Original Research Paper | Medical Science | Volume : 5 ¦ Issue : 1 ¦ Jan 2020 ¦ e-ISSN : 2456-5040

EFFECT OF GARLIC (ALLIUM SATIVUM) AS HYPOTENSIVE AGENT IN TWO AGE GROUPS OF HYPERTENSIVE ADULTS

Morales Escobar Michell Alexandra [1], Flores Herrera Diana Itzel [1], Alonso Ricardez Abraham [2], Alonso Trujillo Javier [2]

[1] Undergraduate students in nursing, Facultad de Estudios Superiores Iztacala, Universidad Nacional Autónoma de México.
[2] Professor of research methodology, Degree in nursing, Facultad de Estudios Superiores Iztacala, Universidad Nacional Autónoma de México.

ABSTRACT

High blood pressure has been considered the most widespread health disorder in the world and has been identified as the main risk factor for various health. For this reason, in addition to health education, alternative treatments that can replace drug therapy have been sought in various parts of the world. Thus, it is popularly known that garlic extract (Allium sativum), is able to lower systemic blood pressure in hypertensive people. The mechanism that has been proposed is that some of the components of garlic extract could stimulate the enzyme nitric oxide synthase in vascular endothelial cells causing a vasodilatory effect, which could be reflected in a decrease in blood pressure.

Objective: To test effect of Allium sativum on blood pressure in hypertensive adults. ***Material and methods:*** Experimental study. Two age blocks were formed; 40 to 60 years old and 70 to 85 years old. The subjects that made up the blocks were randomized to assign one of the three doses used; 0, 500 or 1000 mg / day of Allium sativum to complement his pharmacological therapy. ***Results:*** A statistically significant decrease was found only in the systolic blood pressure of subjects of 70 to 85 years old who consumed 1000 mg/day. ***Conclusion:*** Hypotensive effect of Allium Sativum is still uncertain, in hypertensive adults, however, experimental evidence of a dose-dependent effect discriminating between systolic and diastolic blood pressure was obtained. We suggest strengthening health care at the first level of care.

KEYWORDS: Hypertension, prehypertension, Garlic, Allium, Adult.

INTRODUCTION:

Arterial hypertension is a multiple etiology syndrome characterized by a persistent increase ≥ 140 mm Hg for systolic blood pressure (SBP) and ≥ 90 mm Hg for diastolic blood pressure (DBP), thus representing a risk factor associated with cardiovascular morbidity and mortality that affects approximately one billion people worldwide (Chobanian et al., 2003).

Considering the magnitude of this health problem that arterial hypertension represents, various prevention policies have been generated, which were disclosed in The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of Arterial Hypertension. These policies, once implemented, resulted in important recommendations aimed at health education as a specific Nursing activity, such as the one that states that blood pressure control should be extended to people considered prehypertensive, is that is, those presenting SBP 120-139 mm Hg / DBP 80-89 mm Hg (Chobanian et al., 2003).

Importantly, health prevention and education policies include relevant changes in the lifestyle of prehypertensive people, some of them are increased physical activity, planning strategies to lose weight and some changes in diet, such as for example, higher consumption of vegetables and sometimes the incorporation of dietary supplements. The role of the Nurse in these tasks is essential.

Regarding consumption of vegetables, some authors recommend consumption of garlic (Allium sativum) in a dosage form through capsules, since it is believed that garlic has hypotensive effects in humans (Banerjee, Mukherjee and Maulik, 2003; Higdon and Lawson, 2005). It is known that garlic has played an important dietary and medicinal role in the history of mankind. The reducing properties of garlic blood pressure have been related to the production of hydrogen sulfide (Benavides et al., 2007). On other hand, it has been proposed by various authors, that content of allicin, released from alliin and enzyme alliinase has inhibitory effects of angiotensin II as well as vasodilatory effects in animal and human cells (Al-Qattan, Khan, Alnaqeeb and Ali, 2003; Al-Qattan, Thomson, Al-Mutawa'a, Al-Hajeri, Drobiova and Ali., 2006; Kaye, et al, 2000).

