

## Assessment of Quality of Life in a Randomized Clinical Trial of Candesartan Only or in Combination With DASH Diet for Hypertensive Patients

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### Abstract

**Objectives.** A randomized clinical trial was used to compare the effects of an angiotensin type 1 receptor inhibitor, candesartan, singly or in combination with a reducing sodium diet, the DASH diet, on the quality of life (QOL) in outpatients with hypertension.

**Methods.** After a 2-week wash out period with placebo, 102 patients with mild to moderate hypertension were randomly assigned to receive candesartan (8 to 16 mg per day), and 99 patients were assigned to follow the DASH diet in addition to the same dose of candesartan, both for 16 weeks. Patients completed the Subjective Symptoms Assessment Profile questionnaire, just before treatment and at the end of treatment. ANOVA was used to analyze the QOL-score changes over time and compare treatments.

**Results.** Resting blood pressures were significantly reduced by the combination of candesartan and DASH diet ( $p < 0.005$ ). Significant improvement was demonstrated for the mental component scores after 16 weeks of treatment with the combination of candesartan and DASH diet ( $p < 0.03$ ).

**Conclusions.** Angiotensin type 1 receptor blockade with a therapeutic dosage of candesartan maintains significant control of blood pressure and may improve QOL-scores, especially when combined with a reducing sodium diet.

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### Key Words

■Hypertension

■Antihypertensive therapy (candesartan)

■Diet (DASH)

■Quality of life

### INTRODUCTION

Research has found that diet affects the development of high blood pressure. Recently, two studies showed that following a particular eating plan, the Dietary Approaches to Stop Hypertension (DASH) diet, and reducing the amount of sodium consumed lowers blood pressure. This diet is low in saturated fat, cholesterol and total fat, and emphasizes fruits, vegetables and low fat dairy foods, which are naturally lower in sodium than many other foods.

Quality of life (QOL) has been the subject of numerous research studies with hypertensive treat-

ments<sup>1-5</sup>. QOL guided treatment may improve the patient's psychological status and improve compliance to antihypertensive agents. The QOL for hypertensive patients can be assessed using specific questionnaires. The Subjective Symptoms Assessment Profile (SSAP) questionnaire is a reliable tool for the evaluation of QOL. The 42 questions are designed to evaluate physical and social functions, emotional problems, mental health, the level of pain and general health perception.

This randomized study was designed to assess the additive efficacy of DASH diet on treatment with an angiotensin type 1 inhibitor, candesartan,

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in lowering blood pressure and improving QOL in hypertensive patients.

### SUBJECTS AND METHODS

In this study, 201 hypertensive outpatients from 14 antihypertensive centers were enrolled. Hypertension was defined as seated diastolic blood pressure ranging from 95 - 110 mmHg during the washout period. Patients with systolic blood pressure over 220 mmHg or diastolic blood pressure over 110 mmHg during the washout period, severe heart failure, renal or hepatic disease were excluded.

Patients in the candesartan group took a 8 mg candesartan tablet in the morning. The candesartan dosage was increased to 16 mg for the next 8 weeks if the diastolic blood pressure was  $\geq 90$  mmHg after the first phase of treatment. Hydrochlorothiazide 12.5 mg was added during the last 4 weeks if blood pressure was uncontrolled. The total duration of the treatment period was 16 weeks.

Patients on the DASH diet were given a weekly menu that allowed a daily sodium level of either 2,400 mg, or by making the noted changes, 1,500 mg. The DASH eating plan is based on 2,000 calories a day. Everyday menus inform the patient about the food group to be followed, such as grains, vegetables, fruits, low fat dairy foods, meats, poultry, fish, nuts, dry beans, fats and oils, and sweets, the daily servings and the serving sizes. Patients before randomization had been asked whether they could follow the DASH diet. They had a small training period to see whether the DASH diet was comparable to their current food habits, and if their answer was strictly positive they were enrolled in the study. A notebook was given to all patients on the DASH diet to keep track of what they ate for breakfast, lunch and dinner every day. Calories per item were calculated and if the responsible physicians considered that some patients declined from the DASH eating plans, they were excluded.

