Effects of Garlic on Blood Pressure in Patients With and Without Systolic Hypertension: A Meta-Analysis

Kurt M Reinhart, Craig I Coleman, Colleen Teevan, Payal Vachhani, and C Michael White

BACKGROUND: Garlic has been suggested to lower blood pressure; however, studies evaluating this parameter have provided conflicting results.

OBJECTIVE: To examine the effect of garlic on blood pressure in patients with and without elevated systolic blood pressure (SPB) through meta-analyses of randomized controlled trials.

METHODS: A systematic search of MEDLINE, CINAHL, and the Cochrane Central Register of Controlled Trials was conducted to identify randomized controlled trials in humans evaluating garlic's effect on blood pressure. All databases were searched from their inception through June 26, 2008, using the key words garlic, *Allium sativum*, and allicin. A manual search of published literature was used to identify additional relevant studies. To be included in the analysis, studies must have been written in English or German and reported endpoints of SBP or diastolic blood pressure (DBP). Studies whose population had a mean baseline SBP greater than 140 mm Hg were evaluated separately from those whose population had lower baseline blood pressures. Garlic's effect on SBP and DBP was treated as a continuous variable and weighted mean differences were calculated using a random-effects model.

RESULTS: Ten trials were included in the analysis; 3 of these had patients with elevated SBP. Garlic reduced SBP by 16.3 mm Hg (95% CI 6.2 to 26.5) and DBP by 9.3 mm Hg (95% CI 5.3 to 13.3) compared with placebo in patients with elevated SBP. However, the use of garlic did not reduce SBP or DBP in patients without elevated SBP. There was only a minor degree of heterogeneity in the analyses and publication bias did not appear to influence the results.

CONCLUSIONS: This meta-analysis suggests that garlic is associated with blood pressure reductions in patients with an elevated SBP although not in those without elevated SBP. Future research should focus on the impact of garlic on clinical events and the assessment of the long-term risk of harm.

KEY WORDS: allicin, antihypertensive agents, garlic, herbals, hypertension, meta-analysis.

Ann Pharmacother 2008;42:1766-71.

Published Online, 18 Nov 2008, *www.theannals.com*, DOI 10.1345/aph.1L319

A *For Our Patients* summary of this article is available at www.ForOurPatients.info

Garlic, also known as *Allium sativum*, has been touted to have cardiovascular benefits that include lowering blood pressure and plasma lipids as well as an antiplatelet effect.[1] As such, people with hypertension may choose to use garlic for blood pressure lowering, while others with normal blood pressure may choose garlic for non–blood pressure indications.

Over 50 million Americans have hypertension.[2] These patients may be classified by hypertension severity; those whose systolic blood pressure (SBP) is greater than 140 mm Hg or whose diastolic blood pressure (DBP) is greater than 90 mm Hg are classified as having stage I hypertension, while those whose SBP is greater than 160 mm Hg or whose DBP is greater than 100 mm Hg are classified as having stage II hypertension.[2] Blood pressure reductions in hypertensive patients would be beneficial, given the association between hypertension and cardiac disease and stroke. Antihypertensive therapy decreases the incidence of myocardial infarction, heart failure, and stroke. However, blood pressure reductions could predispose normotensive patients to hypotension.

Author information provided at the end of the text.

Controlled trials have been conducted in patients with and without elevated SBP or DBP to evaluate the impact of garlic therapy on blood pressure. In total, these trials had low power to detect differences and showed blood pressure effects ranging from large reductions to small elevations. The objective of our meta-analysis was to examine garlic's effect on SBP and DBP in subjects with elevated SBP, as well as in those without elevated SBP. Patients with elevated SBP may take garlic to lower blood pressure, while those without elevated SBP may take garlic for other reasons; in individuals without elevated SBP, blood pressure reductions could be dangerous.

Methods

DATA SOURCES

We conducted a systematic search of MEDLINE, CINAHL, and the Cochrane Central Register of Controlled Trials to identify literature evaluating garlic's effect on blood pressure. All databases were searched from their inception through June 26, 2008, using the following MeSH terms and key words: garlic, *Allium sativum*, and allicin. Results were limited to randomized controlled trials in humans. A manual search of the literature (ie, review of references in each obtained study) was used to identify additional relevant studies.

