Effects of *Allium sativum* (Garlic) on systolic and diastolic blood pressure in patients with essential hypertension

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Abstract: The present study evaluated the effects of garlic on blood pressure in patients with essential hypertension. Patients (n=210) with stage 1 essential hypertension were divided into 7 groups named as A, B, C, D, E, F and G. Each group comprised of 30 patients. Each patient in group A, B, C, D and E has received garlic tablets at the dose of 300/mg. 600/mg, 900/mg, 1200/mg and 1500/mg in divided doses per day respectively for 24 weeks while Group F & group G were given tablet atenolol and placebo respectively. Blood pressure readings were recorded at weeks 0, 12 and 24. Present study showed significant decrease in both Systolic and Diastolic blood pressure in both dose and duration dependent manner. In each garlic treated group, significant reduction in SBP and DBP (p<0.005) were observed when compared with atenolol (P<0.005) and placebo.

Keywords: *Allium sativum,* garlic, hypertension, systolic blood pressure, diastolic blood pressure.

INTRODUCTION

Hypertension is an unvoiced slayer, since it exists with no apparent symptoms (Ford *et al.,* 2009). It is an imperative global public health problem and is most extensively documented amendable menace for cardiovascular disease, stroke and renal dysfunction (Erem *et al.,* 2009), affecting an estimated 1 billion individuals worldwide (Chobanian *et al.,* 2003). The population of hypertensives is estimated to increase by 60% to 1.56 billion by 2025, (Chockalingam, 2007) which will be approximately 29% of the worldwide adult population (Kearney *et al.,* 2005). The prevalence as well as unawareness about hypertension and its complications is also quite high in Pakistan (Abbas *et al.,* 2009). The only National Health Survey of Pakistan reported shocking fig of about 18 % of adults above 15 years and 33% of adults above 45 years suffering from hypertension. Moreover, despite a high prevalence of hypertension, less than 3 % had their blood pressure (BP) controlled (Jafar *et al.,* 2005).

Owing to the worldwide rise in the incidence and socioeconomic burden of hypertension**,** it is quite important to discover pharmacological preparation which does not only provide good blood pressure control but also proved to be harmless and cost effective. Despite of the introduction of new therapies and education programs, treatment of hypertension remains suboptimal and many hypertensive patients require more than 2 drugs to achieve recommended blood pressure levels (Volpe *et al.,* 2010).

The utilization of natural substances has increased for various diseases amongst general public over last few years not only because of their easy availability without

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prescription, cost and appointment to the health care professionals, but also owing to the belief that natural substances has less adverse effects as compared to synthetic medicines (Vora *et al.,* 2005). *Allium sativum,* otherwise known as Garlic is commonly used around the world for both culinary and medicinal purposes (Rahman, 2001). Keeping in mind, the increasing interest in alternative therapies for hypertension the present study was designed to evaluate the effects of garlic on blood pressure with different doses and comparatively longer duration of 24 weeks in patients with stage 1 essential hypertension.

MATERIAL AND METHOD

This was a 24 week, single-blind, placebo controlled study, conducted simultaneously in different primary health care centers in Karachi, Pakistan in cooperation with registered medical practitioners. Research protocol has been approved by Board of advanced studies and Research of the University of Karachi.

Patients with newly diagnosed stage I essential hypertension (n=210) were enrolled and divided into 7 groups named as A, B, C, D, E, F and G. Each group comprised of 30 patients. Patients in group A, B, C, D and E has received garlic tablets at the dose of 300/mg. 600 mg, 900/mg, 1200 /mg and 1500/mg in divided doses per day respectively for 24 weeks. Group F has received atenolol 100 mg once daily for 24 weeks, while patients in group G were given placebo for same duration.

Prior to enrollment, screening examination was done; inclusion and exclusion criteria were evaluated. Informed and written consent was taken from each study participant. Patients were advised at time of enrollment

not to amend their usual garlic or onion intake and to maintain their usual diet throughout the study period. Patients were also motivated to keep their nutritional plan, physical activity and general life style as constant as possible. The patients were forbidden to take any other drug throughout the study period and were advised to come for follow up at fortnightly interval. At each visit, blood pressure readings were taken in sitting position after giving 10 minute rest to the patient with a mercury sphygmomanometer having cuff size of 14×54 cms.

Inclusion criteria
Patients of either sex, aged between 20-70 years, with newly diagnosed stage 1 essential hypertension (systolic blood pressure between 140 to 159 mmHg and diastolic blood pressure between 90 to 99 mmHg.

