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Protection roles of serum vitamin D levels in the cardiovascular system

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Abstract: Protection roles of serum vitamin D levels in the cardiovascular system. This observational study enrolled 286 young ACI patients with type 2 diabetes mellitus in our Hospital from October 2016 to April 2020 as the study group. 127 healthy individuals as the control group. Serum levels of vitamin D and blood pressure indexes of the two groups were measured and the correlation between vitamin D levels and the clinical phenotype of young cerebral infarction was explored. Significantly higher 25-hydroxyvitamin D was observed in the study group vs. control group. During the day, The values of systolic and diastolic blood pressure and mean blood pressure was well-balanced between the two groups. However, at night and within 24 hours, significant differences in systolic and diastolic blood pressure and mean value were observed between the two groups. The higher the vitamin D level, the greater the decrease in blood pressure at night. Serum 25-hydroxyvitamin D was positively correlated with the reduction of night systolic and diastolic blood pressure. Low levels of 25-hydroxyvitamin D led to a small decrease in blood pressure at night, resulting in a vulnerable cardiovascular system and an increased incidence of cerebral infarction in the young population.

Keywords: 25-hydroxyvitamin D, type 2 diabetes mellitus, acute cerebral infarction, hypertension.

INTRODUCTION

Acute ischemic stroke (ACI) is a common type of stroke in clinical practice, accounting for 70%-80% of strokes with high rates of disability and death (Liu *et al*., 2022). Conventional western medical therapy improves circulation, prevents platelet aggregation, and regulates lipid levels through drugs to unblock blood vessels and reduce thrombus formation, but the efficacy is suboptimal (Dudenkov *et al*., 2021; Chao *et al*., 2020). In traditional Chinese medicine (TCM), the main pathological mechanism of ACI is stasis, phlegm and blockage of the arteries and veins, for which treatment centers on the activation of blood circulation and removal of blood stasis, yet the prognosis remains poor (Kwak *et al*., 2020). At present, the drug for acute ischemic stroke is unavailable, and early diagnosis and treatment are thus urgency for patient prognosis.

Vitamin D exists in the body mainly as 25 hydroxyvitamin D (25-(OH)D3) and 25(OH)D is an intermediate product of lipid metabolism and is involved in lipid metabolism (Theiler-Schwetz *et al*., 2022; Kwak *et al*., 2021). Decreased 25(OH)D levels are inducing factors for cardiovascular diseases such as coronary heart disease and congestive heart failure (Zhang *et al*., 2020). Serum 25-(OH)D3 is stable in blood concentration and participates in a variety of biochemical metabolism; as an example, it can inhibit the renin-angiotensin system to protect the kidney and blood vessels, lower blood pressure and slow down the development of atherosclerosis (Xiao *et al*., 2020). Several studies have shown that serum 25-(OH)D3 has an anti-oxidative stress function and inhibits oxygen overload and oxidative stress, which consequently contributes to the improvement of brain nerve cells (Hsu *et al*., 2020; Małyszko *et al*., 2021; Pelczyńska *et al*., 2020).

In addition, vitamin D levels are negatively correlated with the activity of the renin-angiotensin-aldosterone system (RAAS), enhance endothelial function and prevent secondary hyperparathyroidism (Maghbooli *et al*., 2021). Moreover, evidence suggest that T2DM and cerebral infarction patients are often complicated by vitamin D deficiency and SBP level correlates with the severity of cerebral infarction in T2DM patients (Xiao *et al*., 2021). Nevertheless, no consensus was established between vitamin D supplementation and SBP/DBP levels in ACI patients among previous findings (Kaneva *et al*., 2022).

To this end, the relationship between vitamin D levels and blood pressure in ACI patients demands further research conducted on a bigger cohort of patients.

MATERIALS AND METHODS

Baseline profiles

This observational study enrolled 286 young ACI patients with type 2 diabetes mellitus who were treated in the Department of Neurology of Cangzhou Central Hospital from October 2016 to April 2020 as a study group. Another 127 healthy individuals with similar profiles were included in the control group. This study was ethically approved by the ethics committee of Cangzhou Central Hospital (No. 2014-02/154).

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Inclusion and exclusion criterion

Inclusion criterion 1) patients aged 18 to 60 years old; 2) within 2 weeks onset of symptoms; 3) with diagnosed acute cerebral infarction confirmed by CT/MRI (Larsson *et al*., 2018).

