AJPS, 2018, Vol. 18, No.2 **Date of acceptance: 5-8-2018**

Effect of Vitamin D3 Supplement on Biochemical Markers and Blood Pressure Reading in Hypertensive patients as A secondary Prevention

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DOI: https://doi.org/10.32947/ajps.18.02.0371

Abstract:

Hypertension is the most significant risk factors for cardiovascular morbidity and mortality. It has two classes according to causes of the high blood pressure (Primary and Secondary). This study was intended to evaluate the potential benefit of vitamin D3 supplementation as a secondary preventive therapy for hypertensive patients. It is a prospective randomized controlled study was carried out on 40 patients visiting the Imam Al-Hussein medical city / Karbala and conducted from Sep 2016 to May 2017. The patients were allocated into group1; include 20 hypertensive patients presented with vitamin D deficiency assigned to receive conventional therapy for hypertension with vitamin D3 (100000 IU) orally every 2 weeks for 8 weeks, and group 2; include 20 hypertensive patients presented with vitamin D deficiency assigned to receive anti hypertension therapy only. Ethical committee approval and written consent of patients were obtained. Results revealed that the effect of vitamin D3 supplementation on both angiotensin II level and endogenous vitamin D levels were significantly clear regardless of age group, gender, BMI, duration of disease, and smoking status, except for systolic and diastolic blood pressure, TC, and LDL-c was affected particularly by age group and the duration of disease.

Key words: Hypertension; Vitamin D3; Patient demographic characteristics

تأثير تناول فيتامين د3 على بعض القراءات البايوكيميائية وقراءات ضغط الدم واستخدامه كعلاج ثانوي في المرضى الذين يعانون من ارتفاع ضغط الدم

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الخلاصة:

ارتفاع ضغط الدم هو واحد من أهم عوامل الخطورة لامراض القلب والأوعية الدموية والوفيات. كما يمكن ان يقسم الى قسمين وفقا لأسباب ارتفاع ضغط الدم (الابتدائي والثانوي (هذه الدراسة احتمالية عشوائية تهدف إلى تقييم الفائدة المحتملة من مكملات فيتامين D3 كعلاج وقائي ثانوي لمرضى ارتفاع ضغط الدم. تم إجراء الدراسة على 40 مريضا خلال زيارتهم مدينة الإمام الحسين (ع) الطبية / كربلاء لأخذ العلاج من سبتمبر 2016 إلى مايو 2017. تم الحصول على موافقة اللجنة الأخلاقية وموافقة خطية من المرضى وتم تقسيم المرضى الى مجموعتين الاولى المجموعة التي تتناول فيتامينD3 مع علاج الضغط المقرر والمجموعة الثانيةالتي تتناول علاج الضغط فقط لمدة شهرين من العلاج للمجموعتين. كما اوضحت النتائج ان التاثير الايجابي للفيتامين على تعديل مستوى الانجيوتنسين وفيتامين د بالجسم لايتعلق بالخصائص

الديموغرافية للمريض لكلا المجموعتين بما يخص العمر ونوع الجنس ووزن الجسم ومدة المرض والتدخين عدا بعض التاثير للعمر و مدة المرض على قياس ضغط الدم ومستوى الكولستيرول بعد العلاج بالفيتامين .

الكلمات المفتاحية: ارتفاع ضغط الدم ؛ فيتامين D3 ؛ خصائص المريض الديموغرافية.

Introduction:

Hypertension(HTN) is one of the most significant risk factors for cardiovascular morbidity and mortality[1][2].The management of secondary prevention in individuals diagnosed with CVD or another occlusive arterial disease is based on the recent update of JNC Guidelines [3].Advice to stop smoking[4], personalized information on modifiable risk factors including physical activity[5], diet[6] alcohol intake, weight and tight control of blood pressure and glucose in those with diabetes[7] are also warranted.

Considerable evidence suggest that a large portion of the population have low levels of vitamin D, which may adversely affect the cardiovascular system (CVS), including elevating levels of parathyroid hormone, activating the RAAS, and increasing insulin resistance, hence leading to hypertension and left ventricular hypertrophy, metabolic syndrome/diabetes mellitus, systemic inflammation, and increased risk of atherosclerosis and CVD events[8]. However, only a few studies examined effects of vitamin D therapy on vascular function, and so far results were contradictory[9]

Accordingly, this study is designed prospectively to evaluate the potential effectiveness of vitamin D3 supplementation according to specific patient characteristics particularly gender, BMI, duration of disease,and smoking status.