For the above, a non-pharmacological panorama is opened for the development of research projects regarding the prevention of arterial hypertension, and with it, reduce the risk of cardiovascular disease. We refer to the study of garlic consumption as a hypotensive agent.

Animal studies have suggested that garlic consumption reduces blood pressure, but primary studies in humans and unsystematic reviews have reported mixed and often conflicting and uncertain results. At present, interest in alternative medicine, specifically naturopathic medicine, has grown, therefore, in different parts of the world studies have begun and developed in which the effect of garlic preparations on blood pressure in various biological models has been investigated.

In Mexico, data from the National Institute of Statistics, Geography and Informatics (INEGI), reveal that there is a significant proportion of citizens who do not have sufficient resources to access private health services, and in many cases these people are also not benefited by the public policies and programs of prevention of arterial hypertension, since they are located in a socioeconomic level of poverty or extreme poverty. Some specific data that demonstrate the above are following: In 2015, 17.8% of Mexican population was not affiliated with any public health service, that is, about 21 million people. 13.1% of Mexicans receive monetary income from sources other than work, such as government assistance programs. 22.2% of Mexicans over 18 were hungry and did not eat all day, while in the case of minors, it was 14% of this group who have stayed a full day without trying food (INEGI, 2015).

This problem allows us to direct the purpose of this research towards a design that can demonstrate and provide scientific evidence, of effect that garlic has on blood pressure in hypertensive subjects, especially in adults over 40 years, in which this disease begins to Increase your frequency

Based on previous knowledge, some mechanisms are known through which garlic lowers blood pressure. Thus, in endothelial cell cultures, it has been shown that an aqueous extract of fresh garlic effectively inhibits activity of adenosine deaminase (ADA), which contributes to antihypertensive activity and vasoprotective effects of garlic (Gonzales, 2014, p.61).

Garlic extract lowers systemic blood pressure in hypertension, because in vivo, garlic stimulates enzymatic activity of nitric oxide synthase (ONS) in vascular endothelial cells, which leads to increased oxide synthesis nitric (ON) and with it, arterial diameter is increased. The decrease in blood pressure is also result of hyperpolarization of smooth muscle cells in blood vessels and / or inhibition of opening of calcium channels in muscle tissue. The inhibition of angiotensin enzyme, modulation of prostaglandin synthesis or those chemical compounds that affect the atherosclerotic process, may also play a role in blood pressure changes. (Ankri, 1997, p. 2286)

Recent studies suggest that the production of ON is decreased in patients with arterial hypertension. ON is the endogenous product of oxidation of L-arginine and has a vasodilator effect of what has been called a relaxing factor derived from endothelium (Forte, 1997, p. 937).

Cockroft (1997) suggested that baseline ON production, rather than stimulated, is abnormal in arterial hypertension. Forte (1997) conducted studies to directly estimate the production of ON in patients with untreated arterial hypertension through the measurement of inorganic nitrate synthesis, which is final product of ON oxidation in humans; At the end, data obtained suggested that total body production of ON in patients with arterial hypertension is decreased below baseline. Bathaei (2008), in a meta-analysis about effects of garlic on blood, observed that in each of eight randomized studies, preparation of dried Kwai garlic was used, at doses of 600 to 900 mg daily, during minus 4 weeks in 415 subjects. The results showed an average decrease in systolic blood pressure (SBP) of 7.7 mm Hg (95% CI: 4.3-11) and a decrease in diastolic blood pressure (DBP) of 5 mm Hg (95% CI: 2.9- 7.1).