Exclusion criterion 1) patients with progressive stroke, transient ischemia attack, cerebral infarction with posterior cerebral hemorrhage and cerebral arteritis; 2) with tumor, injury and parasites caused cerebral embolism; 3) pregnant and of childbearing potential or breastfeeding.

Methods

SBP, DBP and pulse rate

The arterial pulse analyzer (Sphygmocor, AtCor Medical, Australia) was used to perform non-invasive measurements on the patient and the operation was carried out in strict accordance with the instruction. The patient's radial artery pulse wave was recorded for 10 seconds and was converted to the central arterial pulse wave group through the instrument's built-in conversion program, so as to obtain the corresponding central artery SBP and DBP. At the strongest part of the right radial artery, the number of beats was documented for 1min with the index finger and middle finger and the measurement was repeated at 1 min intervals. The mean value of the two measured values is the pulse rate.

Fasting blood lipids and vitamin D

5mL of fasting venous blood was secured from the participants and stored in a separating gel accelerator tube, followed by a centrifuge for 10min to obtain the serum, which was stored in a refrigerator at -80°C for assays. An automatic biochemical analyzer (Hitachi 7600-010, HITACHI, Japan) was used to determine blood lipid indexes and an enzyme-linked immunosorbent method was used to determine 25-hydroxyvitamin D (Haida Biotechnology, China).

STATISTICAL ANALYSIS

All data were expressed as (x±s) and the analysis was performed using a t-test. All the analyses were done by SPSS software (version 25, SPSS, Inc., Chicago, IL, USA). All analyses were deemed as statistical significance with a threshold of 0.05.

RESULTS

Baseline data

The baseline characteristics such as age, BMI, HDL, LDL, TG, Hg, BPC and WBC was well-balanced between the two groups (P>0.05) (table 1).

Blood pressure

There was no marked difference in 24h SBP, 24h DBP, Day SBP, Day DBP,and Day MAP between the two groups (P>0.05). The mean values of 24h MBP, Night SBP, Night DBP and Night MAP were significantly different between the two groups (P<0.001). (table 2).

