Original article

Calcidiol serum levels and blood pressure responses in normotensive patients with dietary goat milk

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Abstract

Background: Calcidiol (25-hydroxyvitamin D or 25(OH) D) is the active form of vitamin D that can be measured in the blood. Vitamin D functions as a regulator of blood pressure and a vitamin D deficiency is associated with an increased risk of hypertension. Goat's milk is thought to have anti hypertensive effect. That is likely due to the amount of vitamin D found in goat's milk, but requires further investigation. This research was conducted to analyze the effect of consuming goat's milk on blood pressure and its relationship with calcidiol serum in normotensive patients. ***Materials and Methods*:** The design of this research was experimental laboratory with randomized pretest-posttest with a control group using 18 sedentary women aged 18-19 years. The treatment was 250 ml/day of goat's milk given in the morning after breakfast for 110 days. The data were analyzed by the statistical t-test ($p<0.05$). ***Results:*** A significant decrease of systolic blood pressure ($p=0.00$) and no significant decrease of diastolic blood pressure ($p=0.51$) were observed in the trial group. Levels of calcidiol serum did not increase significantly ($p=0.06$) after consuming goat's milk in the trial group. ***Conclusion*:** It can be concluded that goat's milk can decrease blood pressure but does not affect calcidiol serum in normotensive patients. Further research is needed to determine the effect of goat's milk on blood pressure in hypertensive patients.

Keywords: *blood pressure; 25-hydroxyvitamin D; vitamin D; goat milk; hypertension*

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Headlines

Consuming goat milk regularly can lower blood pressure but the decrease of blood pressure does not occur through increased secretion of serum 25-hydroxyvitamin D. Goat's milk has the potential to be developed as an antihypertensive agent, but further research is required to determine the mechanism of action of goat's milk in controlling blood pressure and as an antihypertensive agent.

Introduction

Currently, numerous studies explain that vitamin D plays a role in regulating blood pressure.[1,2] Vitamin D or Cholecalciferol has many physiological functions, including: as a blood pressure regulatory, estrogen biosynthesis, inflammation, regulator of calcium homeostasis and rennin–angiotensin system (RAS), and regulating the activity of vascular muscles.[1,2] Vitamin D directly regulates blood pressure.[1,2] Vitamin D deficiency is associated with higher predisposition and risk of various diseases, including: osteoporosis, cardiovascular disease (CVD), and hypertension. Calcidiol levels are a biomarker of the state of vitamin D in the body.[3]

Several studies have shown that there is an inverse relationship between levels of calcidiol serum and blood pressure, with reports that low levels of calcidiol increase blood pressure and is a predictable cause of hypertension.[1,2,3] Supplementation of vitamin D in controlling blood pressure in patients with hypertension has been studied.[1,2] However, further studies must address how the consumption of goat's milk can lower blood pressure and if it stimulates the secretion of calcidiol.

The main source of vitamin D is from exposure to the sun while smaller amounts of vitamin D are found in foods such as goat's milk.[4-6] Goat's milk contains vitamins A, B, C, D and E.[4-6] Consuming goat's milk regularly could be expected to lower blood pressure, and it is believed to be useful as an antihypertensive. However, the influence of the consumption of goat's

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milk in controlling blood pressure is still unclear. Goat's milk can also stimulate increased serum 25-hydoxyvitamin D, but still needs further study. The purpose of this study was to analyze the effect of regular consumption of goat's milk on blood pressure and its relationship with calcidiol serum levels in normotensive patients.

Materials and Methods

This study was an experimental laboratory using a randomized pretest-posttest with a control group. The sample included 18 sedentary women aged 18-19 years. Criteria for the research subjects are: female, healthy, completely follow the research procedures, not to consume foods and supplements (other than goat's milk), and normal blood pressure (according to criteria of JNC-8). Subjects were divided into two groups, namely: (1) control group (not given goat's milk) and (2) trial group (given goat's milk). Selection of subject research was conducted by simple random sampling. The trial was fresh goat's milk, 250 ml/day, given in the morning after breakfast, for 110 days.