Exclusion criteria
Patients having history of allergy to garlic or β-blockers, patients with stage 2 & 3 hypertension, pregnant or lactating women, patients having history of ischemic heart disease, established coronary artery disease, heart failure, bradycardia, liver and kidney dysfunction, Patients who taking systemic steroids, androgens, or any other drug known to have interaction with antihypertensive agents and if they are known to have any other concurrent medical illness.

STATISTICAL ANALYSIS

Statistical analysis was done by using one-way analysis of variance (ANOVA) followed by Tukey post-hoc test. Statistical P value less than 0.05 was considered significant.

RESULTS

Table 1 shows the demographic distinctiveness of the study population. The patients were men (60%) and women (40%). The mean age was 48 years in garlic treated group and 50 years in atenolol treated group (range 25-70 years) (table 1). Modifications in the systolic and diastolic blood pressure were evaluated at week 0 and week 12 and week 24 (tables 2 & 3).

Table 1: Demographic data of hypertensive patients

	Placebo treated group (n=30)	Garlic treated group(n=150)	Atenolol treated group (n=30)
Men	16	90	17
Women	14	60	13
Age (years)	45±4.87	48±5.04	50±5.80
Body weight (kg)	66.5±7.45	68.2±10.45	65±9.80
Height (cm)	166.4±7.63	165.2±8.8	167.60±9.20

Among the 210 patients initially registered in this study, 192 patients have completed the study protocol. Out of

the dropped 18 patients, 3 patients were dropped from placebo treated group, 2 due to vague abdominal discomforts and headache and refused to continue the protocol while 1 patient was found to have uncontrolled high blood pressure and was dropped at 5th week of the study. The remaining patients were dropped from different garlic treated groups, 8 has not return for follow-up after 4 weeks of study due to unidentified reason, 4 patients say no to give the blood samples for biochemical analysis so were forbidden to continue the study. 3 patients were dropped in the garlic treated group G, who reported heart burn in the first week of study and refused to take any further treatment.

Table 2: Changes in Systolic blood pressure from week 0 to week 12 and week 24 after treatment with garlic at different doses, placebo and Atenolol

Groups	Week 0 (n=30)	Week12 (n=27)	Week24 (n=27)
GA Garlic 300 mg	145.0± 0.706	143.4± 0.669	142.7± 0.644**
GB Garlic 600 mg	145.3± 0.792	143.6± 0.645	141.0± 0.577***
GC Garlic 900 mg	145.0± 0.800	141.8± 0.706**	138.9± 0.569***
GD Garlic 1200 mg	143.9± 0.818	140.8± 0.811**	137.2± 0.861***
GE Garlic 1500 mg	145.2± 0.679	141.6 ± 0.696***	137.6± 0.587***
GF Atenolol 50/100 mg	147.8± 0.898	139.3± 0.896***	138.6± 0.815***
GG Placebo	130.9± 0.892	129.7± 0.944	130.7± 0.850

(P<0.05);*(P<0.005) when compared from week 0 n=no of patients
Figures are in (Mean±SEM)
All observations were measured in mmHg.
GA=Garlic 300 mg, GB=Garlic 600 mg, GC=Garlic 900 mg, GD=Garlic 1200/mg, GE=Garlic 1500/mg, GF=Atenolol, GG=placebo

The result in the present study showed significant drop off in both SBP and DBP in both dose dependent and duration dependent manner when compared with placebo and standard antihypertensive agent Atenolol (tables 2 and 3).

Significant fall in SBP was observed with garlic at all doses when compared with placebo at week 0, week 12 and week 24 (table 2 and fig. 1). When compared statistically, on week 12 and 24 significant difference (P<0.005) was seen between garlic at all doses and placebo treated groups. When different doses of garlic are compared, significant difference was seen between different doses with greater and comparable reduction in systolic blood pressure observed at higher doses of 900 mg, 1200/mg and 1500/mg.