Life study modification, such as smoke cessation and training, was encouraged as complimentary measures to both treatments for all patients.

#### Blood pressure measurements

Blood pressure measurements were taken with a standard mercury sphygmomanometer by the same physician of each antihypertensive center, after 10 min rest in a sitting position. Two seated measurements were taken within a 5-min period and the

mean of the two measurements was used.

#### Quality of life measurement

The QOL dimensions were measured using the SSAP questionnaire which was completed at the baseline and 16-week visit. This questionnaire was designed to survey health related QOL issues for clinical research. The 42 questions are associated with general and mental health, body pain, vitality, physical, emotional and social functioning. The self administered questionnaire uses a 10-grade scale. The higher the score, the better the patient. The validity, reliability and utility of the questionnaire have been established across various clinical studies<sup>6,7</sup>.

#### Statistical analysis

Data are presented as mean  $\pm$  standard error (SE). Comparisons between baseline and end-treatment measurements were analyzed by the paired *t*-test. A *p* value  $< 0.05$  was considered statistically significant. ANOVA was used to assess the effect of treatments on QOL dimension scores.

### RESULTS

Two hundred one patients completed the study, as presented in **Table 1**. The mean  $\pm$  SEM daily dose of candesartan given over the 16-week therapy treatment was  $11.5 \pm 2.5$  mg for the candesartan group ( $n = 102$ ), and  $10.6 \pm 2.1$  mg for the group allocated to candesartan plus DASH diet group ( $n = 99$ ). Hydrochlorothiazide was also given to 11 patients of the candesartan group and 9 patients of the candesartan plus DASH diet group.

Resting blood pressure was significantly reduced in both groups. All results are summarized in **Table 2**, **Fig. 1** and **Fig. 2**. The results were similar even if patients who received hydrochlorothiazide were eliminated.

Diastolic blood pressure was normalized ( $\leq 85$  mmHg) in 66 patients (64.7%) treated with candesartan and in 72 patients (72.7%) treated with candesartan and the DASH diet. The changes in QOL-scores for the two treatment groups are presented in **Table 3**.

Eleven of the 201 participants in the trial did not complete the questionnaire. No statistical difference was demonstrated comparing the two treatment groups.

The effects of treatments on biochemical measurements are summarized in **Table 4**. Candesartan

**Table 1 Patient characteristics**

	Candesartan group (n = 102)	Candesartan plus DASH diet group (n = 99)
Age( yr )	53.5 ± 8.4	54.1 ± 7.7
Baseline SBP( mmHg )	149.3 ± 5.8	148.7 ± 6.2
Baseline DBP( mmHg )	98.9 ± 3.6	99.1 ± 4.1
Women	34( 33.3% )	31( 31.3% )

Continuous values are mean ± SE.

DASH = Dietary Approaches to Stop Hypertension ; SBP = systolic blood pressure ; DBP = diastolic blood pressure.

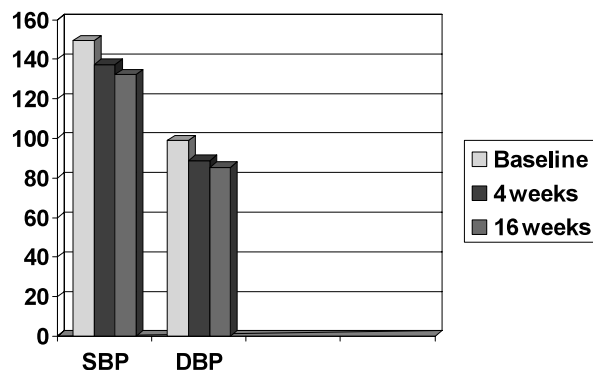
**Table 2 Effects of candesartan and candesartan plus DASH diet on resting blood pressure**

	Candesartan			Candesartan plus DASH diet		
	Baseline	8 weeks	16 weeks	Baseline	8 weeks	16 weeks
SBP( mmHg )	149.3 ± 8.8	137.4 ± 6.2*	132.3 ± 5.9* <sup>†</sup>	148.7 ± 9.2	133.8 ± 5.5*	127.7 ± 5.1* <sup>†</sup>
DBP( mmHg )	98.9 ± 4.6	88.7 ± 5.8*	85.4 ± 6.2* <sup>†</sup>	99.1 ± 4.9	84.8 ± 6.2*	82.1 ± 5.4* <sup>†</sup>

