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Original Articles

THE EFFECTS OF CAPTOPRIL ON PULMONARY AND SYSTEMIC ARTERIAL PRESSURES IN HIGH-ALTITUDE PULMONARY HYPERTENSION

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ABSTRACT

The purpose of this investigation was to assess the effect of captopril on both systemic (P_a) and pulmonary arterial pressures (P_{PA}) in patients with high-altitude pulmonary hypertension (HAPH). Seventeen patients (mean age 44±6.8 years) with HAPH and mild to moderate systemic arterial hypertension were included in the study. All patients underwent right heart catheterization with measurements of systolic P_{PA} ($P_{PA, syst}$), mean P_{PA}, ($\overline{P}_{PA}$) and diastolic P_{PA} ($P_{PA, diast}$). After 4 weeks placebo phase patients with a $P_{PA, syst}$>25 mmHg, $\overline{P}_{Pa}$>15 mm Hg and systemic diastolic blood pressure ($P_{a, diast}$)>100 mmHg were given captopril (50-75 mg at 8 am) for a period of 12 weeks. The statistical evaluation of the results was made using Student's t-test. It was found that captopril significantly decreases P_{PA} and P_a.

Keywords: Captopril, pulmonary hypertension, systemic hypertension, high-altitude pulmonary hypertension.

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INTRODUCTION

There presently seems to be considerable controversy concerning the underlying pathophysiologic mechanisms and the treatment of high-altitude pulmonary hypertension (HAPH). Previous studies[1-4] have reported the salutary effects of different vasodilators such as hydralazine, phentolamine, isoproterenol and nifedipine in the management of pulmonary hypertension. On the other hand, long-term use of these medications is limited by the development of undesirable side-effects such as activation of sympathetic influences, increase in renin level or a reduced number of favorable responders to treatment among the patients.[3-5] These considerations appear to be more important in cases of HAPH with concurrent systemic hypertension.

Angiotensin-converting enzyme (ACE) inhibitors are currently used in the treatment of hypertension. These drugs are free of side-effects such as disturbances in lipid metabo-

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lism.[6-9] However, the influence of ACE inhibitors on pulmonary and systemic hypertension in HAPH patients is at present not clearly understood.

The aim of the present study was to determine the effects of the long-acting ACE inhibitor Capoten on pulmonary and systemic pressures during a one month course of treatment of high-altitude pulmonary and systemic hypertension.

MATERIALS AND METHODS

Subjects used in this study were 17 outpatients (4 male) aged 40-58 years, with stable mild to moderate essential hypertension and HAPH. Exclusion criteria were severe or secondary systemic and pulmonary hypertension, myocardial infarction within the previous year, arrhythmia, angina pectoris, significant abnormal clinical laboratory values, major organ failure, psychosis and current medication with other agents known to affect blood pressure. Written informed consent was obtained from each subject. Patients on current antihypertensive therapy were gradually withdrawn from this treatment; new therapy was begun directly.

Following a 4-week placebo phase, patients with a systolic pulmonary artery pressure ($P_{PA,\ syst}$)>25 mmHg, mean pulmonary artery pressure ($\bar{P}_{PA}$)>15 mmHg and systemic diastolic arterial blood pressure ($P_{a,\ diast}$)>100 mmHg received Capoten (50-75 mg at 8 am) for a period of 12 weeks. Monthly recordings of systemic arterial blood pressure ($P_{a,\ syst}$, $P_{a,\ diast}$), P_{PA}($P_{PA,\ syst}$, $\bar{P}_{PA,\ diast}$) and heart rate (HR) were taken according to the American Heart Association's recommendation and each patient was questioned about adverse drug reactions.

Observed values from the end of the placebo phase were compared with those at the end of the 12th week treatment phase using Student's t-test. The level of statistical significance was taken as $P<0.05$.

Table I. Changes in heart rate, systemic and pulmonary arterial blood pressures during Capoten therapy in patients with high-altitude pulmonary hypertension (mean±SD).

Variable	Baseline	Placebo	12 weeks
$P_{PA,\ syst}$(mmHg)	42±5	40±7	28±3*
$\bar{P}_{PA}$(mmHg)	33±4	31±5	21±3*
$P_{PA,\ diast}$ (mmHg)	24±2	23±3	16±2*
$P_{a,\ syst}$(mmHg)	158±10	156±9	140±8*
$P_{a,\ diast}$(mmHg)	106±6	104±4	86±3*
HR (beats/min)	68±5	66±5	68±5

$P_{PA,\ syst}$= systolic pulmonary artery pressure, $\bar{P}_{PA}$= mean pulmonary artery pressure, $P_{PA,\ diast}$= diastolic pulmonary artery pressure, $P_{a,\ syst}$= systemic systolic arterial pressure, $P_{a,\ diast}$= systemic diastolic arterial pressure.