Examination of serum 25-hydroxyvitamin D levels was conducted using Chemiluminescense Immunoassays (CLIA). Systolic and diastolic blood pressure were measured using mercury sphygmomanometer with the auscultator method. The examination of blood pressure and calcidiol serumlevels were before and after the trial. The data were analyzed by the test of homogeneity of variance of Levine's test ($p<0.05$), the test of normality of Kolmogorov-Smirnov ($p<0.05$) and a statistical t-test ($p<0.05$).

This research has received approval from the Ethics Committee for Medical and Health Research, Faculty of Medicine, Syiah Kuala University, Banda Aceh, Aceh-Indonesia, based on the letter number: 304/KE/FK/2015. All of the study subjects had to provide written permission before the examination and treatment.

Results

Table 1 shows that the characteristics of the research subjects such as: age (years), weight (kg), height (cm^2), and body mass index (BMI=kg/m^2). The characteristics across the trial and control groups were not significantly different ($p>0.05$).

Table 1. Physiologic and anthropometric features of subjects

	Trial group Mean±SD	Control group Mean±SD
Age (years)	18.77±0.44	18.66±0.50
Weight (kg)	51.77±8.60	47.72±3.91
Height (cm^2)	154.33±2.69	153.56±2.12
BMI (kg/m^2)	21.80±3.98	20.25±1.77

In order to confirm homogeneity of variance, the Levine-test ($p<0.05$) was used and the Kolmogorof-Smirnov ($p<0.05$) test was used to determine whether the data were normally distributed. Data were found to be homogeneous and normally distributed. The average changes in systolic and diastolic blood pressure and calcidiol serum levels in all the subjects before and after consuming goat's milk are shown in table 2.

Table 2. Effect of goat's milk supplementation on blood pressure and calcidiol serum levels in normotensive patients

Group	Variable	Before trial Means±SD	After trial Means±SD	t-test	p-value
Control	Systolic (mmHg)	112.22±9.71	110.00±8.66	-1.51	0.16
	Diastolic (mmHg)	75.55±5.27	80.00±0.00	2.53	0.03*
	25-hydroxyvitamin D (ng/mL)	14.38±3.35	13.52±2.88	0.90	0.39
Trial	Systolic (mmHg)	101.11±9.27	93.33±5.00	-3.5	0.00*
	Diastolic (mmHg)	70.00±7.07	67.78±9.71	-0.68	0.51
	25-hydroxyvitamin D (ng/mL)	13.56±2.75	14.27±2.25	2.17	0.06

Discussion:

Results showed that consuming goat's milk regularly resulted in significantly ($p=0.05$) lower systolic blood pressure (7% reduction). Goat's milk did not significantly reduce ($p=0.51$) diastolic blood pressure (3.17% reduction). The regular consumption of goat's milk did not significantly increase ($p=0.06$) levels of calcidiol serum (5% increase). This study suggests that the decrease in blood pressure due to the regular consumption of goat's milk has no effect on the

levels of 25-hydroxyvitamin D serum. The findings indicate that goat's milk can lead to a decrease in blood pressure, but the mechanism of action of goat's milk in lowering blood pressure was not through an increase in the secretion of 25-hydroxyvitamin D. That is likely due to several reasons, namely: (1) the dose of goat's milk was not enough to raise levels of calcidiol serum, suggesting a need for the continuation of this research using a higher dosage of goat's milk, (2) This study uses female subjects who wear the veil so that exposure to the sun is reduced, (3) The study was conducted on patients with normal blood pressure, so it is necessary to do a comparison with hypertensive patients using variable doses of goat's milk, (4) This research is being continued by using goat's milk with varying doses and methods of research are different by measuring several hormones related to blood pressure control.