Thaslima et al. (2018) included 30 patients with arterial hypertension in their study. SBP and DBP were measured before and after garlic intake for a period of 15 days. For the SBP in first measurement they obtained 141 mm Hg and in second measurement 136 mm Hg. Initial DBP was 90 mm Hg and final measurement was 88 mm Hg. The authors suggest that effect could depend on duration and dose used in treatment. Ried (2013) evaluated effects of garlic on blood pressure in patients with arterial hypertension. His study showed a significant decrease in both SBP and DBP, both in terms of dose and duration. In each group treated with garlic, a significant reduction in SBP and DBP ($p < 0.005$) was observed compared to group that received atenolol and placebo group. Finally, Ried, Frank, Stocks, Fakler and Sullivan (2008), observed an average decrease of 4.6 ± 2.8 mm Hg for SBP in a group of hypertensive subjects who consumed garlic. The objective of this research is to verify the effect of Allium Sativum as a hypotensive agent in older adults.

MATERIAL AND METHODS:

An experimental, prospective, longitudinal and analytical investigation was carried out. A Completely Randomized Design Block (CRDB) was used, where independent variable (factor considered causal) was dose administered to subjects in three intensities (0, 500 and 1000 mg) and dependent variable was blood pressure (systolic and diastolic).

Basic research design:

$Rb_{1\ n=5}$ O_1 Dose = 0 mg O_2

$Rb_{1\ n=5}$ O_1 Dose=500 mg O_2

$Rb_{1\ n=4}$ O_1 Dose = 1000 mg O_2

$Rb_{2\ n=5}$ O_1 Dose = 0 mg O_2

$Rb_{2\ n=4}$ O_1 Dose = 500 mg O_2

$RB_{2\ n=4}$ O_1 Dose = 1000 mg O_2

Where:
R = Randomized allocation to experimental doses

B1 = Block of subjects 40 to 60 years old

B2 = Block of subjects 70 to 85 years old

n = Sample size

O1 = Measurement of blood pressure before treatment

O2 = Measurement of blood pressure after treatment

Random assignment of subjects of each block (40 to 60 years / 70 to 85 years) was made to experimental doses (0, 500 and 1000 mg). A blood pressure measurement (standard technique) was performed before and after having consumed garlic in previously established doses, for 15 calendar days. A previously calibrated cuff baumanometer was used to measure systolic and diastolic pressure of each of experimental units.

Experimental units:

25 Adults of both sexes with age from 40 to 85 years. All presented alterations in blood pressure (prehypertension or arterial hypertension) and agreed to participate in the study by committing to consume doses of garlic assigned for a period of 15 days, without suspending their single pharmacological treatment and antihypertensive control. Subjects who had two or more pharmacological treatments and who were using diuretic drugs were excluded. In the database, incomplete records or clear transcription errors were deleted.

Sampling technique:

Subjects were grouped into two blocks, according to their age. First block (n = 14): 40 to 60 years and Second block (n = 13): 70 to 85 years. All were assigned a folio number so that that number could be used in random assignment of experimental doses.

In tables 1 and 2, assignment of subjects of each of experimental doses can be observed. The assignment was simple random.

Table 1: Random assignment of first block subjects to each of experimental doses.

First block	Dose (mg)	Subjet	Dose (mg)	Subjet	Dose (mg)	Subjet
40 a 60 years old n = 14	0	11	500	4	1000	12
	0	3	500	2	1000	9
	0	6	500	13	1000	7
	0	10	500	14	1000	1
	0	5	500	8	1000	

Table 2: Random assignment of second block subjects to each of experimental doses.

Second block	Dose (mg)	Subjet	Dose (mg)	Subjet	Dose (mg)	Subjet
70 a 85 years old n = 13	0	3	500	9	1000	4
	0	1	500	2	1000	11
	0	10	500	6	1000	12
	0	5	500	8	1000	7
	0	13	500		1000	

Ethical aspects:

All subjects decided to sign an informed consent letter and thereby voluntarily agreed to participate in this study.

