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ORIGINAL ARTICLE

Effect of Vitamin D on Arterial Stiffness in People with Type 2 Diabetes and Intermediate Chronic Kidney Disease

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ABSTRACT

Background: The aim of this study was to investigate the effect of vitamin D therapy on arterial stiffness on diabetic type 2 with intermediate chronic kidney diseases patients**.**

Study design: This was a cross sectional study conducted at Sialkot Medical College, Sialkot for six months from September 2022 to February 2023.

Methods: There were 160 participants in total included both male and female gender. The age range was 40-75 years, but majority participants included male 90%. The pulse wave velocity (PWV), 2000 wave unit was measured the arterial stiffness. In an approved laboratory, biochemical parameters such vitamin D, FGF-23, iPTH were assessed by enzyme linked immunoassay, and chemiluminescence immunoassay.

Results: A total of 160 participants who were randomly assigned to receive either a placebo (n = 60) or vitamin D (n = 100) were qualified for analysis. The eGFR, serum calcium, phosphate, HbA1c, total cholesterol level, and albumin excretion in both groups did not change significantly throughout therapy; p>0.005. Vitamin D deficiency was significantly increase, p <0.001** in participants, then increased aortic-PWV in the vitamin D therapy group compared to the placebo group. Ao-PWV did not change significantly at the end of the treatment, P>0.005. There is no significant impact of vitamin D on arterial stiffness.

Conclusion: In T2DM with moderate CDK, the aortic-PWV, augmentation index, and pressure measurements of arterial stiffness were all substantially higher in the vitamin D deficient group compared to the vitamin D sufficient group.

Keywords: Chronic kidney disorder, Diabetes type 2, Pulse wave velocity, Aortic.

INTRODUCTION

Deficits in vitamin D are cyclically made worse in the winter and spring because of the reduced amount of outdoor exercise.[1] Obesity is a key risk factor for vitamin D insufficiency, in along with having a greater body mass index waist measurement, overall fat mass, and % of total mass. People with type 2 diabetes are approximately twice as probable as those without the disease to be vitamin D inadequate.[2, 3] The measurement of arterial stiffness using pulse wave velocity (PWV) is quick, painless, and scientifically proven. The arterial stiffness was found while determining the central aortic augmentation index by quantifying the aortic augmented pressure as a small percentage of the pulse rate. The separation between PWV and AI, however, might have a wide range of probable explanations. Height, diabetes, obesity, and sex are among variables that significantly impact (augmentation index) AI. [4, 5] Approximately 30–50% of the general population suffers from vitamin D insufficiency, which is fairly frequent and linked to the breakdown of endothelial cells has increased of the blood arteries, patients with severe renal diseases, which on dialysis according to recent clinical evidence. 6 The finding is sensitive to being interpreted incorrectly, though, because healthy persons are less likely to experience a vitamin D shortage and may spend more time outside and receive skin-to-sun contact. Vitamin D therapy had used for heart vessels protection to individuals with vitamin D insufficiency since vitamin D has anti-atherosclerotic properties.[7, 8] A well-established independent predictor of incident hypertension, cardiovascular disease, and overall mortality is arterial stiffness. It is a sign of atherosclerotic disease and is connected to increased calcification and decreased bone mineral density. The impact of subclinical inflammation on the process of stiffening in hypertension patients generally, and in high-risk hypertensive patients who have CKD in particular, is receiving more attention. The increase of Ao-PWV in patients with renal diseases is a risk factor for fatalities, and connected to an impairment in renal function. There is conflicting information regarding how active vitamin D medication affects vascular indices and cardio-renal biomarkers in patients with and without CKD. [9, 10] Arterial stiffness and vitamin D insufficiency in type 2 diabetes could be connected through insulin resistance. Due to both conventional risk factors including diabetes mellitus and hypertension as well as CKD-specific risk factors, patients with chronic kidney disease have an elevated risk of unfavorable long-term outcomes that are mostly linked to cardiovascular diseases (CVDs). [11]

We investigated the effect of vitamin D therapy on arterial stiffness in vitamin D deficient people with type 2 diabetes and intermediate chronic renal impairment.

METHODOLOGY

This was a cross sectional study conducted at Sialkot Medical College, Sialkot for six months from September 2022 to February 2023. A total number of the participants n= 160 were randomized to placebo (n=60) and Vitamin D (n=100). Inclusion criteria: at the screening visit, the following values were normal: corrected serum calcium, normal phosphate, and iPTH between 30-200, pg/mL. Exclusion criteria: included cardiovascular, non-diabetic, obstructive renal disease, an iPTH≥ 200 pg/mL, and arterial vasculature. Changes from baseline were seen in the Ao-PWV, augmentation index, brachial and central systolic and diastolic blood pressure, estimated GFR, and serum calcium and phosphate levels after six months of vitamin D treatment as comparison to a placebo. The biochemical parameters such active and inactive vitamin D level, FGF-23 were assessed by enzyme linked immunoassay, and iPTH by chemiluminescence immunoassay. Data were gathered, put into SPSS version 21 for descriptive statistical analysis, and percentages and frequencies were calculated.