STUDY SELECTION

To be included in the analysis, studies must have been written in English or German and reported endpoints of SBP or DBP. Crossover studies were included as long as they provided a 2-week or longer washout period between treatments. Studies were excluded if they were not randomized, double-blind, or placebo-controlled; if they lacked enough data for statistical pooling (eg, did not report any measures of variance); or if they did not report a baseline SBP. Two investigators (CT, PV) independently reviewed all identified abstracts or full publications for inclusion and exclusion criteria. Any disagreements were resolved through discussion with a third investigator (KMR).

DATA ABSTRACTION

Using a predefined data-abstraction tool, 3 investigators (CT, PV, KMR) independently recorded data for each included trial, with disagreements resolved through discussion. Extracted data were verified by a fourth investigator (CMW). The following information from each included trial was recorded: first author; year of publication; age and sex of the study population; type, brand, and dose of garlic being studied; and the washout period (if it was a crossover trial). When data were presented individually for different treatment groups within a study, values were recorded as a range of the reported means. For each study, the baseline and last reported SBP and DBP values were recorded along with measurements of variance.

DATA SYNTHESIS AND ANALYSIS

Studies with patients exhibiting a mean baseline SBP of greater than 140 mm Hg (and thus representative of stage I hypertensive patients) were analyzed separately from those with a lower mean baseline SBP in order to distinguish garlic's effects on hypertensive and nonhypertensive patients.

The mean change in SBP and DBP parameters from baseline was treated as a continuous variable and the weighted mean difference was calculated as the difference between the mean in the garlic and placebo groups. A DerSimonian and Laird random-effects model (a variation on the inverse variance method, which incorporates an assumption that the different studies are estimating different, yet related, treatment effects) was used in calculating the weighted mean difference and its 95% confidence interval. For parallel trials, net changes in each of these study parameters were calculated as the difference (garlic minus placebo) of the changes (baseline minus follow-up) in these mean values (also referred to as the change score). For crossover trials, net changes were calculated as the mean difference in values at the end of the garlic and placebo periods. Since variances for net changes were not reported directly for most studies, they were calculated from confidence intervals, p values, or individual variances for intervention and control groups/periods. For parallel trials in which variances for paired differences were reported separately for each group, we calculated a pooled variance for net change by standard methods. When the variance for paired differences was not reported, we calculated it from variances at baseline and at the end of follow-up. As suggested by Follmann et al.,[3] we assumed a correlation coefficient of 0.5 between initial and final values. We assumed equal variances during the trial and between intervention and placebo groups. Weighted mean differences were calculated using StatsDirect, version 2.6.2 (StatsDirect Ltd., Cheshire, England) and a random effects model.

Statistical heterogeneity was assessed by calculating a Cochrane Q statistic whereby a p value less than 0.10 was considered to represent significant heterogeneity between the trials. In addition, the level of heterogeneity was also assessed with I^2 values where an I^2 less than 25%, between 25% and 75%, and greater than 75% would represent a minor, moderate, or high degree of heterogeneity, respectively. Publication bias was tested through visual inspection of funnel plots as well as the calculation of Egger's weighted statistic (StatsDirect, version 2.6.2).

Results

Figure 1 displays the number of citations initially found upon conducting our search strategy and the number of studies excluded through the application of our prespecified inclusion and exclusion criteria. Ten trials were ultimately included in our meta-analyses: 3 studies evaluating patients with a baseline mean SBP greater than 140 mm Hg[4-6] and 7 involving patients with lower SBPs[7-13] (Table 1). One study reported the effects on both supine and standing blood pressures; however, the data presented for standing pressures lacked information needed for statistical pooling and