Patients and Methods

This is a prospective randomized controlled study conducted from Sep 2016 to May 2017. Forty candidate patients, age range 40-70 years, 20 male and 20 female, were selected during their visit to the local hospital. All patients were diagnosed as hypertensive patients at stage I or IIand were assessed to have vitamin D deficiency (> 20 ng/ml). The patients were allocated to two main groups including 20 hypertensive patients presented with vitamin D deficiency assigned to receive conventional therapy for hypertension with vitamin D3 (100000 IU) orally(group 1), and 20 hypertensive patients presented with vitamin D deficiency assigned to receive conventional therapy for hypertension only (group2).

Angiotensin II (Ag II) was estimated using a competitive immunoluminometric assay by using autoanalyzerinstruments Maglumi AII[10]. The reference values of Ag II is 25 -125 pg/ml. Vitamin D was estimated using a competitive protein binding assay[11], and the reference value is 30-60 ng/ml(12). GPT and lipid profile were estimated using autoanalyzer Mindray instrument. Glucose also was measured by diagnostic kit provided by (SPINREACT) company from Spain according to a method of Borham and Trindoer (1972)[13, 14], which is based on enzymatic oxidation of glucose to form glucouronic acid and hydrogen peroxide(H2O2) by the action of glucose oxidase enzyme. The systolic (SBP) and diastolic blood pressure (DBP) was measured usingautomatic blood pressure monitor supplied by Rossmax Company.

Statistical analysis

Collected data was introduced into Microsoft Excel 2016 and loaded intoIMB-SPSS V 23 software for statistical analysis. A P-value less than 0.05 is considered as discrimination point of significance of results.

Results

After adjustment of the baseline means for treatment and control groups according to the covariance analysis and taking the difference between mean of groups post-treatment and adjusted baseline mean, Table (1) show the overall effect of vitamin D3 supplement on different biochemical markers and blood pressure

readings regarding age, gender, BMI, duration of disease and smoking status of the hypertensive patients.

Results revealed that vitamin D3 supplements produce a highly significant change (P <0.01) in serum Angiotensin II level in treatment group compare to control in both age groups (<60 years and ≥ 60 years) after 2 months of treatment. Also, the highly significant change was noticed according to gender, BMI (<30 and ≥ 30) kg/m2, duration of disease (<10yr and ≥10yr), smoking status. The mean difference in endogenous vitamin D level was highly significant change (P <0.01) in the treatment group after vitamin D3 supplements compare to control in all studied variables as mentioned above.

Results in the Table (1) show that vitamin D3 supplements did not produce any change (P <0.05) in serum blood sugar in the treatment group compared to control in all studied variables as well. Vitamin D3 supplements produce a significant change (P >0.05) in TC and LDL cholesterol of age group <60 years, and also a significant change (P >0.05) in LDL cholesterol when the duration of disease is ≥ 10 years. All other studied variables did not any change (P <0.05) in both treatment and control groups.

Moreover, results presented in Table (1) showed that vitamin D3 supplements produce a highly significant change (*P* <0.01) in SBP in the treatment group compared to control in age group <60 years, duration of disease ≥ 10 years, and in smoker patients. In addition, there was a significant change (*P* <0.05) in patients with BMI <30 kg/m^2.

Regarding the change in DBP, vitamin D3 supplements produce a highly significant change (*P* <0.01) in the treatment group compared to control in age group ≥ 60 years, female gender, BMI less than 30, duration of disease ≥ 10 years, and in smoker patients. Besides, a significant change (*P* <0.05) was noticed in patients with BMI ≥ 30, duration of disease ≥ 10 years, and non-smoker patients.

Finally, Table (1) showed that there was no significant change (*P*> 0.05) in the atherogenic index after vitamin D3 supplements in the treatment group compared to control regarding age, gender, BMI, duration of disease, and smoking status after 2 months of treatment.

