IS CAPTOPRIL EFFECTIVE IN PRIMARY PULMONARY HYPERTENSION?

TATSUO KOKUBU, M.D., YUKIO KAZATANI, M.D., MAREOMI HAMADA, M.D.
KEISUKE MATSUZAKI, M.D., TAKETOSHI ITO, M.D., KAZUTAKA NISHIMURA, M.D.
TAKAAKI OCHI, M.D., FUMIYOSHI DAIMON, M.D., AND TADAFUMI JOH, M.D.*

Several vasodilating agents have been used for the treatment of primary pulmonary hypertension (PPH). However, no effective therapy is currently available for this distressful disease. We tried to use an angiotensin-I converting enzyme inhibitor, captopril, for one woman suffering from PPH. Her initial treatment with furosemide, digoxin and spironolactone had shown little effect. Further administration of captopril improved her clinical condition from NYHA IV to II and made it possible to treat her at our out-clinic. No adverse effect has been found. We would like to appreciate captopril as one of the effective drugs in the treatment of PPH.

MANY reports concern the etiology and pathophysiology of primary pulmonary hypertension (PPH). However, they still remain obscure. In its natural course, death occurs several years after the onset of symptoms such as exertional dyspnea, syncope and chest pain. Although several pulmonary vasodilating agents

have recently contributed to the treatment of PPH,¹⁻⁷ an effective therapy has not been established for this distressful disease. In this report, we will present a patient who showed a significant improvement of symptoms and laboratory data with an oral administration of angiotensin-I converting enzyme inhibitor, captopril.

TABLE I DATA ON CARDIAC CATHETERIZATION

Pulmonary capillary wedge pressure	6 mmHg
Pulmonary artery pressure	100/36 (56) mmHg
Right ventricular pressure	100/12 mmHg
Right atrial pressure	10/2 (5) mmHg
Aortic pressure	106/66 (79) mmHg
Cardiac index	2.0 L/min/m ²

Key Words:

Primary pulmonary hypertension
Captopril

Case Report

The patient, a 53 year old female, had dyspnea at rest, syncopal attack and chest pain, with a functional capacity of class IV of the NYHA. Her hematological and routine laboratory findings were normal. A chest X-ray showed marked cardiac enlargement and protrudent main pulmonary artery with peripheral tapering. Her ECG exhibited typical right ventricular hypertrophy. Echocardiography revealed the right ventricular dilatation and marked pericardial effusion. Cardiac catheterization confirmed her diagnosis of PPH (Table I).

The treatment, started initially with a combin-

(Received December 11, 1981; accepted April 23, 1982)

The Second Department of Internal Medicine, Ehime University School of Medicine, and *Ehime Central Hospital, Ehime, Japan

Address for correspondence: Tatsuo Kokubu, M.D., The Second Department of Internal Medicine, Ehime University School of Medicine, Shigenobu, Onsen-gun, Ehime 791-02, Japan

Fig.1. Clinical course of the patient.

TABLE II CHANGES OF HEMODYNAMIC PARAMETERS ONE HOUR AFTER A SINGLE ORAL ADMINISTRATION OF 50 mg OF CAPTOPRIL

	Before	After one hour
Mean pulmonary artery pressure	64 mmHg	49 mmHg
Pulmonary vascular resistance	1131 dyn·s·cm ⁻⁵	818 dyn·s·cm ⁻⁵
Cardiac index	2.46 L/min/m ²	2.56 L/min/m ²

ed administration of 0.25 mg of digoxin and 40 mg of furosemide daily had brought no remarkable improvement. Further administration of 75 mg of spironolactone and an increment of furosemide doses up to 80 mg daily, still showed little effect. However, the administration of captopril, 25 mg orally, three times daily, significantly improved the symptoms and laboratory data. After 4 weeks of captopril therapy, dyspnea at rest disappeared. The central venous pressure and the cardiothoracic ratio decreased from 15 to 7.5 cmH₂O and from 72 to 58%, respectively. Pericardial effusion was also reduced. Her clinical course is summarized in Fig. 1.

Hemodynamic parameters were analyzed one hour after a single oral administration of 50 mg of captopril. Mean pulmonary artery pressure fell from 64 to 49 mmHg. Pulmonary vascular resistance decreased from 1131 to 818 dyn·s·cm⁻⁵. Cardiac index did not change significantly (2.46 to 2.56 L/min/m²) (Table II). The results

observed in this patient, may suggest the noteworthy effectiveness of captopril in PPH. After discharge, she is in fairly good condition on 75 mg of captopril. No adverse effect of the drug has been found.

The effectiveness of captopril on congestive heart failure has been reported⁸. The action mechanism of captopril on pulmonary vascular beds is not fully understood⁹. From our present experience, administration of captopril, may be considered one of the promising therapies for PPH.

Acknowledgement

We are grateful to Sankyo Pharmaceutical Co. for kindly supplying of captopril.

REFERENCES

1. RUSKIN JN, HUTTER AK: Primary pulmonary

- hypertension treated with oral phentolamine. *Ann Intern Med* 90: 772, 1979
2. KLINKE WP, GILBERT JAL: Diazoxide in primary pulmonary hypertension. *N Engl J Med* 302: 91, 1980
 3. PANTANO JA: Isoproterenol in primary pulmonary hypertension. *N Engl J Med* 302: 919, 1980
 4. RUBIN LJ, PETER RH: Oral hydralazine therapy for primary pulmonary hypertension. *N Engl J Med* 302: 69, 1980
 5. CAMERINI F, ALBERTI E, KLUGMANN S, SALVI A: Primary pulmonary hypertension: Effects of nifedipine. *Br Heart J* 44: 352, 1980
 6. WATKINS WD, PETERSON MB, CRONE RK, SHANNON DC, LEVINE L: Prostacyclin and prostaglandin E₁ for severe idiopathic pulmonary artery hypertension. *Lancet* 8177: 1083, 1980
 7. KAMBARA H, FUJIMOTO K, WAKABAYASHI A, KAWAI C: Primary pulmonary hypertension: Beneficial therapy with diltiazem. *Am Heart J* 101: 230, 1981
 8. ADER R, CHATTERJEE K, PORTS T, BRUNDAGE B, HIRAMATSU B, PARMLEY W: Immediate and sustained hemodynamic and clinical improvement in chronic heart failure by an oral angiotensin converting enzyme inhibitor. *Circulation* 61: 931, 1980
 9. NIARCHOS AP, ROBERTS AJ, LARAGH JH: Effects of the converting enzyme inhibitor (SQ 20881) on the pulmonary circulation in man. *Am J Med* 67: 785, 1979