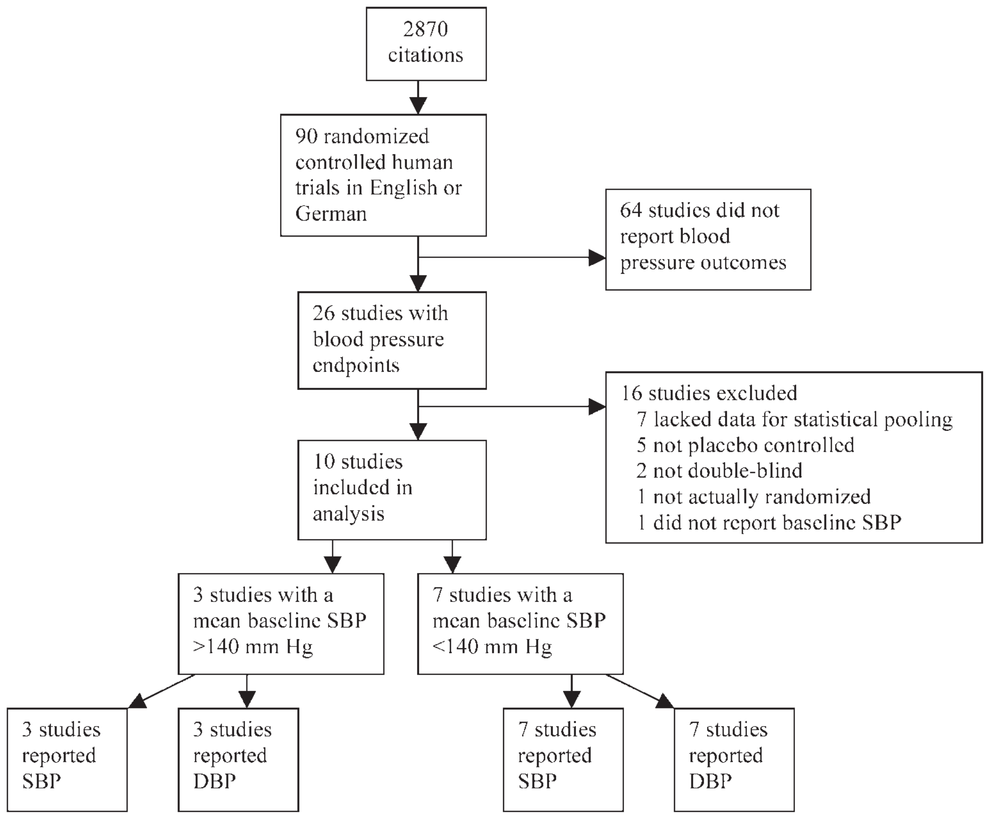

Figure 1. Flow diagram representing study selection. DBP = diastolic blood pressure; SBP = systolic blood pressure.

Table 1. Study Characteristics

Reference	Pts. (N)	Design	Type of Garlic	Daily Dose	Brand[a]	Mean Baseline SBP or Range (mm Hg)[b]	Mean Baseline DBP or Range (mm Hg)[b]
Mean baseline SBP <140 mm Hg (normotensive)							
Isaacsohn (1998)[13]	50	parallel	GP	900 mg	Kwai	119–123	72–73
Jain (1993)[7]	42	parallel	GP	900 mg	Kwai	128–129	82–83
Macan (2006)[8]	48	parallel	AGE	10 mL	Kyolic	122–127	74–82
Saradeth (1994)[9]	52	parallel	GP	600 mg	Kwai	125	81–82
Simons (1995)[11]	28	crossover	GP	900 mg	Kwai	127	80
Williams (2005)[12]	15	crossover	AGE	2.4 g	Kyolic	135	82
Zhang (2000)[10]	27	parallel	GO	12.3 mg	Cardiomax	109–117	64–72
Mean baseline SBP >140 mm Hg (hypertensive)							
Auer (1990)[4]	47	parallel	GP	600 mg	Kwai	161–171	97–102
Santos(1993)[6]	52	parallel	GP	900 mg	Kwai	143–144	89
Vorberg (1990)[5]	40	parallel	GP	900 mg	Kwai	144–145	87–91

AGE = aged garlic extract; DBP = diastolic blood pressure; GO = garlic oil; GP = garlic powder; SBP = systolic blood pressure.
[a]Kwai = Kwai brand garlic (Lichtwer Pharma GmbH, Berlin, Germany); Kyolic = Kyolic garlic (Wakunaga of America Co., Ltd., Mission Viejo, CA); Cardiomax = Cardiomax garlic (Seven Seas Ltd., Hull, UK).
[b]For studies reporting mean baseline SBP and DBP for garlic and placebo groups independently, both values are reported here as a range. Some studies reported mean baseline values for the study population as a whole and are represented by single values.

were not included.[4] Only 1 study was known to be funded by a source other than the garlic manufacturer.[12]

The results of the meta-analysis are displayed in Figure 2. In patients with elevated baseline SBP, garlic reduced SBP by 16.3 mm Hg (95% CI 6.2 to 26.5) and DBP by 9.3 mm Hg (95% CI 5.3 to 13.3) compared with placebo. However, reductions of only 0.5 mm Hg in SBP (95% CI –2.1 to 3.1) and 0.9 mm Hg in DBP (95% CI –0.9 to 2.7) were found in the group without elevated SBP.