Their decision to leave study was respected at time they wished. They learned about the potential risks of garlic consumption and when considering them of minimal risk they decided to participate. The above was accompanied by condition that none of participants would suspend their pharmacological treatment and would continue to be under supervision of their doctor, who was expected to be aware of their participation in this study.

Statistical analysis plan:

For each block, measures of central tendency and variability of systolic and diastolic pressure were calculated before and after dose corresponding to each treatment. Prevalence of high blood pressure and arterial hypertension was calculated.

Comparison of means was made using Student's "t" test for before - after measures and prevalence comparison was performed using McNemar test, for numerical and categorical variables respectively (Alonso, 2019). The level of significance was set at ≤ 0.05

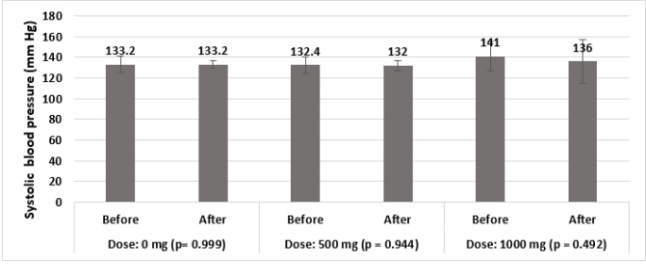
RESULTS:

Comparison of mean systolic and diastolic pressures:

Completely randomized block design allows us to analyze results in a multivariate way. Below are results obtained in this investigation, at first comparison of means of systolic and diastolic pressure, before and after dose of garlic applied (0, 500 and 1000 mg), both for first block and for second.

Secondly, comparisons are presented before - after prevalences obtained from subjects with high blood pressure and arterial hypertension, by doses applied in group of 40 to 60 years and in group of 70 to 85 years.

Figure 1 shows that there were no significant differences between mean systolic pressure before and after each dose in block of subjects 40 to 60 years of age ($p > 0.05$). In Figure 2, result showing a statistically significant decrease in systolic blood pressure with a dose of 1000 mg in group of adults aged 70 to 85 years is highlighted. Decrease in blood pressure went from 156 to 143 mm Hg ($p = 0.010$), however, they are still arterial hypertension figures.



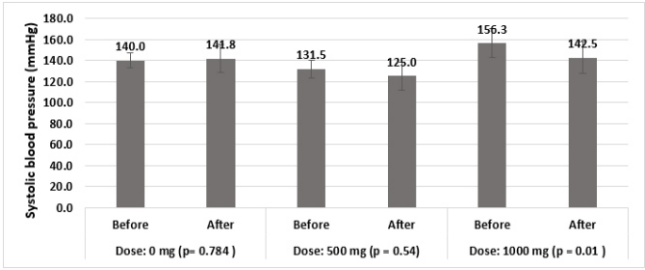
Source: Field work. Own measurements.

Figure 1: Comparison of systolic pressure before and after intervention of block of 40 to 60 years. Garlic dose results of 0, 500 and 1000 mg are shown.

Mean ± DS.

Student's "t" test for before-after measures.

Level of significance ≤ 0.05.



Source: Field work. Own measurements.

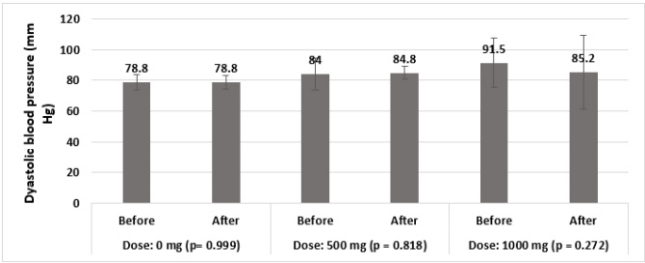
Figure 2: Comparison of systolic pressure before and after intervention of 70 to 85 year block. Garlic dose results of 0, 500 and 1000 mg are shown.

Mean ± SD.

Student's "t" test for before - after measures.

