorus and parathyroid hormone levels were determined at baseline and after the treatment. Serum 25 (OH) D levels were measured with by chromatographic method. All patients were treated with vitamin D (in the first 8 weeks, 50000IU/week of Ergocalciferol, in the remaining 6 weeks 14000IU/day Cholecalciferol and 1000mg/day Calcium) and followed for 14 weeks, while their routine medical therapy was not changed during the follow-up period.*

Results: *The mean levels of serum calcium and albumin were increased significantly after the treatment (9.17±0.67 vs. 9.45 ± 0.42 mg/dL, p=0.017, 3.96 ± 0.45 vs. 4.06 ± 0.35 g/dL, p=0.035, respectively). Serum parathyroid hormone levels were decreased significantly (81.28 ± 71.27 vs 52.26 ± 19.12 pg/mL, p=0.003), while ejection fraction was increased significantly (36.3 ± 6.52 vs. 38.55 ± 6.06 %, p<0.001) after the treatment.*

Conclusion: *Vitamin D supplementation in patients with advanced systolic heart failure can lead to improvement of systolic function via its effects on parathyroid hormone, calcium and phosphorus.*

Keywords: *Heart failure, vitamin D supplementation, ejection fraction.*

ÖZET

Amaç: *Bu çalışmada eşzamanlı vitamin D eksikliği olan evre III-IV sistolik kalp yetmezliği hastalarında vitamin D takviyesinin kardiyak fonksiyonlar üzerine etkisi araştırıldı.*

Metod: *Bu prospektif çalışmaya vitamin D eksikliği olan 33 evre III-IV sistolik kalp yetmezliği hastası (13 kadın, ortalama yaş 66,82 ± 10, 41 yıl, 35-86 yaş aralığı 35-86) alındı. Serum 25-hidroksivitamin D seviyeleri < 20 ng/mL ise vitamin D eksikliği olarak kabul edildi. Tedavi öncesi ve sonrasında tüm hastaların sol ventrikül ejeksiyon fraksiyonu, interventriküler septum ve arka duvar kalınlığı Area-Length metodu ile ölçüldü. Ek olarak tüm hastaların tedavi öncesi ve sonrası serum albumin, kalsiyum, fosfor ve paratiroid hormon seviyeleri ölçüldü. Serum 25 (OH) D seviyeleri kromatografik metot ile ölçüldü. Tüm hastalar vitamin D ile tedavi edildi (ilk 8 hafta 50000 IU/hafta Ergocalciferol, kalan 6 haftada 14000 IU/gün Cholecalciferol ve 1000 mg/gün kalsiyum) ve 14 hafta takip edildi. Hastaların rutin medikal tedavileri takip periyodunda değiştirilmedi.*

Sonuçlar: *Tedaviden sonra ortalama serum kalsiyum ve albumin seviyeleri önemli olarak yükseldi (sırasıyla 9,17 ± 0,67 ve 9,45 ± 0,42 mg/dL, p=0,017, 3,96 ± 0,45 ve 4,06 ± 0,35 g/dL, p=0,035). Tedaviden sonra sol ventrikül ejeksiyon fraksiyonu önemli olarak artarken (% 36,3 ± 6,52 ve 38,55 ± 6,06, p<0,001) serum paratiroid hormon seviyeleri önemli olarak azaldı (81,28 ± 71,27 ve 52,26 ± 19,12 pg/mL, p=0,003).*

Sonuç: *İleri sistolik kalp yetmezliği olan hastalarda vitamin D takviyesi paratiroid hormon, kalsiyum ve fosfor üzerine etkileri yoluyla sistolik fonksiyonda düzelmeye yol açabilir.*

Anahtar Kelimeler: *Kalp yetmezliği, vitamin D takviyesi, ejeksiyon fraksiyonu*

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INTRODUCTION

Vitamin D deficiency or insufficiency is a common health problem worldwide. In numerous epidemiological and observational studies low vitamin D levels have been linked to cardiovascular diseases, serum lipid disorders, inflammation, glucose metabolism disorders, weight gain, infectious diseases, multiple sclerosis, mood disorders, declining cognitive function, impaired physical functioning, and all-cause mortality (1-4). Although the underlying mechanism is not clear, hyperparathyroidism secondary to vitamin D deficiency, low serum calcium and phosphorous levels or vitamin D deficiency itself may play a role in this relationship. Intracellular calcium has a central role in systolic and diastolic cardiac functions. Phosphorous is also an essential element for ATP and energy production. Hyperparathyroidism secondary to vitamin D deficiency increases insulin resistance which is associated with diabetes, hypertension, inflammation and increased cardiovascular risk (5-7). Vitamin D deficiency itself leads to activation of renin-angiotensin-aldosterone system, systemic arterial hypertension and left ventricular hypertrophy (8).

In numerous studies vitamin D has been shown to be significantly linked to mortality, and is thought to be a predictor of survival (9-11). However, the results of interventional studies with vitamin D supplementation for prevention or improvement of worst prognosis is still inconclusive. In this prospective study we investigated the effect of vitamin D supplementation on cardiac functions in patients with stage III-IV cardiac failure and vitamin D deficiency.