Statistical heterogeneity was minor, as denoted by an I^2 value less than 25% in all analyses, and was not considered significant by means of the Cochrane Q statistic ($p > 0.10$ for all analyses). Publication bias was unlikely for the analyses in patients without elevated baseline SBP since the Egger's statistic was greater than 0.05; however, it could not be calculated in the analysis of subjects with elevated baseline SBP due to the small number of studies.

Discussion

Garlic appears to significantly reduce SBP and DBP by 16 and 9 mm Hg, respectively, in patients with a mean

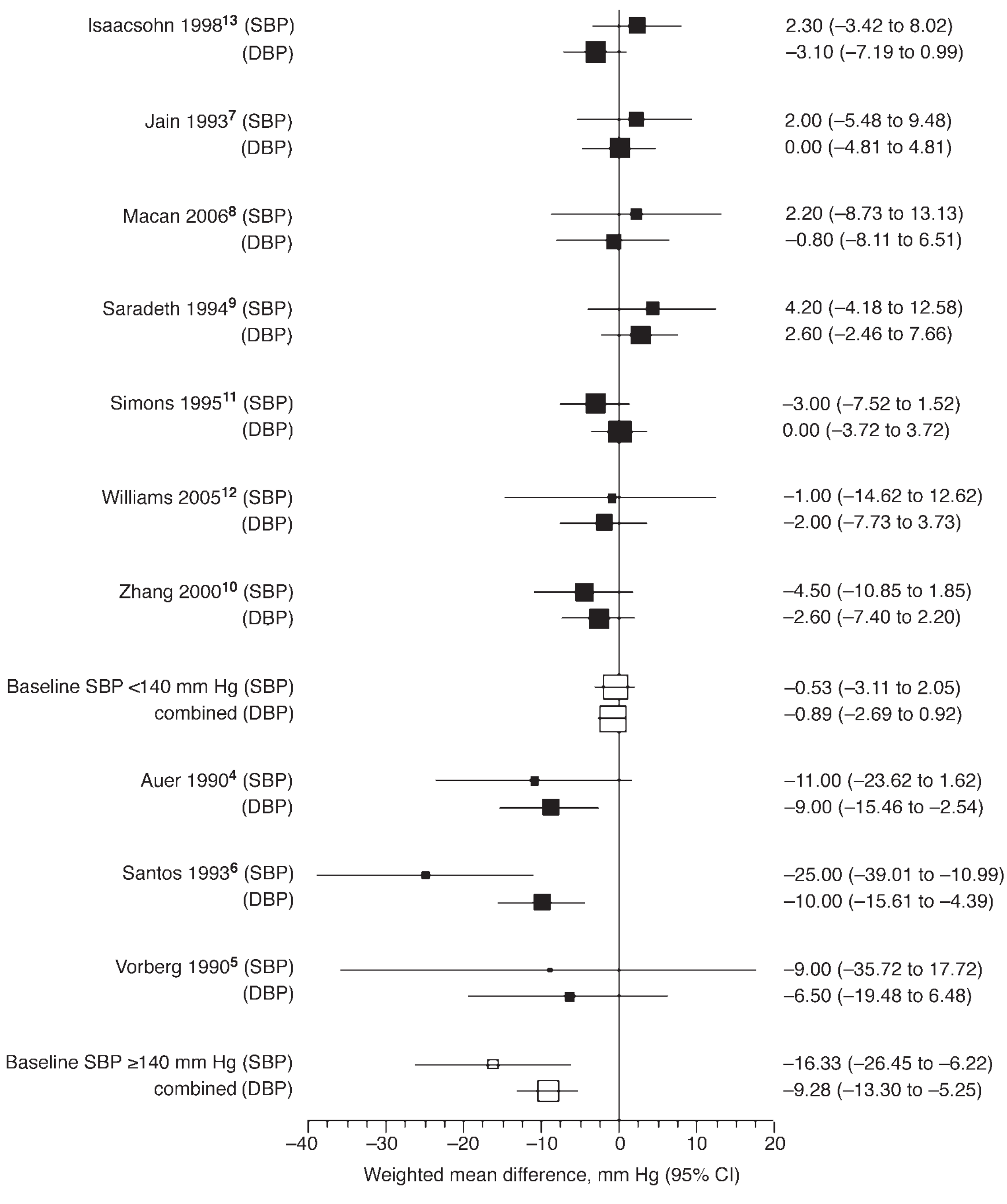

Figure 2. Forest plot results on garlic's impact on SBP and DBP. DBP = diastolic blood pressure; SBP = systolic blood pressure.