Goat's milk may also lower blood pressure through other mechanisms. Some results of experimental studies suggests that goat's milk effects the control of blood pressure and has the potential to prevent and treat hypertension.[4-8] Results of clinical trials showed that the proteins in goat's milk have the potential to improve some diseases, including: cardiovascular disease, hypertension, metabolic syndrome, and the incidence of many chronic diseases.[6,8] Clinical trial results also showed that goat's milk has the potential to regulate blood pressure.[7,8] Goat's milk can be used as an anti-hypertensive.[5-8] The protein content of goat milk casein is allegedly one of the factors that affects the role of goat's milk as an anti-hypertensive.[7] Goat's milk contains two kinds of proteins, namely: caseins and whey proteins.[7] Casein hydrolysis of goat milk effectively lowers blood pressure and acts as a therapy for patients with hypertension.[7] Both of these proteins contain lots of angiotensin-converting enzyme (ACE) inhibitor peptides, which can be extracted from both the goat milk proteins.[6,7] Goat's milk is one of the main sources of ACE inhibitor peptides.[5,6,7]

The angiotensin-converting enzyme (ACE) inhibitor is in the first line drugs used for the management of hypertension.[9,10,11] ACE inhibitors work by inhibiting the secretion of aldosterone and vasopressin, and not by blocking the action of angiotensin II and does not interact directly with other components of the renin angiotensin aldosterone system (RAAS).[9,12,13] RAAS is a target to control blood pressure in people with hypertension.[12,13] RAAS is a hormone that is formed by renin. Angiotensinogen, with the help of renin, is hydrolyzed to angiotensin-I, which, with the support of ACE is hydrolyzed to angiotensin-II. Angiotensin II is a potent vasoconstrictor and associated with hypertension.[12,13]

Some of the literature suggests that blood pressure is also associated with high levels of vitamin D.[14-17] Goat's milk is a source of vitamin D derived from food.[4-6] Vitamin D plays a role in controlling blood pressure through several channels, namely: controls the levels of calcium and phosphorus, suppress proliferation of vascular smooth muscle, inhibits the secretion of parathyroid hormone, and regulates RAAS.[12,13] Vitamin D is a fat-soluble vitamin stored in fat tissue and the liver.[1,16] Vitamin D has two types, namely: ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3).[1,16] Vitamin D in circulation binds to vitamin D-binding protein to then be transported to the liver. In the liver, vitamin D is converted into calcidiol, also called 25-hydroxyvitamin D or [25(OH)D].[14-16] Calcidiol is the active form of vitamin D and it is most often found in the blood. Thus, so the levels of calcidiol will describe the status of vitamin D in the body.[2]

Recent research has found that low levels of calcidiol are associated with increased blood pressure.[19-25] This is presumably because of the role of calcidiol in regulating the function of RAAS.[19-23] Other studies have also found that there is an inverse relationship between levels of calcidiol and the renin-angiotensin levels.[26-29] Goat's milk can also lower blood pressure through the stimulation of the secretion of Nitric Oxide (NO).[8] Results of in vitro studies have found that people who regularly consume goat's milk will exhibit increased levels of NO released by endothelial cells of blood vessels. NO is known as a potent vasodilator and also acts as a cardioprotective and antiatherogenic agent.[8]

Conclusion:

It can be concluded that: consuming goat's milk regularly has the potential to significantly reduce systolic blood pressure but not to significantly decrease diastolic blood pressure in normotensive patients. Regular consumption of goat's milk does not significantly increase calcidiol serum levels in normotensive patients. Consuming goat's milk can lower blood pressure but the decrease of blood pressure does not occur through increased secretion of calcidiol serum levels. Goat's milk has the potential to be developed as an antihypertensive, but requires further research to be able to determine its mechanism in controlling blood pressure and as an antihypertensive agent.