Level of significance ≤ 0.05.

Figure 3 shows comparisons of diastolic blood pressure, before and after doses applied in block of 40 to 60 years. There were no significant differences (p> 0.05). Same result was observed in 70 to 85 year old block as can be seen in Figure 4.



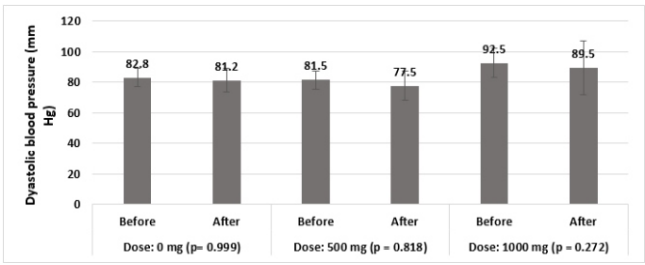
Source: *Field work. Own measurements.*

Figure 3: Comparison of diastolic pressure before and after intervention of block from 40 to 60 years. Garlic dose results of 0, 500 and 1000 mg are shown.

Mean ± SD.

Student's "t" test for before - after measures.

Level of significance ≤ 0.05.



Source: *Field work. Own measurements.*

Figure 4: Comparison of diastolic pressure before and after intervention of block from 40 to 60 years. Garlic dose results of 0, 500 and 1000 mg are shown.

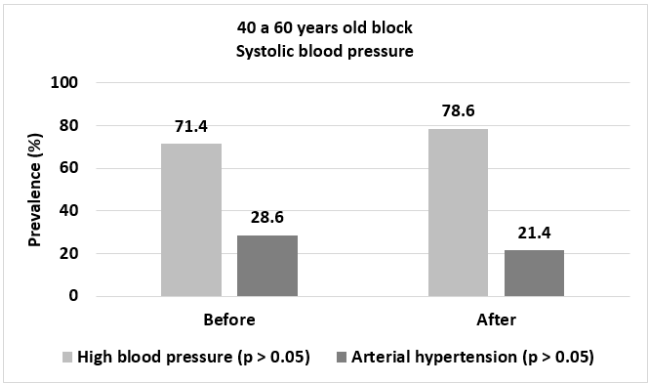
Mean ± SD.

Student's "t" test for before - after measures.

Level of significance ≤ 0.05.

Comparison of prevalence of high blood pressure and hypertension:
Subjects with systolic blood pressure values <140 mm Hg, were categorized as High blood pressure, and when they had ≥ 140 mm Hg, they were classified in arterial hypertension category. In case of diastolic pressure, values <90 mm Hg fell into category of High blood pressure, but values ≥ 90 mm Hg were classified as arterial hypertension.

Based on the above criteria, the prevalence of subjects with high blood pressure and arterial hypertension was obtained. Comparisons between the prevalences before and after each of doses applied showed that there are no significant differences. However, for a better description of these results, you can see figures from 5 to 8.

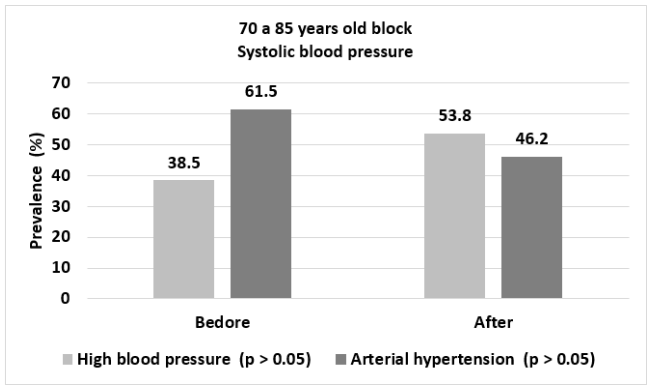


Source: *Field work. Own measurements.*

Figure 5: Comparison of prevalences in 40 to 60 year old block. Systolic pressure was classified into two categories: High blood pressure and arterial hypertension.

