

experience unacceptable hypokalemia may achieve similar blood pressure control without hypokalemia when switched to low-dose combination therapy with benazepril and hydrochlorothiazide.

The tolerability of an antihypertensive regimen is important because treatment may fail if adverse effects cause patients to discontinue therapy. Few patients in this study were withdrawn because of drug-related adverse effects. The majority of the patients were able to tolerate their medications.

Benazepril has been shown to be an effective and well-tolerated antihypertensive medication when given alone once daily or in combination with another agent. In this study, all benazepril/hydrochlorothiazide combinations statistically significantly reduced blood pressure from baseline values when compared with placebo. The greatest overall antihypertensive efficacy, as measured by reduction in mean SDBP, was achieved by the benazepril hydrochloride/hydrochlorothiazide, 20/25 mg, group.

It is interesting to note that two lower-dose combinations, benazepril hydrochloride/hydrochlorothiazide, 5/6.25 mg and 10/12.5 mg, produced antihypertensive effects comparable with those of the benazepril hydrochloride, 20 mg, and hydrochlorothiazide, 25 mg, groups. This suggests that combination therapy with lower doses of each component is as effective as monotherapy with higher doses of either agent alone. Furthermore, use of low-dose combination therapy may allow for effective control of blood pressure while reducing the potential for adverse effects.¹³ Having a choice of dose combinations gives the clinician greater flexibility in tailoring antihypertensive therapy to the particular needs of the individual patient.

Accepted for publication July 24, 1995.

This study was supported by a research grant from Ciba Pharmaceuticals, Summit, NJ.

Reprint requests to Oklahoma Cardiovascular and Hypertension Center, University of Oklahoma, 5850 W Wilshire Blvd, Oklahoma City, OK 73132-4904 (Dr Chrysant).

REFERENCES

1. Whalen J. Definition of the effective dose of the converting-enzyme inhibitor benazepril. *Am Heart J.* 1989;17:728-734.
2. Reams GP, Lau A, Bauer JH. Effect of benazepril monotherapy in subjects with hypertension associated with renal dysfunction. *J Clin Pharmacol.* 1989;29:609-614.
3. Weinberger MH, Black HR, Lasseter KC, et al. Diurnal blood pressure in patients with mild-to-moderate hypertension treated with once-daily benazepril hydrochloride. *Clin Pharmacol Ther.* 1990;47:608-617.
4. Moser M, Abraham PA, Bennett WM, et al. The effects of benazepril, a new angiotensin-converting enzyme inhibitor, in mild to moderate essential hypertension: a multicenter study. *Clin Pharmacol Ther.* 1991;49:322-329.
5. Smith WM, Gomez HJ. The use of benazepril in hypertensive patients age 55 and over. *Clin Cardiol.* 1991;14(suppl 4):IV79-IV82.
6. Whalen J, Skalky C, DeSilva J, Weber M. Peak and trough effects of benazepril in mild-moderate hypertension. *Am J Hypertens.* 1989;2(5, pt 2):45A. Abstract 1178.
7. Guyene TT, Bellet M, Sassano P, Serrurier D, Corvol P, Menard J. Crossover design for the dose determination of an angiotensin converting enzyme inhibitor in hypertension. *J Hypertens.* 1989;7:1005-1012.
8. Schoenberger JA. Emerging benefits of angiotensin converting enzyme inhibitors versus other antihypertensive agents. *Am J Med.* 1988;84(suppl 4A):30-35.
9. Bodin F, Serrurier D, Clementy J, Mugnier J, Bellet M. Efficacy of a fixed combination of benazepril and hydrochlorothiazide as first-line therapy in elderly hypertensive patients. *Curr Ther Res.* 1992;51:1-10.
10. Hansson L. Rationale for combination therapy. *Br J Clin Pharmacol.* 1987;23:S15-S19.
11. Ruoff G. ACE inhibitors and diuretics: the benefits of combined therapy for hypertension. *Postgrad Med.* 1989;85:137-139.
12. Pickering TG. The use of angiotensin converting enzyme inhibitors in combination with other antihypertensive agents. *Am J Hypertens.* 1991;4:735-785.
13. Chrysant SG. Antihypertensive effectiveness of low-dose lisinopril-hydrochlorothiazide combination. *Arch Intern Med.* 1994;154:737-743.
14. Weber MA. Safety issues during antihypertensive treatments with angiotensin converting enzyme inhibitors. *Am J Med.* 1988;84(suppl 4A):16-23.
15. Shindler DM, Kostis JB. Lisinopril: mechanism of action, safety, and efficacy. *Intern Med.* 1989;10:92-100.
16. Kostis JB. Angiotensin converting enzyme inhibitors, II: clinical use. *Am Heart J.* 1988;116:1591-1605.
17. Chrysant SG, McDonald RH, Wright JT, et al. Perindopril monotherapy in hypertension: a multicenter comparison of two dosing regimens. *Clin Pharmacol Ther.* 1993;53:479-484.

Members of the Benazepril Study Group

Participating Investigators

Florida Heart Group, Orlando: Louis Acierno, MD; Department of Family Medicine, Jefferson Medical College, Philadelphia, Pa: Peter Amadio, Jr, MD; New Orleans (La) Institute of Clinical Investigations: John Angelo, DO; Department of Family Medicine, East Carolina School of Medicine, Greenville, NC: Doyle M. Cummings, PharmD; Hypertension Services and Diagnostic Laboratory, Los Angeles, Calif: Vincent DeQuattro, MD; Veterans Affairs Hospital, Dayton, Ohio: Steven Cohen, MD, and Tom Evans, MD; Jackson's Hospital, Montgomery, Ala: Henry A. Frazer, PharmD, Malcolm Brown, MD; Department of Medicine, Albert Einstein Medical School, Bronx, NY: William Frishman, MD; Nephrology Associates, Buffalo, NY: Theodore Herman, MD; Pediatric Nephrology, University of Florida College of Medicine, Gainesville: Abdollah Iravani, MD; Department of Medicine, University of Kansas Medical Center, Kansas City: Bruce Johnson, MD; Family Health Center, South Portland, Me: John E. Kazilionis, DO; National Medical Research Corp, Hartford, Conn: Benjamin Levy, MD; Department of Cardiology, Strong Memorial Hospital, Rochester, NY: Chang-seng Liang, MD, PhD; Nutritional Medicine Clinic, Birmingham, Mich: Charles P. Lucas, MD; Hypertension Program, University of Cincinnati (Ohio) Medical Center: Paul MacCarthy, MD; Hypertension Clinic, Methodist Hospital, Houston, Tex: Edward B. Nelson, MD; Newport Clinical Research Center, Newport Beach, Calif: Sidney Rosenblatt, MD; Booth Memorial Hospital, Flushing, NY: Bruce Spinowitz, MD; Duke Hypertension Clinic, Brown Stone Inn Medical, Durham, NC: Laura Svetkey, MD; Ogden (Utah) Clinic: C. Basil Williams, MD; Arms, Dodge, Robinson, Wilburn, and Crouch Inc, Kansas City, Mo: Barry C. Wood, MD; and Massachusetts General Hospital, Boston: Randall Zusman, MD.