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References:

1. Jorde R, Figenschau Y, Emaus N, Hutchinson M, and Grimnes G. Serum 25-Hydroxyvitamin D Levels Are Strongly Related to Systolic Blood Pressure But Do Not Predict Future Hypertension. *Hypertension*. 2010; 55:792-798. https://doi.org/10.1161/HYPERTENSIONAHA.**109.**143990.
2. Dorjgochoo T, Shu XO, Xiang YB, Yang G, Cai Q, Li H, Ji BT, et al. Circulating 25-hydroxyvitamin D levels in relation to blood pressure parameters and hypertension in the Shanghai Women's and Men's Health Studies. *Br J Nutr*. 2013; **108**(3): 449–458. https://doi.org10.1017/S0007114511005745.
3. Martini LA and Wood RJ. Vitamin D and blood pressure connection: update on epidemiologic, clinical, and mechanistic evidence. *Nutrition Reviews*. 2008; **66**(5):291-297. https://doi.org/10.1 11 1/j.1753-4887.2008.00035.x.
4. Ulusoy BH. Nutritional and Health Aspects of Goat Milk Consumption. *Akademik Gıda.* 2015; **13**(1):56-60. http://www.academicfoodjournal.com.
5. Zenebe T, Ahmed N, Kabeta T and Kebede G. Review on Medicinal and Nutritional Values of Goat Milk. *Academic Journal of Nutrition*. 2014; 3(3):30-39. https://doi.org/10.5829/idosi.ajn.2014.3.3.93210.
6. Mwenze PM. Functional Properties of Goats' Milk: A Review. *Research Journal of Agriculture and Environmental Management.* 2015; **4**(9):343-349. http://www.apexjournal.org.
7. Lee KJ, Kim SN, Ryu JS, Shin HS and Lim JW. Separation and Purification of Angiotensin Converting Enzyme Inhibitory Peptides Derived from Goat's Milk Casein Hydrolysates. *Asian-Aust. J. Anim. Sci.* 2005; **18**(5):741-746. http://ajas.info/upload/pdf/18_117.pdf.
8. Sunagawa K, Kishi T, Nagai A, Matsumura, Nagamine I and Uechi S. Goat Meat Does Not Cause Increased Blood Pressure. *Asian Australas. J. Anim. Sci*. 2014; 27(1):101-114. https://dx.doi.org/10.5713/ajas.2013.13325.