McNemar test.

Significance level ≤ 0.05

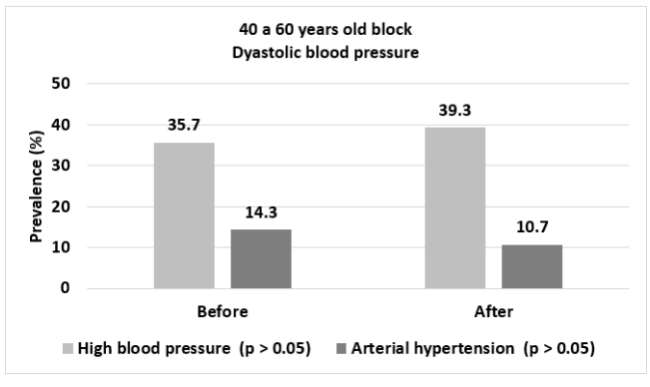


Source: *Field work. Own measurements.*

Figure 6: Comparison of prevalences in 70 to 85 year old block. Systolic pressure was classified into two categories: High blood pressure and Hypertension.

McNemar test.

Significance level ≤ 0.05

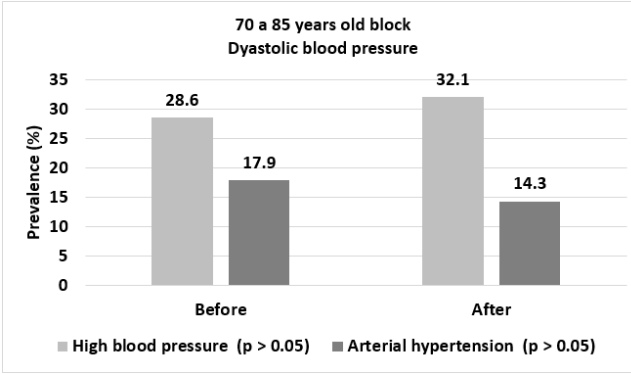


Source: *Field work. Own measurements.*

Figure 7: Comparison of prevalences in the 40 to 60 year old block. Diastolic pressure was classified into two categories: High blood pressure and arterial hypertension.

McNemar test.

Significance level ≤ 0.05



Source: *Field work. Own measurements.*

Figure 8: Comparison of prevalences in the 70 to 85 year old group. Diastolic pressure was classified into two categories: High blood pressure and Hypertension.

McNemar test.

Significance level ≤ 0.05

DISCUSSION:

Some authors such as Bathaei (2008), Ried et al. (2008) and Thaslima et al. (2018) have observed a hypotensive effect of garlic, however, results of this research do not coincide with theirs.

It has been written about possible biological mechanisms that could explain decrease in blood pressure after garlic intake. Among them we have one proposed by González (2014) who points to the inhibition of enzyme adenosine deaminase as responsible for such a decrease.

Also, Ankri (1997), noted that an increase in intravascular nitric oxide could have vasodilatory effects and consequently a decrease in blood pressure could be observed.

In our case, no significant decrease in blood pressure was generally observed after experimental subjects took 500 and 1000 mg of garlic every day for 15 days, except in the age group of 70 to 85 years, who they took a dose of 1000 mg of garlic for 15 days. The difference between blood pressure before and after garlic treatment in this group was statistically significant ($p = 0.010$).

A first explanation about null effect of garlic in most of participating subjects, whether in 40 to 60 year old block or in 70 to 85 year old block, is possible alteration of vascular economy. It is known that arteriosclerotic process is more frequent after 40 years of age. The arteries increase in thickness also lose their elasticity and cause blood pressure to increase.

Such thickening occurs at expense of intimate layer by the accumulation of cells and matrix deposition; There is also fragmentation of internal elastic membrane, increase and changes in crossing of collagen within vascular mean, which decreases elasticity of this layer. (Ramos C, 2010, p. 5)

These endothelial damages probably cancel out both vasodilator effect of adenosine deaminase and nitric oxide, mechanisms proposed by authors such as Ankri (1997) and González (2014).