METHODS

This prospective study was carried out in 33 patients (13 women, mean age of 66. 82 ± 10. 41 years, ranging from 35-86 years) who have advanced cardiac failure (stage III-IV) and vitamin D deficiency. Within previous six month acute coronary syndrome or percutaneous coronary angioplasty, existence of known malignancy, chronic renal failure, primary or tertiary hyperparathyroidism, granulomatous disease or using of drugs effecting vitamin D metabolism were exclusion criteria. Experimental protocol of this study was approved by local human ethics committee and informed consent was obtained from each subject. Serum vitamin 25 (OH) D values less than 20 ng/mL were accepted as vitamin D deficiency. All patients' left ventricular systolic and diastolic diameter, interventricular septum and posterior wall thickness were measured using transthorasic echocardiography by Area-Length method. These measurements were evaluated according to American Echocardiography Society guidelines by GE Vivid 4 Expert Machine. In addition, all patients' serum albumin, calcium, phosphorous and parathyroid hormone levels were determined. Serum 25 (OH) D levels were measured with Shimadzu LC 20AD/T machine (Kyoto, Japan) by chromatographic method. All patients were treated with vitamin D (in the first 8 weeks, 50000IU/week of Ergocalciferol, in the remaining 6 weeks 14000IU/day Cholecalciferol and 1000mg/day Calcium) and followed for 14 weeks, while they underwent the current cardiac treatment. All measurements were repeated at the end of 14 weeks. Statistical analysis was conducted using Number Cruncher Statistical System 2007&PASS and 2008 Statistical Software programs. Distribution of parameters was tested by Kolmogorov Smirnov. Comparisons between pre- and post-treatment levels of the parameters were made using paired T test. Ninetyfive percent confidence intervals are reported. Alpha was set at 0.05.

RESULTS

The mean levels of serum calcium and albumin were increased significantly after the vitamin D treatment (9.17 ± 0.67 vs. 9.45 ± 0.42 mg/dL, p=0.017, 3.96 ± 0.45 vs. 4.06 ± 0.35 g/dL, p=0.035, respectively). Serum parathyroid hormone levels were decreased significantly (81.28 ± 71.27 vs 52.26 ± 19.12 pg/mL, p=0.003), while left ventricular ejection fraction was increased significantly (36.3±6.52 vs. 38.55±6.06 %, p<0.001) after the vitamin D treatment (Table 1).

Weight change, mortality and hospitalization requirement did not occur during the 14 weeks of follow up.

DISCUSSION

The results of this study show beneficial effect of vitamin D supplementation on left ventricular ejection fraction in patients with stage III-IV systolic heart failure. The increase of left ventricular ejection fraction with vitamin D supplementation is associated with improvement of biochemical results of vitamin D deficiency. Vitamin D receptor exists in almost

every human cell. Therefore, it is not surprising that vitamin D has a broader role overall and cardiovascular health. Numerous experimental animal and cell culture studies showed that vitamin D receptor activation has a central role of prevention arterial hypertension, myocardial hypertrophy, foam cell formation from macrophage, expression of endothelial adhesion molecules and smooth muscle cell proliferation (12-15). Most of observational studies found that vitamin D deficiency was associated with an adverse cardiovascular risk profile such as obesity, arterial hypertension, diabetes mellitus, hyperlipidemia, parathyroid hormone, and inflammation (16-20).

Vitamin D deficiency is frequently reported in patients with heart failure (21, 22). The results of a few intervention studies evaluated the effect of vitamin D supplementation on myocardial function are inconclusive. Vitamin D supplementation with doses using for osteoporosis treatment is neither proven to be beneficial nor harmful in cardiovascular diseases (10). Review of 8 randomized studies by Wanget et al concluded that vitamin D supplements at moderate to high doses may reduce CVD risk, whereas calcium supplements seem to have minimal cardiovascular effects (23). In a randomized controlled trial in patients on chronic dialysis Mose et al reported that six months of cholecalciferol treatment did not improve 24-h blood pressure, arterial stiffness or cardiac function (24). Effects of vitamin D supplementation in high risk elderly patients presenting with acute coronary syndrome also warrants further investigation (25).

At present, it is largely unclear whether vitamin D supplementation can significantly improve cardiovascular outcomes. The results of present study show that vitamin D supplementation contributes to improvement of systolic function in patients with vitamin D-deficient advanced stage systolic heart failure. Improvement seen systolic function with vitamin D supplementation is associated with increased serum calcium and decreased serum parathyroid hormone levels. Our study has some limitations such as the small number of cases and the absence of a control group.

CONCLUSION

The results of this study show that vitamin D supplementation in patients with vitamin D-deficient stage III or IV systolic heart failure leads to increase in left ventricular ejection fraction. Further large-scale randomized controlled studies are required to see long-term mortality outcomes of improvement in left ventricular ejection fraction.

Table 1: Results of pre-and post-treatment parameters.

Parameter	Pre-treatment	Post-treatment	P
Serum albumin (g/dL)	3.96 ± 0.45	4.06 ± 0.35	0.035
Calcium (mg/dL)	9.17 ± 0.67	9.45 ± 0.42	0.017
Parathyroid hormone (pg/mL)	81.28 ± 71.27	52.26 ± 19.12	0.003
Phosphorus (mg/dL)	3.34 ± 0.65	3.39 ± 0.56	0.633
Ejection fraction (%)	36.3 ± 6.52	38.55 ± 6.06	<0.001

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