e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(11); 377-380

Original Research Article

An Observational Study to Determine the Link between Vitamin D and Cellular Senescence Measured With the Enzyme Telomerase in Pre-HTN

Rasikh M. Azaz Alim

Assistant Professor, Department of Physiology, ICARE Institute of Medical Science and Research & Dr BC Roy Hospital, Haldia, West Bengal, India

Received: 10-07-2023 / Revised: 15-08-2023 / Accepted: 22-09-2023
Corresponding Author: Dr. Rasikh M. Azaz Alim
Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to explore the link between Vitamin D and cellular senescence measured with the enzyme telomerase in pre-HTN.

Methods: The present study was conducted from in the Department of Physiology. Inclusion criteria for the pre-hypertensive group (pre-HTN) (n =75) were both genders between 18 and 25 years of age with SBP between 120 and 139 mmHg and DBP between 80 and 89 mmHg in apparently healthy individuals. The controls (n = 75) population were healthy individuals with 18-25 years of age with SBP between 100 and 119 mmHg and DBP between 60 and 79 mmHg.

Results: The study population included 150 apparently healthy individuals. 75 were pre- hypertensive with the age of 22.58±1.56 and the age of controls was 18.82±1.24. Out of 150, 45 males, 30 females were in pre- HTN group and 40 males, 35 females were in the control group. A significant difference was not found between-group differences in height and waist-hip ratio. However, pre- HTN group subject's BMI ($P < 0.001$) and weight ($P < 0.001$) was more compared to controls. In pre-HTN group, significantly higher HR ($P < 0.001$), SBP ($P < 0.001$), DBP ($P < 0.001$), MAP ($P < 0.001$), and RPP ($P < 0.001$) were seen when compared to controls. No significant difference was seen in PP but it was slightly high in pre-HTN group and negatively associated with Vitamin D. High telomerase levels have correlation with waist-hip ratio, SBP, DBP, MAP, and RPP but no significant correlation was seen with BMI, HR, and PP.

Conclusion: It can be concluded that reduced Vitamin D levels in pre-HTN may cause derangements of cardiovascular homeostatic mechanism, enhance the speed of cellular senescence measured by telomerase.

Keywords: Hypertension, Vitamin D, cellular senescence

Introduction

High blood pressure (hypertension) is a serious risk factor for cardiovascular diseases, such as coronary artery disease, myocardial infarction, or stroke, if untreated. [1] Study results revealed that vitamin D deficiency ameliorates the development of hypertension (HT). [1,2] Vitamin D deficiency (25-OH-D < 30 ng/mL) is an independent risk factor for high blood pressure and is involved in the promotion of cardiovascular mortality. [3] It is well known that vitamin D is involved in calcium homeostasis and bone metabolism, and that supplementation in the elderly can reducing the fracture risk. [4]

Arterial hypertension (AH) is a common condition involving the arterial blood pressure (BP) being too high. This means that the force of blood pushing against the walls of the arteries is constantly elevated. This change affects the heart, which needs to work hard to pump sufficient amounts of blood in the body. [5] HT is traditionally defined as a persistent BP measured as ≥140/90 mmHg. [6] Maintenance of a normal BP is dependent on the balance between the cardiac output and the vascular resistance throughout the organism. Furthermore, the cardiac output is dependent on the stroke volume and heart rate (HR). [7]

Even though it is fairly impossible to find a clear underlying cause for most HT cases, there are still various risk factors that can lead to HT. Age, family history, obesity, lack of exercise, smoking, excessive salt diet, high alcohol consumption, and even pregnancy, are a few among the known risk factors responsible for the development of HT. [5] Besides lifestyle risk factors, prescribed drugs, such as oral contraceptives, non-steroidal anti-inflammatory drugs, ciclosporin, erythropoietin (EPO), and glucocorticoids (steroid hormones), may also raise the BP and induce HT. [8] Physiological maintenance of a normal BP is dependent on the

balance between cardiac output and the vascular resistance of the system. There is an interchange between electrical, biochemical, and mechanical forces to control the BP. The electrical component is the sympathetic nervous system; the biochemical component is the renin–angiotensin–aldosterone system (RAAS), neurotransmitters (e.g., norepinephrine (noradrenaline)), or cytokines; and the mechanical component is the HR and the vasodilation/vasoconstriction of the arterioles. Thus, HT occurs when vascular regulation results from malfunctioning in the arterial BP control mechanisms of the body. [7]

The aim of the present study was to explore the link between Vitamin D and cellular senescence measured with the enzyme telomerase in pre-HTN.