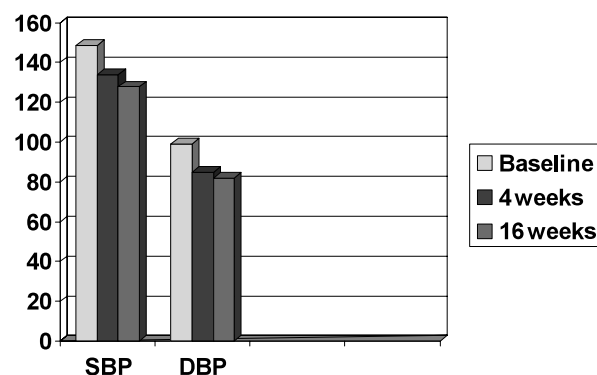
Values are mean ± SE.

\*p < 0.001 vs baseline, <sup>†</sup>p < 0.05 vs baseline.

Abbreviations as in Table 1.



**Fig. 1 Effects of candesartan on blood pressure**  
Abbreviations as in Table 1.



**Fig. 2 Effects of candesartan plus DASH on blood pressure**  
Abbreviations as in Table 1.

**Table 3 Changes in QOL-scores for the two treatment groups**

	Candesartan			Candesartan plus DASH diet		
	Baseline	16 weeks	p value	Baseline	16 weeks	p value
Physical function	86	87	NS	86	89	NS
Pain	77	78	NS	76	79	NS
Mental health	61	63	NS	61	66	0.029
Emotional status	70	73	NS	69	74	0.038
Vitality	67	68	NS	66	70	0.045

QOL = quality of life. Other abbreviation as in Table 1.

**Table 4** Effects of both treatments on biochemical measurements

	Candesartan		Candesartan plus DASH diet	
	Baseline	16 weeks	Baseline	16 weeks
Creatinine( mg/dl )	0.92 ± 0.2	0.93 ± 0.3	0.91 ± 0.3	0.92 ± 0.3
Uric acid( mg/dl )	4.8 ± 1.4	4.6 ± 1.9	4.8 ± 1.6	4.5 ± 2.1
Sodium( mg/dl )	144 ± 3	143 ± 4	142 ± 3	143 ± 3
Potassium( mg/dl )	4.2 ± 0.4	4.4 ± 0.3	4.1 ± 0.4	4.2 ± 0.5

Values are mean ± SE.

Abbreviation as in Table 1.

singly or in combination with the DASH diet did not affect any biochemical values. No serious adverse effects were reported with candesartan. Patient compliance and dosage titration for both treatments were compatible.

### DISCUSSION

This study demonstrated that candesartan was effective to reduce blood pressure in mild to moderate hypertension, as reported by other authors<sup>8-13</sup>. Candesartan normalized blood pressure( diastolic blood pressure  $\leq$  85 mmHg )and maintained good long-term control of blood pressure in 54% of treated patients, without significant side effects. The addition of a sodium reducing diet, the DASH diet, increased this control to 64%.

Blood pressure can be unhealthy even if it stays only slightly above the optimal level of less than 120/80 mmHg. The higher blood pressure rises above optimal, the greater the health risk. In the past, researchers tried to find clues about what in the diet affects blood pressure. These studies were done mostly with dietary supplements and their findings were not conclusive. Then, scientists supported by the National Heart, Lung, and Blood Institute( NHLBI )conducted two key studies<sup>14,15</sup>. The first was called DASH, for Dietary Approaches to Stop Hypertension, and tested nutrients as they occur together in food. Its findings showed that blood pressure was reduced with an eating plan that is low in saturated fat, cholesterol, and total fat, and emphasizes fruits, vegetables, and low fat dairy foods. This eating plan, known as the DASH diet, also includes whole grain products, fish, poultry and nuts. It is reduced in red meat, sweets, and sugar-containing beverages. It is rich in magnesium, potassium and calcium, as well as protein and fiber.