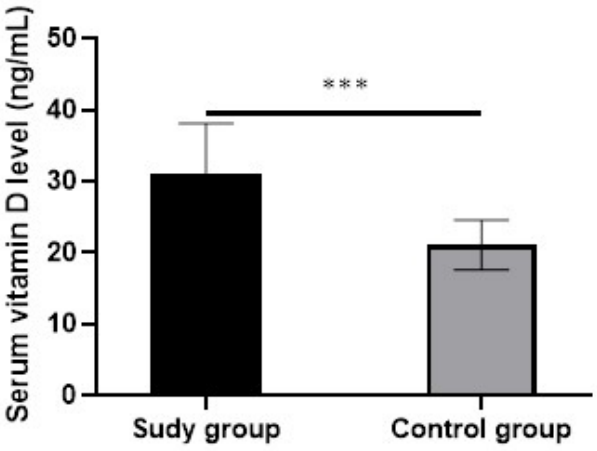

Fig. 1: Serum 25-hydroxyvitamin D levels

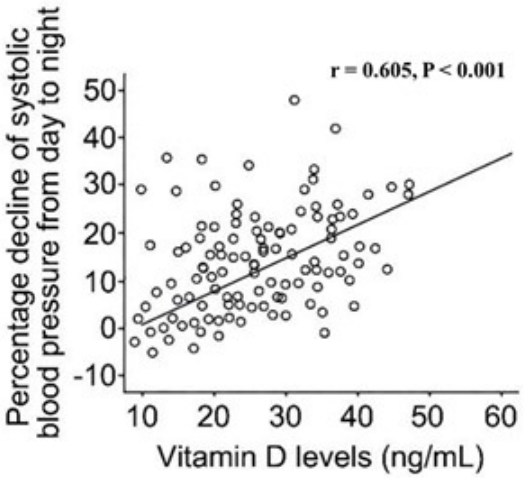

Fig. 2: Correlation analysis between serum vitamin D level and SBP

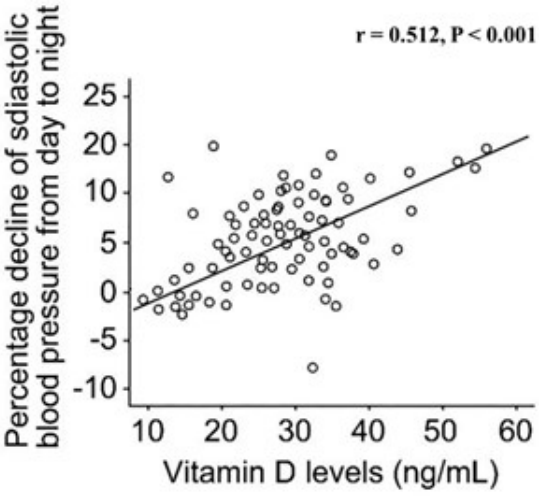

Fig. 3: Correlation analysis between serum vitamin D level and DBP

Table 1: Comparison of general information

	Control group	Study group	*P*
Age (years)	38.4±8.9	36.9±6.4	0.279
BMI (kg/m2)	25.9±4.9	27.9±6.2	0.415
HDL (mg/dL)	38.9±6.3	38.5±2.3	0.236
LDL (mg/dL)	124.4±17.6	129.9±14.3	0.193
TG (mg/dL)	148.8±13.1	152.3±12.1	0.672
Hg (g/L)	14.6±2.8	14.8±1.6	0.184
BPC (×109/L)	287.6±73.6	289.1±80.9	0.901
WBC (×109/L)	6.8±0.9	6.6±1.2	0.348

Table 2: Comparison of blood pressure

	Control group	Study group	*P*
24h SBP (mmHg)	127.3±9.2	133.9±8.2	0.162
24h DBP (mmHg)	81.9±6.4	84.8±2.1	0.298
24h MBP (mmHg)	93.5±3.2	99.9±4.8	<0.001
Day SBP (mmHg)	137.2±10.2	137.6±5.3	0.438
Day DBP (mmHg)	87.2± 5	88.7±3.7	0.195
Day MAP (mmHg)	103.6±4.7	104.7±4.2	0.173
Night SBP (mmHg)	122.6±7.8	132.9±8.2	<0.001
Night DBP (mmHg)	75.4±2.3	82.9±3.7	<0.001
Night MAP (mmHg)	89.4±2.9	99.7±3.8	<0.001

Serum vitamin D levels

In the control group, the serum vitamin D level was 31±7.1ng/mL and it was 21.1±3.5ng/mL in the study group (P<0.001).(fig. 1)

Correlation analysis between serum vitamin D level and SBP

As shown in fig. 2, a positive correlation between vitamin D levels and changes in SBP during the day and night was observed (r=0.605, P<0.001).

Correlation analysis between serum vitamin D level and DBP

As shown in fig. 3, there existed a positive correlation between vitamin D levels and DBP changes during the day and night (r=0.512, P<0.001).

DISCUSSION

The present findings exhibited that the vitamin D levels of the control group were significantly higher versus ACI hypertensive patients and that vitamin D levels are associated with the decrease in night SBP and DBP. Evidence showed that for patients with hypertension, proper reduction in night blood pressure might lead to higher cardiovascular risks (Zhao *et al*., 2019). Therefore, in this study, the correlation between vitamin D and SBP and DBP was explored to determine the role of vitamin D levels in ACI patients.

Hypertension is the main cause of cardiovascular disease, stroke and renal failure. Although the root cause of the night-time blood pressure decline has not been fully elucidated, trials have studied the relationship between vitamin D and essential hypertension (Kaneva *et al*., 2022). In America, the vitamin D level of healthy adults is inversely proportional to blood pressure. Additionally, a trial conducted on the data of 5414 patients from 2003 to 2006 showed that the prevalence of hypertension and prehypertension decreased linearly with the increase of serum vitamin D levels. Studies have shown that people with older age, obesity, poor sleep quality, autonomic dysfunction and higher sympathetic nerve activity and inflammation are more susceptible to cerebral infarction (Badimon *et al*., 2019). In recent years, the prevalence of cerebral infarction and type 2 diabetes mellitus has shown an increasing trend. Therefore, whether there are certain changes in serum vitamin D levels in young ACI patients, and whether there is a correlation between vitamin D levels and young ACI deserves further research.