Materials and Methods

The present study was conducted from in the Department of Physiology, ICARE Institute of Medical Science and Research & Dr BC Roy Hospital, Haldia, West Bengal, India for one year .Inclusion criteria for the pre- hypertensive group (pre-HTN) (n =75) were both genders between 18 and 25 years of age with SBP between 120 and 139 mmHg and DBP between 80 and 89 mmHg in apparently healthy individuals. The controls (n = 75) population were healthy individuals with 18– 25 years of age with SBP between 100 and 119 mmHg and DBP between 60 and 79 mmHg.

Individuals suffering from diabetes, hypertension, endocrine disorders, kidney diseases, and hypertensive patients already receiving medication were not considered to take part in this research. The volunteers were asked to not participate in heavy exercises, not drink alcohol and coffee 1 day before the data collection. Baseline, anthropometric parameters were recorded before recording of the BP by sphygmomanometer as per standard protocol. [9] Then, 5 ml of blood was collected, allowed to clot, and subjected to centrifugation to separate the serum. Serum was stored at –80°C for processing of Vit-D and telomerase levels as per the instructions provided in the commercially available kits.

Statistical analysis was done to analyze the data. To study the between-group differences, independent t-test, to assess the correlation of vitamin D with telomerase and other parameters, Pearson's correlation coefficient analysis was applied.

Results

Table 1: Comparison of anthropometric characteristics between pre-HTN and controls

Parameters	Pre-HTN (*n*=75)	Controls (*n*=75)	*P*-value
Age	22.58±1.56	18.82±1.24	0.460
Gender (male/female)	45/30	40/35	1.390
Height (cm)	172.28±8.72	169.71±8.52	0.316
Weight (kg)	65.45±10.40	58.42±8.72	<0.001
BMI (k/m^2)	23.17±4.66	23.67±4.72	<0.001
Waist to hip ratio	0.90±0.12	0.87±0.07	0.474

The study population included 150 apparently healthy individuals. 75 were pre- hypertensive with the age of 22.58±1.56 and the age of controls was 18.82±1.24. Out of 150, 45 males, 30 females were in pre- HTN group and 40 males, 35 females were in the control group. A significant difference was not found between-group differences in height and waist-hip ratio.

Table 2: Comparison of cardiovascular parameters between pre-HTN and controls

Parameters	Pre-HTN (*n*=75)	Controls (*n*=75)	*P*-value
HR (BPM)	87.43±4.76	82.48±4.82	<0.001
SBP (mmHg)	122.18±4.82	114.6±5.55	<0.001
DBP (mmHg)	81.69±4.07	74.36±4.90	<0.001
PP (mmHg)	41.69±4.96	39.01±5.65	0.172
MAP (mmHg)	93.57±2.84	87.73±3.75	<0.001
RPP	10960.82±702.78	9082.78±488.82	<0.001

However, pre- HTN group subject's BMI ($P < 0.001$) and weight ($P < 0.001$) was more compared to controls. In pre-HTN group, significantly higher HR ($P < 0.001$), SBP ($P < 0.001$), DBP ($P < 0.001$), MAP ($P < 0.001$), and RPP ($P < 0.001$) were seen when compared to controls. No significant difference was seen in PP but it was slightly high in pre-HTN group and negatively associated with Vitamin D.

Table 3: Comparison of Vitamin D and telomerase levels between pre-HTN and controls

Parameters	Pre-HTN (*n*=100)	Controls (*n*=100)	*P*-value
Vitamin D (ng/ml)	19.21±4.36	21.03±6.34	0.048
Telomerase (IU/ml)	35.85±16.84	7.05±4.96	<0.001

High telomerase levels have correlation with waist-hip ratio, SBP, DBP, MAP, and RPP but no significant correlation was seen with BMI, HR, and PP.

Discussion

Hypertension is a common health problem, one of the leading costs to the health care system, and a significant cause of mortality and morbidity worldwide. [10] Hypertension is also one of the most common and influential risk factors of cardiovascular disease including myocardial infarction, cerebral stroke, congestive heart failure, peripheral vascular disorders and kidney disease. [11] It has been estimated that eliminating high blood pressure would reduce the occurrence of stroke by 35% and heart attacks by 18%. [12,13] To reduce the burden of hypertension, a multicomponent lifestyle intervention that includes weight loss, increased physical activity, restricted sodium and alcohol consumption, and adherence to a Dietary Approach to Stop Hypertension like diet with plenty of fruits, vegetables, and low-fat dairy items and little saturated fat is needed. [14] Moreover, improved vitamin D status has been proposed as an easily modifiable risk factor. [15]