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Table 3: Changes in Diastolic Blood Pressure from week 0 to week 12 and week 24 after treatment with Garlic at different doses, placebo and Atenolol

Groups	DBP Week 0 (n=30)	DBP Week 12 (n=27)	DBP Week 24 (n=27)
GA Garlic 300 mg	93.15± 0.543	91.89± 0.540	91.70± 0.514
GB Garlic 600 mg	93.11± 0.521	91.74± 0.390**	89.74± 0.379***
GC Garlic 900 mg	92.79± 0.515	90.00± 0.617**	88.63± 0.512***
GD Garlic 1200 mg	92.97± 0.494	89.75± 0.475***	86.70± 0.598***
GE Garlic 1500 mg	91.93± 0.446	89.59± 0.370***	86.96± 0.454***
GF Atenolol 50/100 mg	98.26± 0.657	92.04± 0.561***	89.15± 0.494***
GG Placebo	94.33±0.430	95.26±0.418	95.37±0.221

(P<0.05);*(P<0.005) when compared from week 0 n=no of patients
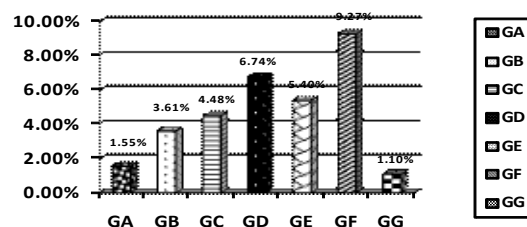Figures are in (Mean±SEM)
All observations were measured in mmHg.
GA=Garlic 300/mg, GB=Garlic 600/mg, GC=Garlic 900/mg, GD= Garlic 1200/mg, GE=Garlic 1500/mg, GF=Atenolol, GG=placebo

Significant reduction in diastolic blood pressure was observed with garlic at all doses when compared with placebo at week 0, week 12 and week 24 (table 3, fig. 2). When compared statistically, on week 12 and 24, highly significant difference (P<0.005) was seen between garlic at all doses and placebo treated groups. The difference in DBP on the average showed slightly higher reduction among garlic treated groups as compared to placebo at week 24 as compared to week 12. Highly significant reduction in DBP was seen at higher doses of garlic as compared to lower doses, when compared from week 0 to week 24. Garlic preparation used in our study was found to produce significant and analogous reduction in both systolic and diastolic blood pressure when compared with atenolol at week 12 and 24 (table 2&3; figs. 1 & 2).
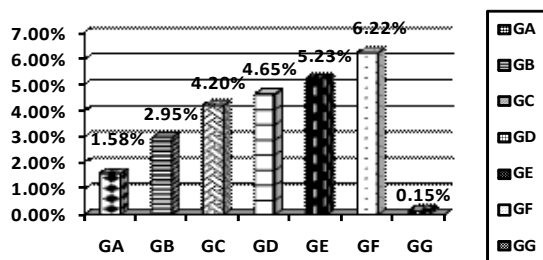
Fig. 1: % Changes in Systolic Blood Pressure from week 0 to week 24 with Garlic (different doses), Atenolol and Placebo.
GA=Garlic 300/mg, GB=Garlic 600/mg, GC=Garlic 900/mg, GD=Garlic 1200/mg, GE=Garlic 1500/mg, GF=Atenolol, GG=placebo.

Fig. 2: % Changes in diastolic blood pressure from week 0 to week 24 with Garlic (different doses), Atenolol and Placebo.
GA=Garlic 300/mg, GB=Garlic 600/mg, GC=Garlic 900/mg, GD=Garlic 1200/mg, GE=Garlic 1500/mg, GF=Atenolol, GG=placebo.

DISCUSSION

The present study monitored the antihypertensive effects of garlic with respect to its ability to incite a decrease in systolic and diastolic blood pressure and to discover the time taken for this reduction in comparison with 'placebo' and one of the standard antihypertensive agent 'Atenolol' in patients with stage 1 essential hypertension. Blood pressure measurements were evaluated at baseline i.e at week 0, week 12 and week 24.

The results observed in the present study demonstrated significant reduction in both systolic and diastolic blood pressure when compared from week 0 to week 12 and week 24. The reduction in SBP and DBP was found to be significantly higher when compared with placebo but analogous when compared with atenolol. Greater reduction in blood pressure is observed at higher doses of garlic and with the increase in the duration of therapy.

Although animal studies (Han *et al.*, 2011; Elkayam *et al.*, 2001; Al-Qattan *et al.*, 2001; Banerjee *et al.*, 2002; Han *et al.*, 2011) showed beneficial antihypertensive effects of garlic, however clinical trials (Zhang *et al.*, 2001; Turner *et al.*, 2004; Qidwai *et al.*, 2000; Pittler *et al.*, 2007; Ackermann *et al.*, 2001) on garlic preparations and blood pressure in humans remained unconvincing and inconsistent. The present study is unique from previous clinical trials as this is the first time that effects of garlic were observed in comparison with atenolol, in a duration and dose dependent manner in patients with stage 1 essential hypertension for comparatively longer duration of 24 weeks.