Vitamin D plays a role in the process of lymphocyte proliferation, cell differentiation and cytokine secretion. It participates in the regulation of the immune system and the population with higher inflammation is prone to ACI. There is a certain correlation between vitamin D and ACI as previously reported (Nitsa *et al*., 2018). Vitamin D has two biologically active forms in the human body, namely, cholecalciferol, vitamin D3 and ergocalciferol, vitamin D2. D3 is mainly synthesized in the human body using 7-dehydrocholesterol as a raw material by the skin under ultraviolet radiation and D2 is obtained from food or medicine (Sunkara *et al*., 2019). Traditionally, vitamin D was thought to regulate physiological activity in humans and animals and was closely related to bone and phosphorus metabolism, but in recent years, with gradual

development of scientific research, vitamin D has been found to be negatively associated with the incidence of cardiovascular disease. Studies have shown that the incidence of cerebral infarction and abnormal serum vitamin D levels is closely related, with patients with serum vitamin D levels above baseline experiencing a 40% lower risk of cerebrovascular disease than those below baseline levels. In the present study, the serum vitamin D level in the study group was significantly lower than that in the control group, which may be attributed to the fact that young people are less involved in outdoor activities. For hypertensive patients, proper reduction of night blood pressure including SBP and DBP has a certain protective effect on the cardiovascular system (Tousoulis *et al*., 2020).

Furthermore, no significant fluctuation in blood pressure between the two groups during the day was found in the present study; but at night and within 24 hours, the two groups were different in SBP, DBP and the mean blood pressure. It can be assumed that the decrease in blood pressure at night in the study group may contribute primarily to the disease. Of note, through correlation analysis, vitamin D is positively correlated with the reduction of night SBP and DBP. The higher the vitamin D level, the greater the reduction in night blood pressure, better protection from cardiovascular disease and the lower the incidence of ACI. It agrees with the previous studies in which a strong negative correlation between serum vitamin D levels and the risk of hypertension was also observed (Lin *et al*., 2021; Ricke et al., 2022; Zhao *et al*., 2023).

However, there are some limitations to this study that should be outlined. This was a single-center observational study with a small number of patients and a low level of evidence. In addition, the association between vitamin D levels and blood pressure alone could not verify whether vitamin D supplementation reduced the risk of hypertension. This study might provide an innovative point of view and the findings are needed to be validated in future studies.

CONCLUSION

Serum 25-hydroxyvitamin D was positively correlated with the reduction of night systolic and diastolic blood pressure. Low levels of 25-hydroxyvitamin D led to a small decrease in blood pressure at night, resulting in a vulnerable cardiovascular system and an increased incidence of cerebral infarction in the young population.

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REFERENCES

Badimon L, Chagas P and Chiva-Blanch G (2019). Diet and cardiovascular disease: Effects of foods and nutrients in classical and emerging cardiovascular risk factors. *Curr. Med. Chem.,* **26**(19): 3639-3651.

Chao G, Zhu Y and Fang L (2020). Correlation between hashimoto's thyroiditis-related thyroid hormone levels and 25-hydroxyvitamin D. *Front. Endocrinol. (Lausanne)*, **11**(1): 4.

Dudenkov DV, Mara KC, Maxson JA, Thacher TD (2021). Serum 25-hydroxyvitamin D values and risk of incident cardiovascular disease: A population-based retrospective cohort study. *J. Steroid Biochem. Mol. Biol.,* **213**(11): 105953.

Hsu S, Hoofnagle AN, Gupta DK, Gutierrez OM, Peralta CA, Shea S, Allen NB, Burke G, Michos ED, Ix JH, Siscovick D, Psaty BM, Watson KE, Kestenbaum B, de Boer IH and Robinson-Cohen C (2020). Race, ancestry, and vitamin D metabolism: The multi-ethnic study of atherosclerosis. *J. Clin. Endocrinol. Metab.,* **105**(12): e4337-e4350.

Kwak JH, Hong YC and Choi YH (2020). Serum 25-hydroxyvitamin D and hypertension in premenopausal and postmenopausal women: National Health and Nutrition Examination Surveys 2007-2010. *Public Health Nutr.,* **23**(7):1236-1246.

Kwak JH and Choi YH (2021). Sex and body mass index dependent associations between serum 25-hydroxyvitamin D and pulse pressure in middle-aged and older US adults. Sci. Rep., **11**(1): 9989.

Kaneva AM, Potolitsyna NN and Bojko ER (2022). Association of serum 25-hydroxyvitamin D with metabolic disturbances in adolescents. *Am J Hum Biol.,* **34**(12): e23802.

Liu Y, Shi L, Lin Y, Zhang M, Chen F, Li A and Liu Y (2022). Relationship between serum 25-hydroxyvitamin D and target organ damage in children with essential hypertension. *J. Hum. Hypertens.,* **36**(7): 604-609.