SBP greater than 140 mm Hg at baseline. This level of reduction is comparable to reductions seen with some prescription antihypertensive drugs and lends credence to the future exploration of garlic as an antihypertensive drug.[14] It is promising that observational studies not involving garlic found that blood pressure reductions in this range reduce the risk of coronary events and stroke by approximately 30% and 46%, respectively.[15-17] However, unlike other antihypertensives, the actual impact of garlic on cardiovascular and cerebrovascular events is not known. At this time, this lack of outcomes data should preclude garlic's use instead of standard antihypertensives such as thiazide diuretics, calcium-channel blockers, and angiotensin-converting enzyme (ACE) inhibitors. Also, garlic is not known to have the beneficial effects outside of blood pressure reduction seen with several other antihypertensives, such as the renoprotective effects of ACE inhibitors and does not have compelling indications for use.

Larger-scale clinical trials are needed to allow an adequate sample size to be assessed for adverse effects. While garlic can cause bad breath and body odor,[18] we cannot adequately evaluate the risk of clinical adverse effects associated with chronic use. It is possible that garlic administration has potentially serious adverse effects that were not reported in these studies; for example, an interaction between garlic and aspirin as well as other agents used to prevent thrombosis. For the time being, this is another reason not to use garlic in lieu of standard antihypertensive drugs for the treatment of hypertension.

Garlic did not impact blood pressure when we evaluated studies in which subjects' mean baseline SBP was below 140 mm Hg. This is a pharmacologic phenomenon that has been reported with some antihypertensive medications: as blood pressure gets closer to normal, antihypertensives have an attenuated effect.[14] In only 2 of the 7 studies were the average baseline SBPs at or below 120 mm Hg, the level considered to be normal SBP. As such, the majority of trials in that analysis represented patients with prehypertension; therefore, we cannot recommend garlic specifically for its blood pressure–lowering effects in patients with prehypertension. Also, the effects of garlic on patients with diastolic hypertension alone were not evaluated. Garlic may have clinical utility in reducing total cholesterol and providing an antiplatelet effect[1]; because it may not lower blood pressure in patients with normal blood pressure, the risk of hypotension should be minimal.

Our findings are bound by several limitations. Beyond typical limitations of meta-analyses such as the inability to control the biases of included studies, ours is limited by our use of aggregate data. We grouped patients into categories based on mean baseline blood pressure, and there are a range of blood pressures that make up the mean, which could result in aggregation or ecological bias. In other words, some subjects included in the elevated SBP analysis could have had normal or even low blood pressure and some subjects in the studies used for the nonelevated SBP analysis may have had high blood pressure. Secondly, garlic products are not controlled by the Food and Drug Administration and therefore could theoretically have numerous constituents. It is possible that there are inter- and intrabrand differences in the concentrations of active constituents of garlic products, their bioavailability, and contaminants that could have increased heterogeneity; however, this was not seen in our meta-analysis. In our analysis of studies with patients whose mean baseline SBP was greater than 140 mm Hg, only the Kwai brand of garlic was used, but other brands of garlic were used in 3 of the 7 studies in which patients had a lower mean baseline SBP. Other brands of garlic require evaluation in hypertensive subjects. Because funding by the manufacturer of Kwai could not be ruled out for the 3 studies used in the elevated SBP analysis, further, independently funded studies with Kwai are also warranted. Overall, although the results of this meta-analysis show a promising future for garlic as an antihypertensive, much more research is needed to better characterize its effects.

Conclusions

In hypertensive patients, our meta-analysis found that garlic selectively lowered SBP by 16 mm Hg and lowered DBP by 9 mm Hg. On the other hand, garlic did not lower blood pressure in nonhypertensive subjects. Future research focused on a larger number of hypertensive subjects may validate this finding and assess garlic's long-term risk of harm.