The study population included 150 apparently healthy individuals. 75 were pre- hypertensive with the age of 22.58±1.56 and the age of controls was 18.82±1.24. Out of 150, 45 males, 30 females were in pre- HTN group and 40 males, 35 females were in the control group. A significant difference was not found between-group differences in height and waist-hip ratio. Vitamin D deficiency has recently emerged as a public health problem, affecting almost 50% of the population worldwide. [16] In addition to the reduced exposition to sunlight [17], also genetic and environmental factors have been suggested as a cause of this pandemic, such as pollution, diet, sedentary life style and stress. [18] Moreover, vitamin D is no longer considered as only a pivotal mediator of calcium metabolism and skeletal health, but it also regulates several cell functions, including differentiation and metabolism. This aspect may explain the reason why hypovitaminosis D has been proved to be an independent risk factor for overall mortality in various cohort analyses [19], whereas vitamin D supplementation significantly reduced mortality. [20] Zhao et al [21] in an ongoing report detailed a positive relationship between Vit-D and hypertension and pre-HTN. Forman et al [22] reported a positive relationship between Vit-D and self-revealed occurrence hypertension among 38,388 men from the Health Professionals' follow-up study and 77,531 females from the Nurses' Health Study; a positive affiliation was likewise detailed between Vit-D and hypertension in a subsample of members. Further, a study concentrate from the second Nurses' health study detailed a positive relationship between serum Vit-D and hypertension among 1484 young females. In the NHANES, SBP was demonstrated to be conversely connected with Vit-D among 12,644 participants. [23]

However, pre- HTN group subject's BMI ($P < 0.001$) and weight ($P < 0.001$) was more compared to controls. In pre-HTN group, significantly higher HR ($P < 0.001$), SBP ($P < 0.001$), DBP ($P < 0.001$), MAP ($P < 0.001$), and RPP ($P < 0.001$) were seen when compared to controls. No significant difference was seen in PP but it was slightly high in pre-HTN group and negatively associated with Vitamin D. High telomerase levels have correlation with waist-hip ratio, SBP, DBP, MAP, and RPP but no significant correlation was seen with BMI, HR, and PP. Earlier reports have shown that higher Vitamin D is related to longer telomere length, which underscores the conceivably advantageous impacts of this hormone on cell senescence and age-related conditions. [24] In this study, cellular senescence was assessed using telomerase. This enzyme attempts to inhibit the process of telomere shortening. [25] Since the cell telomere loss appears to result from cell division just to a fractional degree, different components, particularly oxidative stress, were attested to assume a job in the expanded rate for shortening of telomeres. [26] The exact mechanism by which lower Vit-D levels are associated with this cellular senesce is hypothesized dependent on the perceptions recommends that the degrees of the telomerase may really be related to oxidative stress, with higher oxidative stress prompting higher telomerase levels. Cells of nearly complex organism may not have an ability to divide. This marvel was depicted by Hayflick in 1961. [27]

Conclusion

It can be concluded that reduced Vitamin D levels in pre-HTN may cause derangements of cardiovascular homeostatic mechanism, enhance the speed of cellular senescence measured by telomerase.

References

1. Legarth C, Grimm D, Krueger M, Infanger M, Wehland M. Potential beneficial effects of vitamin d in coronary artery disease. Nutrients. 2019 Dec 30;12(1):99.
2. Wimalawansa SJ. Vitamin D and cardiovascular diseases: Causality. The Journal of steroid biochemistry and molecular biology. 2018 Jan 1;175:29-43.
3. Rai V, Agrawal DK. Role of vitamin D in cardiovascular diseases. Endocrinology and Metabolism Clinics. 2017 Dec 1;46(4):1039-59.
4. Delmi M, Rapin CH, Bengoa JM, Bonjour JP, Vasey H, Delmas PD. Dietary supplementation in elderly patients with fractured neck of the femur. The Lancet. 1990 Apr 28;335(8696): 1013-6.