It is likely that it is not really certain which or which garlic ingredients are involved in the reduction of blood pressure, although authors such as Singh and Singh (2008) point out that certain components of garlic (saponins and carbohydrates related to fructose) act as inhibitors of enzyme adenosine deaminase (ADA) in aorta artery.

Adenosine is present in significant amounts in garlic. If ADA enzyme is inhibited, more adenosine is available. In this way adenosine can help dilate blood vessels and relax intramural smooth muscles. Both effects lead to lower blood pressure and could be result of prolonged consumption of garlic powder, which also has a protective effect during aging. In fact, the authors point out that the higher the consumption of garlic powder, levels of enzyme nitric oxide synthetase are increased proportionally and with it levels of nitric oxide (García and Sánchez, 2000, p. 15).

It has been said that garlic inhibits the activity of the Angiotensin I converting enzyme (which transforms Angiotensin I into Angiotensin II), which is a potent vasoconstrictor and, consequently, causes elevated blood pressure. (Gómez, 2011, p. 9). According to our results, the effect of garlic on this converting enzyme does not seem to have occurred in most of our experiments.

Significant decrease in systolic blood pressure in the 70-85 age group that received the 1000 mg / day dose is only case in which one could think that angiotensin I-II converting enzyme inhibition occurred in II, is In other words, only group of subjects that received the highest dose of garlic had a significant decrease in systolic pressure. This also suggests that the mechanism that explains pressure changes in arteries is probably different when it comes to systolic than when it comes to diastolic. It should also be noted that all subjects retained their pharmacological treatments, in parallel to the experimental doses, and as observed in results of tables 1 to 4, there were always high systolic and diastolic pressures, which puts in doubt, not only hypotensive effect of garlic, but also the efficacy of drug treatment, which supposedly controlled his arterial hypertension. It is interesting to ask what is cause that a dose of 1000 mg / day had an effect only in older age group and not in the "younger ones", if it is to be expected that at greater age greater anatomical deterioration.

Ours results show that promotion and education to preserve health, are still better options to avoid the disease. Nursing practice in what is known as the first level of care, represents a high value strategy that should be promoted.

CONCLUSIONS:

Our investigation showed a dose-dependent effect. At a higher dose of garlic it is possible to expect a decrease in blood pressure. However, decrease in blood pressure does not occur homogeneously, but mechanism that leads to decrease in systolic pressure is more sensitive than that which would explain a decrease in diastolic pressure.

Although there is no consensus as to the minimum dose required to obtain beneficial changes, we suggest that it be at least 1000 mg / day, even if it is divided into two doses of 500 mg / day each.

It is evident that age and other factors such as general health status, diet, treatment adherence, dyslipidemias, lifestyle, and overweight / obesity, could influence effectiveness of garlic consumption as a hypotensive agent. However, we conclude that hypotensive effect of garlic (Allium Sativum) is still uncertain according to the results obtained in this work. Therefore, it is suggested to strengthen the practice of Nursing in the first level of care in order to avoid, as far as possible, appearance of diseases such as arterial hypertension.

REFERENCES:

1. Alonso, T.J. y Alonso, R.A. (2019). Investigación en Enfermería. Análisis de datos. Universidad Nacional Autónoma de México, México.
2. Al-Qattan, K.K., Khan, I., Alnaqeeb, M.A., Ali, M. (2003). Mechanism of garlic (Allium sativum) induced reduction of hypertension in 2K-1C rats: a possible mediation of Na/H exchanger isoform-1. Prostaglandins Leukot Essent Fatty Acids. PubMed, 69, 217–222. doi: 10.1016/S0952-3278(03)00087-5.
3. Al-Qattan, K.K., Thomson, M., Al-Mutawa'a, S., Al-Hajeri, D., Drobiova, H., Ali, M. (2006). Nitric oxide mediates the blood-pressure lowering effect of garlic in the rat two-kidney, one-clip model of hypertension. J Nutr, 136, 774S–776S.
4. Ankri, S., et al. (1997). Allicin from garlic strongly inhibits cysteine proteinases and cytopathic effects of Entamoeba histolytica. Antimicrob Agents Chemother, 41(10), 2286-8.
5. Banerjee, S.K., Mukherjee, P.K., Maulik, S.K. (2003). Garlic as an antioxidant: the good, the bad and the ugly. Phytother Res, 17, 97–106. doi: 10.1002/ptr.1281.
6. Bathaei, F., et al. (2008). Cardiovascular Effects of Allium Sativum (Garlic): An Evidence-Based Review. J Teh Univ Heart Ctr, 1, 5-10.
7. Benavides, G.A., et al. (2007). Hydrogen sulfide mediates the vasoactivity of garlic. Proc Natl Acad Sci USA, 104, 17977–17982. doi: 10.1073/pnas.0705710104.
8. Chobanian, A.V., et al. (2003). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. Jama, 289, 2560–2572. doi: 10.1001/jama.289.19.2560.
9. Cockroft, J.R., et al. (1997). Preserved endotelium-dependent vasodilation in patients with essential hypertension. N Engl J Med, 330, 1036-40.
10. Forte, P., et al. (1997). Basal nitric oxide synthesis in essential hypertension. Lancet, 349(9055), 837-42.
11. Garcia J. y Sánchez J. (2000). Efectos cardiovasculares del ajo (Allium sativum). ALAN, 50(3), 1- 23.
12. Gómez, M. (2011). Efectos del ajo sobre la tensión arterial (tesis de maestría). Recuperado de: http://repositori.uib.es/xmlui/bitstream/handle/1 1201/145881/tfm_ 2015-16_MNAH_ amg939_2.pdf?sequence=1&isAllowed=y
13. González, M., et al. (2014). Revisión bibliográfica sobre el uso terapéutico del ajo. Revista Cubana de Medicina Física y Rehabilitación, 6(1), 61-71.
14. Higdon, J. y Lawson, L. (2005). Garlic and Organosulfur Compounds. Micronutrient Information Center. Linus Pauling Institute, Oregon State University. Recuperado de: http://lpi.oregonstate.edu/infocenter/phytochemicals/garlic/#table1 accessed 24 March 08.
15. INEGI. (2015). Encuesta intercensal 2015. Principales Resultados. Recuperado de: https://www.inegi.org.mx/contenidos/programas/intercensal/2015/doc/eic_2015_presentacion.pdf
16. Kaye, A.D., et al. (2000). Analysis of responses of garlic derivatives in the pulmonary vascular bed of the rat. J Appl Physiol, 89, 353–358.
17. Ramos, C., et al. (2010). Comportamiento fisiológico cardiorespiratorio en el adulto mayor durante el ejercicio físico. Correo Científico Médico de Holguín, 14(3), 1- 12.
18. Ried, K., Frank, O. R., Stocks, N. P., Fakler, P., & Sullivan, T. (2008). Effect of garlic on

blood pressure: a systematic review and meta-analysis. BMC cardiovascular disorders, 8, 13. doi:10.1186/1471-2261-8-13)

19. Ried, K., Frank, OR, Stoks, NP. (2013). Aged garlic extract reduces blood pressure in hypertensives: a dose–response trial. European Journal of Clinical Nutrition, 67, 64–70.
20. Singh V y Singh D. (2008). Pharmacological Effects of Garlic (Allium sativum L.). ARBS Annu Rev Biomed Sci; 10:6-26.
21. Thaslima, J., et al. (2018). Effect of garlic on blood pressure in hypertensive patients. Drug Invention Today, 10(11), 2267-2269.