Kurt M Reinhart PharmD, Fellow, Cardiovascular Outcomes, Hartford Hospital, Hartford, CT

Craig I Coleman PharmD, Methods Chief, Health Outcomes, Policy, and Economics Collaborative Group, University of Connecticut and Hartford Hospital

Colleen Teevan BSPharm, PharmD Student, School of Pharmacy, University of Connecticut, Storrs, CT

Payal Vachhani BSPharm, PharmD Student, School of Pharmacy, University of Connecticut

C Michael White PharmD, Director, Health Outcomes, Policy, and Economics Collaborative Group, University of Connecticut and Hartford Hospital

Reprints: Dr. White, University of Connecticut and Hartford Hospital, 80 Seymour St., Hartford, CT 06102, fax 860/545-2277, cmwhite@harthosp.org

References

1. Banerjee SK, Maulik SK. Effect of garlic on cardiovascular disorders; a review. Nutr J 2002;1:4. DOI 10.1186/1475-2891-1-4
2. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003;42:1206-52.
3. Follmann D, Elliott P, Suh I, Cutler J. Variance imputation for overviews of clinical trials with continuous response. J Clin Epidemiol 1992;45:769-73.

4. Auer W, Eiber A, Hertkorn E, et al. Hypertension and hyperlipidaemia: garlic helps in mild cases. Br J Clin Pract 1990;69(suppl):3-6.
5. Vorberg G, Schneider B. Therapy with garlic; results of a placebo-controlled, double blind study. Br J Clin Pract 1990;69(suppl):7-11.
6. Santos OSDA, Grünwald J. Effect of garlic powder tablets on blood lipids and blood pressure—a six month placebo controlled, double blind study. Br J Clin Res 1993;4:37-44.
7. Jain AK, Vargas R, Gotzkowsky S, McMahon FG. Can garlic reduce levels of serum lipids? A controlled clinical study. Am J Med 1993;94:632-5.
8. Macan H, Uykimpang R, Alconcel M, et al. Aged garlic extract may be safe for patients on warfarin therapy. J Nutr 2006;136(3 suppl):793S-5S.
9. Saradeth T, Seidl S, Resch KL, Ernst E. Does garlic alter the lipid pattern in normal volunteers? Phytomedicine 1994;1:183-5.
10. Zhang XH, Lowe D, Giles P, et al. A randomized trial of the effects of garlic oil upon coronary heart disease risk factors in trained male runners. Blood Coagul Fibrinolysis 2000;11:67-74.
11. Simons LA, Balasubramaniam S, Konigsmark MV, Parfit A, Simons J, Peters W. On the effect of garlic on plasma lipids and lipoproteins in mild hypercholesterolaemia. Atherosclerosis 1995;113:219-25.
12. Williams MJ, Sutherland WH, McCormick MP, Yeoman DJ, Jong SA. Aged garlic extract improves endothelial function in men with coronary artery disease. Phytother Res 2005;19:314-9.
13. Isaacsohn JL, Moser M, Stein EA, et al. Garlic powder and plasma lipids and lipoproteins. A multicenter, randomized, placebo-controlled trial. Arch Intern Med 1998;158:1189-94.
14. Sasso FC, Carbonara O, Persico M, et al. Irbesartan reduces the albumin excretion rate in microalbunuric type 2 diabetic patients independently of hypertension. Diabetes Care 2002;25:1909-13.
15. MacMahon S, Peto R, Cutler J, et al. Blood pressure, stroke, and coronary heart disease. Lancet 2000;335:765-74.
16. Cook NR, Cohen J, Hebert P, Taylor JO, Hennekens CH. Implications of small reductions in diastolic blood pressure for primary prevention. Arch Intern Med 1995;155:701.
17. Ogden LG, He J, Lydick E, Whelton PK. Long-term absolute benefit in lowering blood pressure in hypertensive patients according to the JNC VI risk stratification. Hypertension 2000;35:539-43.
18. Ackermann RT, Mulrow CD, Ramirez G, Gardner CD, Morbidoni L, Lawrence VA. Garlic shows promise for improving some cardiovascular risk factors. Arch Intern Med 2001;161:813-24.

Los Efectos de Ajo en la Presión Sanguínea en Pacientes con y sin Hipertensión Sistólica: Un Meta-Análisis

KM Reinhart, CI Coleman, C Teevan, P Vachhani, y CM White

Ann Pharmacother 2008;42:1766-71.

EXTRACTO

TRASFONDO: Se ha sugerido que el ajo baja la presión sanguínea, sin embargo, los estudios que han evaluado éste parámetro han obtenido resultados conflictivos.