The DASH study involved 459 adults with systolic blood pressures of less than 160 mmHg and

diastolic pressures of 80 - 95 mmHg. About 27% of the participants had hypertension. About 50% were women and 60% were African Americans. DASH compared three eating plans: A plan similar in nutrients to what many Americans consume, a plan similar to what many Americans consume but higher in fruits and vegetables, and the DASH diet. All three plans used about 3,000 mg of sodium daily. The results were dramatic: Both the fruits and vegetables plan and the DASH diet reduced blood pressure. But the DASH diet had the greatest effect, especially for those with high blood pressure. Further, the blood pressure reductions came fast, within 2 weeks of starting the plan.

The second study was called " DASH-Sodium ", and looked at the effect on blood pressure of a reduced dietary sodium intake as participants followed either the DASH diet or an eating plan typical of what many Americans consume. DASH-Sodium involved 412 participants. Their systolic blood pressures were 120 - 159 mmHg and their diastolic blood pressures were 80 - 95 mmHg. About 41% of them had high blood pressure. About 57% were women and about 57% were African Americans. Participants were randomly assigned to one of the two eating plans and then followed for a month at each of three sodium levels. The three sodium levels were: a higher intake of about 3,300 mg per day( the level consumed by many Americans ), an intermediate intake of about 2,400 mg per day, and a lower intake of about 1,500 mg per day. Results showed that reducing dietary sodium lowered blood pressure for both eating plans. At each sodium level, blood pressure was lower on the DASH diet than on the other eating plan. The biggest blood pressure reductions were for the DASH diet at a sodium intake of 1,500 mg per day. Those with hypertension saw the biggest reductions, but those without hypertension also had

**Table 5 Tips to reduce salt and sodium**


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Buy fresh, plain frozen, or canned with no-salt-added vegetables.
Use fresh poultry, fish and lean meat, rather than canned, smoked or processed types.
Choose ready-to-eat breakfast cereals that are lower in sodium.
Limit cured foods( such as bacon and ham ) foods packed in brine( such as pickles, pickled vegetables, olives ), and condiments( such as mustard, horseradish, catsup and barbecue sauce )
Be spicy instead of salty. In cooking and at the table, flavor foods with herbs, spices, lemon, lime, vinegar or salt-free seasoning blends. Start by cutting salt use in half.
Cook rice, pasta and hot cereals without salt.
Choose convenience foods that are lower in sodium. Cut back on frozen dinners, mixed dishes such as pizza, packaged mixes, canned soups or broths, and salad dressings-these often contain a lot of sodium.
Rinse canned foods, such as tuna, to remove sodium.

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large decreases. Participants on the 1,500 mg sodium intake, as well those on the DASH diet, had fewer headaches. Other than that and blood pressure levels, there were no significant effects caused by the two eating plans on different sodium levels.

Our patients who followed the DASH diet during their antihypertensive treatment had favorable changes in QOL-scores. Physical function, pain, mental health, emotional status and vitality showed improvement, with a positive impact on their compliance to antihypertensive therapy.

The increase in QOL-scores with antihypertensive treatment is attributed to the favorable effect on blood pressure. When hypertension is well controlled, general well-being, work performance and cognitive function subsequently improve. The inhibition of angiotensin type 1 receptors by candesartan also has an important effect on QOL-scores.

Incorporating a heart-healthy diet into lifestyle in hypertensive patients will help to reduce blood pressure, cholesterol levels, blood sugar level and body weight. Salt retains water, increases body fluid volume and raises blood pressure, and all these factors cause the heart to work harder. Sodium intake is referred to be associated with headaches. The DASH diet restricts salt intake and

the amount of sodium consumed, so has favorable effects on QOL dimensions. It is easy to get started on the DASH diet. The DASH diet requires no special foods and has no hard-to follow recipes. **Table 5** offers some tips on how to reduce the salt and sodium content in your diet.

## CONCLUSIONS

Angiotensin type 1 receptor blockade with candesartan in combination with a low salt diet exerts favorable effects on blood pressure and improves several QOL parameters, such as mental health, emotional status and vitality.

## Appendix

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