RESULTS

A total of 160 participants who were randomly assigned to receive either a placebo (n = 60) or vitamin D (n = 100) were qualified for analysis. The assessments of changes included all subjects who met the criteria for the aortic pulse wave velocity studies. Both groups shared similar demographic characteristics, clinical traits, and drug usage at baseline.

Table 1: Baseline Demographic variables

Variables	Total number of participants N=160(%)	
	Vitamin D group n=100(%)	Placebo group n=60(%)
Age	48-74 years	53-75 years
Gender (M)	90(90%)	54(91%)
(F)	10(10%)	10(17%)
Smoking status YES	5(5%)	3(5%)
NO	95(95%)	57(96%)
Alcohol consumption YES	8(8%)	6(10%)
NO	92(92%)	54(90%)
BMI kg/m2	35.2(5.1)	35.7(6)
Augmentation index%	35(11)	36(12)
SBP mmHg	146.5(22.5)	143.6(20)
DBP mmHg	79.5(14)	73.1(11)
MAP mmHg	103(15)	98(12)
PP mmHg	72.5(21)	71.8(19)
Ao-PWV, m/s	12.4(2.6)	10.4(2.3)
Medications		
RAS inhibitors	75(75%)	43(72%)
SGLT-2 inhibitors	10(10%)	6(11%)
GLP-1 inhibitors	15(15%)	10(17%)

Mean ± SEM: ANOVA SPS 21 Test* p< 0.0; **p<0.0; ***p<0.00:

There were 160 participants in all, split into two groups that received vitamin D treatment and placebo treatment. Males were more prevalent than females in the age group of 40 to 75 years. Overall, 95% and 96% of the participants were non-smokers and 10% were smokers in both group. 92% and 90% of individuals in each group, respectively, did not consume alcohol. Diabetes was present on average for 20.5 years. RAS inhibitors were frequently used, and 75% of individuals were receiving therapy. The SGLT-2 inhibitors were utilized by the 10% and 11% of individuals, whereas the GLP-1 inhibitors were used by the 15% and 17% of people. The usage of anti-diabetic and anti-lipid drugs did not differ significantly across groups.

Table 2: Estimation of Biochemical parameters from baseline between two groups

	Vitamin D group	Placebo control group	P=value
e-GFR ml/min	45.3(11.5)	44.6(10.1)	0.883
1, 25 (OH)2D, pmol/L*	25.5(16.5 to 30.1)	24.1(20.2 to 31.5)	<0.001**
25(OH)D, nmol/L*	44.2(31.2 to 54)	40.8(31.5 to 53.1)	<0.001**
iPTH, pg/mL*	75.5(55 to 110)	69.2(53 to 95)	
Serum Calcium, mmol/L*	3.35(0.3)	2.93(0.3)	0.987
FGF-23	79.5(61 to 92)	73.2(58 to 63)	0.622
Serum Phosphate, mmol/L*	1.22(0.15)	1.25(0.17)	0.555
Heamoglobin, g/L	9.4(l.4)	7.7(1.2)	0.008
Serum Albumin, g/L	45.2(3.6)	45.7(3.6)	0.009
Total cholesterol mmol/L	5.2(1.6)	5.1(1.1)	0.008
LDL mmol/L	1.5(0.3)	1.9(0.5)	0.699
HDL mmol/L	1.6(0.4)	1.4(0.2)	0.008
Urinary albumin excretion	58.3(11 to 140)	25(10 to 225)	0.006

Mean ± SEM: ANOVA SPS 21 Test* p< 0.0; **p<0.0; ***p<0.00:

The eGFR, serum calcium, phosphate, HbA1c, total cholesterol level, and albumin excretion in both groups did not change significantly throughout therapy; p>0.005. But it should be emphasised that throughout therapy, both groups' levels of 1,25(OH-vitD) and 25(OH-vitD) significantly decreased; p<0.005**.

Table 3: Effect of Vitamin D on arterial stiffness at baseline and 6 months of End- treatment with placebo or vitamin D treatment.

Parameters	Vitamin D (n=100) Man difference between baseline and last visit (CI=95%)	P=value % difference between group	Placebo (n=60) Man difference between baseline and last visit (CI=95%)	P=value % difference between group	Between treatment group adjust differences (CI=95%)	P=value % difference between group
Ao-PWV, m/s	0.27(0.26, 0.78)	=0.221	0.55(-0.03, 2.5)	=0.332	0.25(-0.35, 3.03)	=0.321
Augmentation index %	-2.0(-3.1, 1.1)	=0.883	-0.5(-2.1, -1.5)	=0.787	- 0.01(-2.5, 2.1)	=0.882
Central aortic blood pressure	-1.0(-2.0, 0.1)	=0.69	-0.5(-2.2, 0.4)	=0.55	-0.04(-3.09, 2.29)	=0.522
eGFR	-4.4(-5.4, -2.9)	=0.009	-1.4(-2.4, -0.5)	=0.446	-1.33(-4.12, 0.23)	=0.077
iPTH, pg/mL*	-19.1(-21.5,-16.3)	<0.001**	13.5(10.5, 13.2)	<0.001**	-30.4(-15.2, -46.5)	<0.001**
Serum Calcium, mmol/L*	0.01(-0.3, 0.12)	=0.112	0.05(-0.02, 0.10)	=0.233	0.01(-0.02, 0.01)	=0.432
Serum Phosphate, mmol/L*	0.10 (0.15, 0.11),	=0.761	-0.21(-0.11, 0.13)	=0.543	0.01(-0.02, 0.03)	=0.333
FGF-23	42.5(39.9, 44.3)	<0.001**	7(5.5, 8.9)	<0.005	31.2(15.5, 45.5)	<0.001**
Urine Albumin excretion rate	0.1(-0.02, 0.4)	=0.881	0.3(-0.1, 0.3)	=0.121	-0.4(-0.78, 0.2)	=0.432
HbA1c	0.03(-0.23, 0.45)	=0.333	0.40(0.05, 0.34)	=0.323	-0.2(-0.61,0.33)	=0.330

