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Effect of Grape Seed Extract in Subjects with Pre-Hypertension

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Summary

This study was undertaken to determine whether grape seed extracts (GSE) which contain powerful vasodilator phenolic compounds lower blood pressure (BP) in subjects with pre-hypertension. The subjects were randomized into a placebo or an experimental group (GSE at a dose of 300 mg/day) and treated for 8 weeks. Serum lipids and blood glucose were measured at the beginning of the study and at the end. BP was recorded using an ambulatory monitoring device at the start of the treatment period and at the end. Both the systolic and diastolic blood pressures were lower after treatment with GSE as compared with placebo. There were no significant changes in serum lipids or blood glucose values. These findings suggest that GSE could be used as a nutraceutical in a lifestyle modification program for patients with pre-hypertension.

Introduction

Hypertension affects approximately 60% of adults in the U.S. (1) and remains a major cause of morbidity and mortality. Despite the availability of numerous antihypertensive medications, control of blood pressure to optimal levels remains inadequate in most patients. The prevalence of pre-hypertension alone in the U.S. is 31% (1). It is defined by the Joint National Committee on Prevention, Detection, evaluation, and Treatment of High Blood Pressure in its seventh report (JNC 7) as a systolic blood pressure between 120 and 139 mmHg and/or a diastolic blood pressure between 80 and 89mmHg. Current guidelines recommend that these individuals should be managed by dietary and lifestyle modifications alone (2).

There is evidence that a diet rich in vegetables and fruit has a beneficial

effect on blood pressure. This effect has been attributed to the presence of phenolic compounds in the plant products. These compounds have also been shown to have vasodilator effects (3), (4). Of all the phenolic compounds, those derived from grape seeds appear to have received the most attention, possibly because of their involvement with the French Paradox (5). These extracts have also been shown to activate endothelial nitric oxide synthase (eNOS) (3), and up-regulate eNOS in cultured endothelial cells (6).

The investigation reported here was undertaken to examine the effect of a well characterized extract of grape seed on blood pressure in subjects with pre-hypertension. The extract used had been previously shown to cause an endothelium dependent relaxation in guinea pig (7) aortic rings and to reduce blood pressure in humans with the metabolic syndrome (8). The study was designed as a placebo controlled double blind trial.

Methods

The study was approved by the Institutional Review Board of the University of California. The study was conducted on a convenience sample of 66 adults (age 25-80 years) who were screened for pre-hypertension. Those with average day time blood pressures which met the JNC 7 criteria for pre-hypertension (systolic blood pressures between 120 and 139 mmHg and diastolic blood pressures between 80 and 89 mmHg) were enrolled in the trial. The exclusion criteria were as follows: smokers (abstinence for < 1 year), clinical evidence of coronary artery, pulmonary, gastro intestinal or renal disease, consumption of prescription medications and vitamin preparations.

After baseline biochemical and hematological parameters were measured, all subjects commenced a two-week placebo run-in period. At the end of two weeks, the subjects had a second 24 hour ambulatory blood pressure measurement and were randomized subsequently to receive a capsule containing either a placebo or a grape seed extract (300 mg/day). The GSE used in this study was Meganatural BP ® (Polyphenolics Inc., Madera, California). The subjects were advised to maintain their usual level of activity and diet. The latter was monitored by examining a 4-day food diary which was completed at the start and at the end of the study. After a further 8 weeks, a final 24-hour ambulatory blood pressure was recorded and blood was drawn for measurement of biochemical and hematological parameters.

The primary endpoints were the mean day-time systolic and diastolic blood pressures. Secondary endpoints were the changes in serum lipids and oxidized LDL. The oxidized LDL concentrations were measured using an ELISA technique by Shiel Laboratories, New York.

Results

Sixty six subjects were screened for the study and 32 met the criteria for pre-hypertension. Two refused to participate in the trial and remaining 30 were randomized. The baseline clinical data are given in Table 1. There were no significant differences in the baseline parameters in these subjects.

Table 1. Baseline Parameters

	Placebo	GSE
Age (yr)	54±3	50±2.5
Male/female	26.9±1	26.3±2
Total cholesterol (mg/dl)	204±9	200±10
LDL (mg/dl)	134±9	128±9
HDL (mg/dl)	48 ±3	55±4
Triglycerides (mg/dl)	100±12	146±18
Oxidized LDL (mU/l)	43.3±3	41.2±3

At the end of 8 weeks both systolic and diastolic blood pressures in the group receiving GSE were significantly lower than those in the placebo group. These findings are summarized in Table 2.

There were also no changes in the serum total, LDL and HDL cholesterol values in both groups. An interim analysis was performed on the oxidized LDL values after 8 subjects in each group had completed the study. It was found that the baseline values were similar in both groups (Table 1) and the there were no significant changes after two months in either group. No additional measurements were undertaken on the other subjects.

Conclusions

The findings of this randomized controlled trial indicate that GSE when administered at a dose of 300 mg/day reduced both systolic and diastolic blood pressure in subjects with pre-hypertension as defined by JNC 7. The unique aspect of this study is that blood pressure was recorded using a ambulatory device which measured blood pressure over a twenty-four hour period as opposed to a clinic blood pressure measurement. The ambulatory blood pressure values are usually lower than clinic readings. In most individuals, the blood pressure decreases by 10% to 20% during the night. In this report we presented data relating to day-time blood pressures only.

It was found that GSE reduced both systolic and diastolic blood pressure in these subjects with pre-hypertension. JNC 7 recommends that patients with pre-hypertension should be managed by inducing lifestyle changes such as

Table 2. Initial and final blood pressures (mmHg)

	GSE		Placebo	
	Systolic	**Diastolic**	**Systolic**	**Diastolic**
Initial	134 ± 2	79 ± 2	133 ± 2	79 ± 2
Final	126 ± 2	74 ± 2	133 ± 2	81 ± 2
P	**0.003**	**<0.05**	**NS**	**NS**
N = 15: Power at alpha 0.05 is 0.86 for systolic BP				

diet, exercise and stress management. It is suggested that GSE could be used as a nutraceutical adjunct in the management of these patients.

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