9. Ţânţu M, Belu E, Bobescu E , Armean Sm , Armean P, Constantin Mm, Domnariu Cd. Role Of Angiotensin Converting Enzyme (ACE) Inhibitors In Hypertension And Cardiovascular Protection Management. *FARMACIA.* 2014; **62**(3):451-59.
10. Tabassum N. Aliskiren: A new renin inhibitor as anti-hypertensive. *Journal of Applied Pharmaceutical Science.* 2011; 01(03):30-33. http:// www. Japsonline. com.
11. Santoro D, Caccamo D, Lucisano S, Buemi M, Sebekova K, Teta D, and De Nicola L. Interplay of Vitamin D, Erythropoiesis, and the Renin-Angiotensin System. *BioMed Research International*. 2015; 1-11. http:// dx.doi.org/10.1155/2015/145828
12. Otte M, Spier A. The Renin–Angiotensin–Aldosterone System: Approaches to Cardiac and Renal Therapy. *Compendium: Continuing Education for Veterinarians.* 2009; E1-E7. http: CompendiumVet.com.
13. Atlas SA. The Renin-Angiotensin Aldosterone System: Pathophysiological Role and Pharmacologic Inhibition. *Journal of Managed Care Pharmacy.* 2007;**13**(8):S9-S20. http://www.amcp.org.
14. Vaidya A, and Williams JS. Vitamin D in the Pathophysiology of Hypertension, Kidney Disease, and Diabetes: Examining the Relationship Between Vitamin D and the Renin-Angiotensin System in Human Diseases. *Metabolism.* 2012; **61**(4):450–458. https://doi.org/doi:10.1016/j.metabol.2011.09.007.
15. Li YC. Vitamin D: Roles In Renal And Cardiovascular Protection. *Curr Opin Nephrol Hypertens.* 2012; 21(1): 72–79. https://doi.org/10.1097/MNH.0b013e32834de4ee..
16. Pilz S, Tomaschitz A, Drechsler C and de Boer RA. Vitamin D deficiency and heart disease. KidneyInternational Supplements (2011) **1**, 111–115; https://doi.org/10.1038/kisup.2011.26.
17. *Pilz S, Tomaschitz A, Ritz E and Pieber TR.* Vitamin D status and arterial hypertension: a systematic review. *Nat. Rev. Cardiol.* 6, 621–630 (2009); published online 18 August 2009; https://doi.org/10.1038/nrcardio.2009.**135**
18. Ajabshir S, Asif A, and Nayer A. The effects of vitamin D on the renin-angiotensin system. *J Nephropathol.* 2014; **3**(2):41-43. https://doi.org/10.12860/jnp.2014.09.
19. Bhandari SK, Pashayan S, Liu ILA, Rasgon SA, Kujubu DA, Tom TY, and Sim JJ. 25-Hydroxyvitamin D Levels and Hypertension Rates. *The Journal of Clinical Hypertension*. 2011; **3**(3):170–177. https://doi.org/10.1111/j.1751-7176.2010.00408.x.
20. 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; **49**:1063–69. https://doi.org/10.1161/HYPERTENSIONAHA.107.087288.
21. Forman JP, Williams JS, Fisher NDL. Plasma 25-Hydroxyvitamin D and Regulation of the Renin-Angiotensin System in Humans. *Hypertension*. 2010; 55:1283-88. https://doi.org/10.1161/HYPERTENSIONAHA.**109**.148619.
22. Martins D, Wolf M, Pan D, Zadshir A, Tareen N, Thadhani R, Felsenfeld A, Levine B, Mehrotra R, Norris K. Prevalence of cardiovascular risk factors and the serum levels of 25-hydroxyvitamin D in the United States: data from the Third National Health and Nutrition Examination Survey. *Arch Intern Med.* 2007; **167**:1159–65. http://www.archinternmed.com
23. Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, ethnicity, and blood pressure in the Third National Health and Nutrition Examination Survey. *Am J Hypertens.* 2007; 20:713–19. https://doi.org/ 10.1016/j.amjhyper.2007.**01**.017.
24. Judd SE, Nanes MS, Ziegler TR, Wilson PW, Tangpricha V. Optimal vitamin D status attenuates the age-associated increase in systolic blood pressure in white Americans: results from the third National Health and Nutrition Examination Survey. *Am J Clin Nutr* 2008; **87**:136–41. http://ajcn.nutrition.org/.
25. Dorjgochoo T, Shu XO, Xiang YB, Yang G, Cai Q, et al. Circulating 25-hydroxyvitamin D levels in relation to blood pressure parameters and hypertension in the Shanghai Women's and Men's Health Studies. *Br J Nutr*. 2012; **108**(3):449–458. https://doi.org/10.1017/S0007114511005745.
26. Forman JP, Curhan GC, and Taylor EN. Plasma 25-Hydroxyvitamin D Levels and Risk of Incident Hypertension Among Young Women. *Hypertension*. 2008; 52:828-32. https://doi.org/10.1161/HYPERTENSIONAHA.**108.**117630.
27. Goel RK and Lal H. Role of Vitamin D Supplementation in Hypertension. Ind J Clin Biochem. 2011; **26**(1):88–90. https://doi.org/10.1007/s12291-010-0092-0
28. Tamez H, Kalim S, and Thadhani RI. Does Vitamin D Modulate Blood Pressure? *Curr Opin Nephrol Hypertens*. 2013; **22**(2):204–209. https://doi.org/10.1097/MNH.0b013e32835d919b.
29. Tomaschitz1 A, Pilz S, Ritz E, Morganti A, Grammer T, Amrein K, et al. Associations of plasma renin with 10-year cardiovascular mortality, sudden cardiac death, and death due to heart failure. *European Heart Journal*. 2011; **32**:2642–2649. https://doi.org/doi:10.1093/eurheartj/ehr150.