Table (1A): Percent of change between estimated end line (post-treatment) and adjusted estimated baseline(pre-treatment) age and gender readings of different studied variables according to ANCOVA analysis of hypertensive patients

Variables	Groups	Age				Gender			
		<60YR		≥60YR		Male		Female	
		PO-PR	Sig	PO-PR	Sig	PO-PR	Sig	PO-PR	Sig
Ag II pg/ml	G1	-97.05	**	-111.24	**	-101.30	**	-106.79	**
	G2	-0.4		-10.68		4.76		-3.94	
D3 ng/ml	G1	26.27	**	24.49	**	27.78	**	22.47	**
	G2	2.31		-0.42		2.15		0	
FBS mg/dl	G1	-2.51	NS	-0.45	NS	0.73	NS	-4.26	NS
	G2	-2.38		1.85		-1.33		1.351	
TC mg/dl	G1	-32.64	*	-13.65	NS	-10.50	NS	-34.43	NS
	G2	0.131		-13.35		7.6		-22.28	
TG mg/dl	G1	-7.38	NS	-5.52	NS	-6.61	NS	-5.89	NS
	G2	-5.11		0.32		0.70		-5.92	
HDL mg/dl	G1	-4.5	NS	0.62	NS	-1.60	NS	-2.48	NS
	G2	-1.6		1.28		-1.20		0.302	
LDL mg/dl	G1	-27.80	*	-12.19	NS	-7.63	NS	-32.446	NS
	G2	3.70		-15.56		8.71		-20.494	
VLDL mg/dl	G1	-1.47	NS	-1.16	NS	-0.132	NS	-1.177	NS
	G2	-1.02		0.04		0.142		-1.183	
SBP mmHg	G1	-13.6	**	-10.92	NS	-13.23	NS	-11.361	NS
	G2	-4		-13.2		-12.27		-5.139	
DBP mmHg	G1	-6.06	NS	-6.24	**	-5.36	NS	-6.78	**
	G2	-3.94		-1.07		-3.13		-2.026	
Atherognic index	G1	0.007	NS	0.015	NS	0.035	NS	-0.007	NS
	G2	0.018		-0.026		0.01		-0.017	

PO = post-treatment, PR = pre-treatment, NS = non-significant (PV≥0.05),
*= significant (PV<0.05), **= highly significant (PV<0.01)

Table (1B): Percent of change between estimated end line(post-treatment) and adjusted estimated baseline(pre-treatment) duration of disease and smoking status readings of different studied variables according to ANCOVA analysis of hypertensive patients

Variables	Groups	Duration				Smoking			
		<10yr		≥10yr		yes		No	
		PO-PR	Sig	PO-PR	Sig	PO-PR	Sig	PO-PR	Sig
Ag II pg/ml	G1	-120.4	**	-95.89	**	-113.4	**	-103.53	**
	G2	-8.48		4.21		-8.75		-3.47	
D3 ng/ml	G1	23.27	**	26.82	**	28.81	**	23.53	**
	G2	12.1		-0.37		2.38		-0.2	
FBS mg/dl	G1	-1.7	NS	-1.09	NS	-0.63	NS	-1.44	NS
	G2	0.21		-1.12		-2.39		1.4	
TC mg/dl	G1	-8.43	NS	-34.2	NS	-13.734	NS	-26.93	NS
	G2	-8.2		-5.98		-8.09		-4.24	
TG mg/dl	G1	-0.68	NS	-9.53	NS	-12.11	NS	1.15	NS
	G2	-20.53		-6.68		0.01		-5.03	
HDL mg/dl	G1	-1.54	NS	-2.17	NS	-2.41	NS	-1.47	NS
	G2	-3.29		-0.12		-0.25		-0.3	
LDL mg/dl	G1	-6.7	NS	-30.495	*	-8.81	NS	-26.3	NS
	G2	-7.846		-4.062		-8.56		-2.32	
VLDL mg/dl	G1	-0.137	NS	-1.906	NS	-2.42	NS	0.23	NS
	G2	-0.106		-1.337		0		-1	
SBP mmHg	G1	-10.8	NS	-12.3	**	-10.68	**	-13.13	NS
	G2	-14.26		-3.42		-4.27		-13.39	
DBP mmHg	G1	-6.04	*	-6.31	**	-5.09	**	-6.45	*
	G2	-2.69		-2.18		-81.79		-3.1	
Atherognic index	G1	0.026	NS	0.01	NS	0.002	NS	0.027	NS
	G2	-0.007		-0.005		0.007		-0.013	

PO = post-treatment, PR = pre-treatment NS = non-significant (PV≥0.05), * = significant(PV<0.05), **= highly significant (PV<0.01)