OBJETIVO: Examinar el efecto de ajo en la presión sanguínea en pacientes con y sin presión sanguínea sistólica elevada mediante el uso de un meta-análisis de los estudios controlados aleatorizados publicados.

MÉTODOS: Se realizó una búsqueda sistemática de la literatura durante el período de junio de 2008 para identificar los estudios controlados aleatorizados que evaluaban el efecto de ajo en la presión sanguínea. Los estudios que informaban resultados en poblaciones con presiones sanguíneas sistólicas de base de más de 140 mm Hg se evaluaron separadamente de los estudios con sujetos con presiones de base menor. El efecto de ajo en la presión sanguínea sistólica (SBP) y la presión sanguínea diastólica (DBP) se consideró una variable contínua y la diferencia promedio ponderada (weighted mean differences) se calculó utilizando un modelo de efecto aleatorio.

RESULTADOS: Se incluyeron 10 estudios en el meta-análisis. Tres de las investigaciones fueron hechas con pacientes con presión sistólica elevada y 7 con sujetos sin elevaciones en la presión sanguínea sistólica. A base del meta-análisis, se encontró que el ajo redujo la SBP 16.3 mm Hg (95% CI 6.2 y 26.5) y la DPB 9.3 mm Hg (95% CI 5.3 y 13.3) al comparar con el placebo en pacientes que inicialmente presentaban SBP elevada. El ajo no redujo las presiones sanguíneas sistólicas o diastólicas en pacientes que no tuvieran elevacion en SBP. Solo se encontró un pequeño grado de heterogenicidad en el análisis y el sesgo de publicación aparentó no afectar los resultados.

CONCLUSIONES: Este meta-análisis sugiere que el ajo se asocia con reducciones en la presión sanguínea en pacientes con SBP elevado, pero no disminuyó la presión sanguínea en pacientes que no tuvieran SBP elevada. Investigaciones futuras deben enfocar en el impacto de ajo en eventos clínicos y en evaluar el riesgo de daño a largo plazo.

Traducido por Mirza D Martinez

Les Effets de l'Ail sur la Tension Artérielle chez des Patients Porteurs ou non d'Hypertension Systolique: Une Méta-Analyse

KM Reinhart, CI Coleman, C Teevan, P Vachhani, et CM White

Ann Pharmacother 2008;42:1766-71.

RÉSUMÉ

ÉTAT DES CONNAISSANCES: On a suggéré que l'ail avait des propriétés hypotensives. Cependant, les études qui ont porté sur ce sujet ont généré des résultats conflictuels.

OBJECTIFS: Appliquer la méthode de la méta-analyse sur les études randomisées et contrôlées portant sur les effets de l'ail sur la tension artérielle de patients avec et sans tension artérielle systolique élevée.

MÉTHODE: Une révision systématique de la littérature a été réalisée jusqu'en juin 2008 pour identifier les études randomisées et contrôlées qui évaluaient l'effet de l'ail sur la tension artérielle. Les études qui portaient sur une population dont la tension artérielle systolique (TAS) de base >140 mm Hg ont été évaluées séparément de celles portant sur des tensions artérielles de base plus basses. Les effets de l'ail sur la TAS et sur la tension artérielle diastolique (TAD) ont été traités comme une variable continue et la différence moyenne pondérée a été calculée avec le modèle des effets aléatoires.

RÉSULTATS: Dix études ont été incluses dans l'analyse, 3 avec des patients avec une TAS élevée et 7 avec des patients n'ayant pas de TAS élevée. La méta-analyse a révélé une réduction de la TAS de 16.3 mm Hg (IC 95% 6.2 à 26.5) et la TAD de 9.3 mm Hg (IC 95% 5.3 à 13.3) par rapport au placebo chez les patients avec hypertension systolique, mais n'a réduit ni la TAS ou la TAD chez les patients sans atteinte de la tension artérielle à la base. Il y avait un faible degré d'hétérogénéité dans l'analyse et un biais de publication n'a pas semblé influencer les résultats.

CONCLUSIONS: Cette méta-analyse suggère que l'utilisation de l'ail réduit la tension artérielle chez les patients dont la tension artérielle systolique est élevée mais ne présente aucun effet si la tension artérielle initiale n'est pas élevée. Les recherches futures devraient porter sur la survenue d'événements cardiovasculaires et évaluer le risque à long terme.

Traduit par Marc Parent