The findings in present study are in accordance with the previous clinical trials (Andrianova *et al.*, 2002; Sobenin *et al.*, 2009) that compared the antihypertensive effects of "Kwai" with long acting garlic preparation in patients with mild to moderate hypertension and reported

reduction in both systolic and diastolic blood with Allicor, but only in systolic blood pressure with Kwai. The reason for not finding reduction in diastolic blood pressure is not without ambiguity as we found significant reduction in both SBP and DBP with Kwai tablets in both dose and duration dependent manner.

The result in our study also matches with Auer *et al.,* 1990 who reported reduction of diastolic blood pressure from 102 to 91 mmHg after eight weeks and to 89 mmHg after 12 weeks. Our study is also in accordance with double-blind study by Vorberg *et al.*, 1990 that observed the antihypertensive effects of garlic in hypercholesterolemic patients and reported significant reduction in total cholesterol, triglycerides and blood pressure with garlic as compared to placebo. The only difference is in patient's population and study protocol as we have observed the effects of garlic in hypertensive patients in comparison with standard antihypertensive "atenolol" and placebo for longer duration of 24 weeks.

Our findings are also in accordance with McMahon who evaluated the effects of a garlic at a large dose (2400/mg) in patients with severe hypertension and reported a significant reduction in diastolic blood pressure except that we have observed significant reduction in both systolic and diastolic blood pressure with garlic at comparatively lower doses of 900/mg, 1200/mg and 1500/mg.

The antihypertensive effects observed in this study are also in agreement with the meta-analysis by Ried *et al.,* 2008 and Reinhart *et al*., 2008 which advocate garlic supplementation exerts a hypotensive effect compared to placebo, in particular in individuals with high blood pressure (SBP≥140 mm Hg, DBP≥90 mm Hg) and proved a mean decrease of 4.6 ± 2.8 mm Hg for SBP in the garlic group compared to placebo. The hypotensive effects of garlic were reported to be comparable to those of beta-blockers, angiotensin converting enzyme inhibitors (ACEI), and angiotensin II type 1 receptor antagonists (Ried *et al.,* 2008).

It has been reported that decrease in systolic blood pressure of 10-12 mmHg and diastolic blood pressure 5-6 mmHg significantly decrease cardiovascular risk by 8–20% (McInnes, 2005). In the present study a reduction of 7.6 mmHg (5.23%) in SBP and 6.27 mmHg (6.74%) in DBP with garlic at week 24 has been observed as compared to atenolol in which reduction in SBP was 9.2 mmHg (6.22%) and diastolic blood pressure was 9.1 mmHg (9.27%). This confirms our hypothesis that garlic can be a good alternative or addition in antihypertensive regimen for reducing cardiovascular related morbidity.

The present study contradicts with some previous clinical trials (Turner *et al.,* 2004; Capraz *et al.,* 2007) which reported insignificant effect of garlic on blood pressure. The possible reason for this could be the short duration of these studies for only 3 weeks and 8 weeks respectively and were conducted in normolipidemic volunteers.

Garlic ability to lower blood pressure has been linked to its hydrogen sulphide production and allicin content which is reported to have angiotensin II inhibiting and vasodilating effects (McMohan *et al.,* 1993). Garlic was reported to lower BP by modulating the activity of several mechanisms including the prostaglandin system, renin-angiotensin system, and renal tubular transport mechanisms. Another possible mechanism by which garlic might induce its hypotensive effect could be through the direct and indirect vasodilatory actions of NO. Garlic was reported to enhance the synthesis of NO (Al-Qattan *et al.,* 2001). Invention and function of both endothelium-derived relaxing factor (NO) and constricting factors like endothelin-1 is found to be altered with garlic (Tripathi, 2009). The gamma-glutamylcysteines are the compounds present in garlic which may decrease blood pressure, as demonstrated by their ability to inhibit angiotensin-converting enzyme (Omar *et al.,* 2007). Garlic-derived compounds are converted to hydrogen sulfide by red blood cells in vitro (Benavides *et al.,* 2007). Hydrogen sulfide, a gaseous signaling molecule produced by some cells within the body, acts as a vasodilator (relaxes blood vessels) and thus may have cardio protective properties (Lefer, 2008).

CONCLUSION

The present study has demonstrated significant hypotensive effects of garlic as compared to placebo and showed comparable effects with that of atenolol. Garlic could be a good addition in combination therapy for hypertension. Comprehensive clinical trials of longer duration, using standardized garlic preparations are desirable to confirm the findings of present study.

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