Table (1C) :Percent of change between estimated end line(post-treatment) and adjusted estimated baseline(pre-treatment) weight status readings of different studied variables according to ANCOVA analysis of hypertensive patients

Variables	Groups	Weight status			
		BMI <30		BMI ≥30	
		PO-PR	Sig	PO-PR	Sig
Ag II pg/ml	G1	-124.766	**	-85.45	**
	G2	-25.504		16.361	
D3 ng/ml	G1	29.777	**	20.799	**
	G2	2.633		-0.789	
FBS mg/dl	G1	-2.531	NS	-0.383	NS
	G2	-0.239		-0.617	
TC mg/dl	G1	-12.396	NS	-29.854	NS
	G2	-13.304		-4.046	
TG mg/dl	G1	-6.107	NS	-6.449	NS
	G2	-6.593		1.449	
HDL mg/dl	G1	-1.523	NS	-2.209	NS
	G2	-0.977		0.509	
LDL mg/dl	G1	-8.786	NS	-26.191	NS
	G2	-11.874		-5.009	
VLDL mg/dl	G1	-1.221	NS	-1.29	NS
	G2	-1.319		0.29	
SBP mmHg	G1	-12.241	*	-11.032	NS
	G2	-5.659		-13.068	
DBP mmHg	G1	-5.815	**	-6.539	*
	G2	-1.085		-3.861	
Atherognic index	G1	0.5978	NS	0.003	NS
	G2	0.5668		-0.008	

PO = post-treatment, PR = pre-treatment, NS = non-significant (PV≥0.05), * = significant(PV<0.05), ** = highly significant (PV<0.01)

Discussion

There are many risk factors for cardiovascular diseases, and the individual involvement of each risk factor differs between different communities or ethnic groups, the overall involvement of these risk factors is very consistent[15]. Some of these risk factors, for example; age, gender or family history, are immutable, meanwhile many important cardiovascular risk factors are modifiable such as prevention of hypertension, hyperlipidemia, diabetes[16], and obesity as a chief risk of atherosclerosis of the coronary arteries[17]. Body weight and BMI have a positive correlation with BP due to the accumulation of fat(18).Body weight increased with age and then slightly decreased after 50 years, since in advanced age there is a decrease in muscle mass due to reduced amount of protein intake or decrease number and size of muscle fibers in degenerative diseases that associated with the advancing age[19], meanwhile younger subjects have larger energy intake, fat-rich diet, and relatively less energy expenditure[20]. It is well known that high blood pressure increased with age[21]. The prevalence of increased BP is higher among men than women since lower levels of BP among women may be attribuTable to a protective effect of estrogen, besides, most women are non-smoker and non-drinker. [22].Additionally, premenopausal women have more lipoprotein lipase (LPL) activity, meanwhile, men have a higher level of intraabdominal tissue this explains the greater prevalence of dyslipidemia and chronic heart disease (CHD) in men than in women.[18].`

In the present study, the effect of vitamin D3 supplementation on both angiotensin II level and endogenous vitamin D levels were significantly clear in all age group above 40 years old, both gender, BMI less or more than 30 kg /m^2, smoker, and nonsmoker. Also, for the duration of disease less than 10 years and ≥ 10 years, also FBS, TG, HDL-c, VLDL-c and atherogenic index did not show any difference considering patients demographics. Nevertheless, only TC and LDL-c significantly affected by vitamin D3 supplementation in age group <60 years and the duration of disease ≥ 10 years. In this study, the SBP was highly improved by vitamin D3 supplementation in age group <60 years old, duration of disease ≥ 10 years, smokers, and in patients with BMI <30 kg /m^2. Meanwhile, the DBP was significantly improved particularly in age group ≥60 years old and female gender, and regardless of BMI, duration of disease, and smoking status. This effect on DBP can be potentially due to female characteristics mentioned above and the increase in peripheral vascular resistance with aging that affected notably by the decrease in angiotensin II after vitamin D3 supplementation. On the other hand, the effect of supplementation was hard to be noticed on SBP in advanced age because of the age-related decline in cardiac performance. The longer the duration of the disease the more cardiovascular complications in hypertensive patients, this potentially highlights the benefit of vitamin D3 supplementation in this regard.

Conclusion

The effect of vitamin D3 supplementation on both angiotensin II level and endogenous vitamin D levels was significantly clear regardless of age group, gender, BMI, duration of disease, and smoking status.

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