Mean ± SEM: ANOVA SPS 21 Test* p< 0.0; **p<0.0; ***p<0.00:

The baseline and the end of treatment values for Ao-PWV in the vitamin D treatment and placebo treatment groups. Vitamin D therapy for 24 weeks resulted in no significant improvement in Ao-PWV, 0.27(0.26, 0.78), p>0.221 as compared to placebo, 0.55(-0.03, 2.5), p>0.332. Ao-PWV mean adjusted difference between vitamin D treatment group and placebo group was 0.25(-0.35, 3.03) m/s, P=0.321 (CI=95). There is no significant impact of vitamin D on arterial stiffness, including central aortic blood pressures. Serum calcium or phosphate levels did not change significantly between treatment groups (P>0.005). Overall, vitamin D was well tolerated, and there were no significant side events due to hypocalcaemia that were treatment-associated.

DISCUSSION

Vitamin D is crucial for cellular differentiation stimulation and angiogenesis inhibition, in addition to calcium homeostasis and the prevention of bone disease. Additionally, vitamin D inhibits the renin-angiotensin-aldosterone pathway and has vasculoprotective and reno protective effects, among other antihypertensive properties.[12, 13] Vitamin D effects may change the likelihood of developing cardiac metabolic consequences such T2DM, blood pressure and CVD.[14, 15] In previous study to show that AoPWV did not significantly alter with a daily vitamin D intake of 0.25 mcg following treatment, indicating that increased vascular calcification was unlikely at this level. In our study of T2DM with intermediate kidney diseases did not show significant effect on lower level of calcium and phosphate.[16] Vitamin D therapy for 24 weeks resulted in no appreciable improvement in Ao-PWV, 0.27(0.26, 0.78), p>0.221 compared to placebo, 0.55(-0.03, 2.5), p>0.332. Ao-PWV mean adjusted difference (CI=95) between vitamin D treatment group and placebo group was 0.25(-0.35, 3.03) m/s, P=0.321. There is no significant impact of vitamin D on arterial stiffness, including central aortic blood pressures. These findings do not support the claim that vitamin D can reduce arterial stiffness, which would ostensibly benefit the heart and kidneys in diabetics. We were agreed with the previous study. [17, 18] In previous study, in patients with SHPT, VDI, and stage 3 or 4 CKD, ERC was very successful in increasing serum 25OHD and lowering iPTH. While rates with IRC or HDC were much lower, iPTH-lowering response rates with ERC were comparable to daily PLDC, the reference treatment. In CKD patients, ERC is a desirable option to vitamin D hormone treatment.[19] In our study to found that, the iPTH levels

with vitamin D administration was reduced from baseline, median range of -19.1(-21.5,-16.3); P<0.001** until end of treatment. In contrast, the iPTH levels in the placebo group gradually increased over the course of 24 weeks from baseline 13.5(10.5, 13.2); p<0.001** at the end of therapy. We discovered a substantial reduction in iPTH with vitamin D administration, with a mean (CI=95%) difference of -30.4(-15.2, -46.5) pg/mL, p<0.001**. We were agreed with the previous study. [20, 21] In previous study show that, unfortunately, the study's findings were undermined by a baseline imbalance, and further investigations did not corroborate them. Both magnesium and FGF23 appear to have little effect on central arterial stiffness. The difference between treatment groups of FGF-23 levels also significantly higher of 31.2(15.5, 45.5) pg/mL, p<0.001** with vitamin D therapy. Serum calcium or phosphate levels did not change significantly between treatment groups (P>0.005). In our trials, we found that vitamin D administration significantly reduced iPTH at the conclusion of the treatment period as compared to the placebo control group. We were agreed with the previous study. [22, 23]

We were aware that evidence on the effect of vitamin D on arterial stiffness pressures and the augmentation index in individuals with T2DM and chronic renal disease have not been substantial. We were agree with the previous study.

CONCLUSION

In T2DM with moderate CDK, the aortic-PWV, augmentation index, and pressure measurements of arterial stiffness were all substantially higher in the vitamin D deficient group compared to the vitamin D sufficient group.

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