Larsson SC, Traylor M, Mishra A, Howson JMM, Michaelsson K and Markus HS (2018). Megastroke project of the international stroke genetics consortium. serum 25-hydroxyvitamin D concentrations and ischemic stroke and its subtypes. *Stroke,* **49**(10): 2508-2511.

Lin HC, Hao WM and Chu PH (2021). Cadmium and cardiovascular disease: An overview of pathophysiology, epidemiology, therapy and predictive value. *Rev. Port. Cardiol (Engl Ed).,* **40**(8): 611-617.

Maghbooli Z, Sahraian MA, Jamalimoghadamsiahkali S, Asadi A, Zarei A, Zendehdel A, Varzandi T, Mohammadnabi S, Alijani N, Karimi M, Shirvani A and Holick MF (2021). Treatment with 25-hydroxyvitamin D3 (calcifediol) is associated with a reduction in the blood neutrophil-to-lymphocyte ratio marker of disease severity in hospitalized patients with

COVID-19: A pilot multicenter, randomized, placebo-controlled, double-blinded clinical trial. *Endocr Pract.,* **27**(12): 1242-1251.

Małyszko J, Tomaszuk-Kazberuk A, Dobrzycki K, Bachórzewska-Gajewska H, Zorawski M, Koc-Zorawska E, Kobus G and Dobrzycki S (2021). Vitamin D deficiency and anemia is highly prevalent and dependent on the etiology of heart failure: A pilot study. *Cardiol. J.,* **28**(2): 262-270.

Nitsa A, Toutouza M, Machairas N, Mariolis A, Philippou A and Koutsilieris M (2018). Vitamin D in cardiovascular disease. *In vivo*., **32**(5): 977-981.

Pelczyńska M, Grzelak T, Sperling M, Kręgielska-Narożna M, Bogdański P and Czyżewska K (2020). Evaluation of vitamin D fractions in obese hypertensive patients. *Int. J. Environ. Res. Public Health*, **17**(5): 1660.

Ricke DO (2022). Pain adverse events, Bell's Palsy and Guillain-Barré syndrome following vaccination. *J. Mod. Biol. Drug. Discov.,* **1**(1): 3.

Sunkara A and Raizner A (2019). Supplemental vitamins and minerals for cardiovascular disease prevention and treatment. *Methodist Debakey. Cardiovasc. J.,* **15**(3): 179-184.

Tousoulis D, Papageorgiou N (2020). Cardiovascular disease: From diagnosis to therapy. *Curr. Med. Chem.,* **27**(27): 4438-4439.

Theiler-Schwetz V, Trummer C, Grübler MR, Keppel MH, Zittermann A, Tomaschitz A, Karras SN, März W, Pilz S and Gangler S (2022). Effects of vitamin d supplementation on 24-hour blood pressure in patients with low 25-hydroxyvitamin D Levels: A randomized controlled trial. *Nutrients,* **14**(7): 1360.

Xiao P, Dong H, Li H, Yan Y, Cheng H, Liu J, Zhao X, Hou D and Mi J (2020). Adequate 25-hydroxyvitamin D levels are inversely associated with various cardiometabolic risk factors in Chinese children, especially obese children. *BMJ Open Diabetes Res. Care,* **8**(1): e000846.

Xiao J, Lv J, Wang S, Zhou Y, Chen L, Lu J, Zhang X, Wang X, Gu Y and Lu Q (2021). Association of serum 25-hydroxyvitamin D with metabolic syndrome and type 2 diabetes: A one sample Mendelian randomization study. *BMC Geriatr.,* **21**(1): 391.

Zhang M, Michos ED, Wang G, Wang X and Mueller NT (2020). Associations of cord blood vitamin D and preeclampsia with offspring blood pressure in childhood and adolescence. *JAMA Netw. Open,* **3**(10): e2019046.

Zhao D, Liu J, Wang M, Zhang X and Zhou M (2019). Epidemiology of cardiovascular disease in China: Current features and implications. *Nat. Rev. Cardiol.,* **16**(4): 203-212.

Zhao Y, Xie Y, Jia D, Ma C, Wei D and Zhang X (2023). Efficacy of pemetrexed or gemcitabine combined with cis-platinum on patients with advanced non-small-cell lung carcinoma and its effect on Serum miR-365. *J. Mod. Pharmacol. Pathol.,* **1**(1): 9.