5. High Blood Pressure (Hypertension).
6. Elliott WJ. Systemic hypertension. Current problems in cardiology. 2007 Apr 1;32(4):201-59.
7. O'Shea PM, Griffin TP, Fitzgibbon M. Hypertension: The role of biochemistry in the diagnosis and management. Clinica Chimica Acta. 2017 Feb 1;465:131-43.
8. Williams B. Resistant hypertension: an unmet treatment need. The Lancet. 2009 Oct 24; 37 4(9699):1396-8.
9. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, Jones DW, Materson BJ, Oparil S, Wright Jr JT, Roccella EJ. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. hypertension. 2003 Dec 1;42(6):1206-52.
10. Mittal BV, Singh AK. Hypertension in the developing world: challenges and opportunities. American Journal of Kidney Diseases. 2010 Mar 1;55(3):590-8.
11. Holick MF. Vitamin D: important for prevention of osteoporosis, cardiovascular heart disease, type 1 diabetes, autoimmune diseases, and some cancers. Southern medical journal. 2005 Oct 1;98(10):1024-8.
12. Colley RC, Garriguet D, Janssen I, Craig CL, Clarke J, Tremblay MS. Physical activity of Canadian adults: accelerometer results from the 2007 to 2009 Canadian Health Measures Survey. Health reports. 2011 Mar 1;22(1):7.
13. Warburton DE, Charlesworth S, Ivey A, Nettlefold L, Bredin SS. A systematic review of the evidence for Canada's Physical Activity Guidelines for Adults. International journal of behavioral nutrition and physical activity. 2010 Dec;7(1):1-220.
14. Elmer PJ, Obarzanek E, Vollmer WM, Simons-Morton D, Stevens VJ, Young DR, Lin PH, Champagne C, Harsha DW, Svetkey LP, Ard J. Effects of comprehensive lifestyle modification on diet, weight, physical fitness, and blood pressure control: 18-month results of a randomized trial. Annals of internal medicine. 2006 Apr 4;144(7):485-95.
15. Hosseinpanah F, Yarjanli M, Sheikholeslami F, Heibatollahi M, Eskandary PS, Azizi F. Associations between vitamin D and cardiovascular outcomes; Tehran Lipid and Glucose Study. Atherosclerosis. 2011 Sep 1;218(1):238-42.
16. Vitamin D. deficiency. Holick MF. N Engl J Med. 2007;357:266-81.
17. Lucas RM, Ponsonby AL, Dear K, Valery PC, Taylor B, Van Der Mei I, McMichael AJ, Pender MP, Chapman C, Coulthard A, Kilpatrick TJ. Vitamin D status: multifactorial contribution of environment, genes and other factors in healthy Australian adults across a latitude gradient. The Journal of steroid biochemistry and molecular biology. 2013 Jul 1;136: 300-8.
18. Holick MF. Environmental factors that influence the cutaneous production of vitamin D. The American journal of clinical nutrition. 19 95 Mar 1;61(3):S638-45.
19. Pludowski P, Holick MF, Pilz S, Wagner CL, Hollis BW, Grant WB, Shoenfeld Y, Lerchbaum E, Llewellyn DJ, Kienreich K, Soni M. Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality—a review of recent evidence. Autoimmunity reviews. 2013 Aug 1;12(10):976-89.
20. Amer M, Qayyum R. Relationship between 25-hydroxyvitamin D and all-cause and cardiovascular disease mortality. The American journal of medicine. 2013 Jun 1;126(6):509-14.
21. Zhao G. Ford eS, li C, Kris-etherton PM, etherton td, balluz lS. Independent associations of serum concentrations of 25-hydroxyvitamin d and parathyroid hormone with blood pressure among uS adults. J hypertens. 2010;28: 1821-8.
22. Forman JP, Giovannucci E, Holmes MD, Bischoff-Ferrari HA, Tworoger SS, Willett WC, Curhan GC. Plasma 25-hydroxyvitamin D levels and risk of incident hypertension. Hypertension. 2007 May 1;49(5):1063-9.
23. Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, ethnicity, and blood pressure in the Third National Health and Nutrition Examination Survey. American journal of hypertension. 2007 Jul 1;20(7):713-9.
24. Richards JB, Valdes AM, Gardner JP, Paximadas D, Kimura M, Nessa A, Lu X, Surdulescu GL, Swaminathan R, Spector TD, Aviv A. Higher serum vitamin D concentrations are associated with longer leukocyte telomere length in women. The American journal of clinical nutrition. 2007 Nov 1;86(5):14 20-5.
25. von Zglinicki T. Telomeres and replicative senescence: is it only length that counts?. Cancer letters. 2001 Jul 26;168(2):111-6.
26. Von Zglinicki T. Oxidative stress shortens telomeres. Trends in biochemical sciences. 20 02 Jul 1;27(7):339-44.
27. Hayflick L. The limited in vitro lifetime of human diploid cell strains. Experimental cell research. 1965 Mar 1;37(3):614-36.