(*$P<0.001$, differences are significant between baseline value and 12 weeks of treatment).

RESULTS

All 17 patients completed the study. During the placebo phase, there was no significant change in P_a, P_{PA} and HR. However, a significant decrease in both systemic and pulmonary arterial blood pressures ($P<0.001$) was observed following Capoten administration. The largest decrease was noted during the first month of therapy, but a decrease was noted even on the last visit (Table I). There was no significant variation in mean HR. Normalization of systemic blood pressure (i.e., $P_{a,\ diast}$<90 mmHg) was seen in 13 patients on Capoten monotherapy.

DISCUSSION

Previous studies have reported the hemodynamic effects of Capoten on pulmonary circulation.[10,11] Niarchos et al.[11] have shown a significant decrease of both pulmonary and systemic vascular resistance after Capoten treatment in patients with pulmonary hypertension secondary to collagen vascular disease. Some previous experimental findings have also indicated that ACE inhibitors diminish pulmonary pressures in both *in vivo* and *in vitro* conditions.[12] Our results confirmed previous preliminary reports[10-13] and extended them by showing the benefits of Capoten treatment in patients with HAPH and concurrent systemic hypertension. Pulmonary and systemic pressures decreased significantly after Capoten use; however, in the control series, the same parameters remained constant throughout the treatment. There was no significant change in HR. Capoten monotherapy produced an antihypertensive effect in a large group of patients (82.3%). It was well tolerated, with only two patients reporting side-effects (1 diarrhea, 1 dry cough).

The mechanisms responsible for high pulmonary and systemic pressures at high altitudes have still not been clarified. The possible explanation for the salutary vasodilator action of Capoten in HAPH and systemic hypertension is believed to be by influencing the renin-angiotensin system. Several experimental and clinical studies have registered disturbances of neuro-hormonal regulation in the formation of HAPH.[14,15] Milledge et al.[14] have obtained increased levels of plasma renin at high altitudes. It was proposed that the activity of plasma renin is stimulated by hypoxia.[15] It has been demonstrated that 45 minutes of hypoxia (12% oxygen) induces an elevation of plasma renin activity by 50% in subjects with high pulmonary arterial pressures.[15] Although the beneficial effects of Capoten have been shown in studies of longer duration, their underlying mechanisms are presently being subject to further evalua-

tion.

Thus Capoten has a stable favorable effect on systemic and pulmonary artery pressures in patients with HAPH and concurrent systemic hypertension.

REFERENCES

1. Fisher J, Borer JS, Moses JW, et al: Hemodynamic effects of nifedipine versus hydralazine in primary pulmonary hypertension. Am J Cardiol 54: 646, 1984.
2. Luji Herrera E, Bialostozky D, Sabrino A: The role of isoproterenol in pulmonary artery hypertension of unknown etiology. Chest 79: 292, 1981.
3. Rich S, Brundage BH: High dose calcium channel blocking therapy for primary pulmonary hypertension: evidence of long-term reduction in pulmonary arterial pressure and regression of right ventricular hypertrophy. Circulation 76: 135, 1987.
4. Ruskin JD, Hutter AM: Primary pulmonary hypertension treated with oral phentolamine. Ann Intern Med 90: 772, 1979.
5. Shepher AMM, Irving NA: Differential hemodynamic and sympathoadrenal effects of sodium nitroprusside and hydralazine in hypertensive subjects. J Cardiovascular Pharmacology 8: 527, 1986.
6. Kochar MS, Barboriak JJ, Tyson JA, Kalbfleish JH: Effect of beta-blockers and converting enzyme inhibitors on serum lipids. J Clin Pharmacol 24: 422-3, 1984.
7. Malini PL, Strocchli E, Ambrosioni E, Magnani B: Long-term antihypertensive, metabolic and cellular effects of enalapril. J Hypertens 2(Suppl 2): 101-5, 1984.
8. Ohman P, Aurell M, Asplund J: A long-term follow-up of patients with essential hypertension treated with captopril. Acta Med Scand 216: 53-6, 1984.
9. Weinberger MH: Antihypertensive therapy and lipids. Evidence of mechanism and implications. Arch Intern Med 135: 1102-5, 1985.
10. Bertolid LO, Cicero S, Busnardo I, et al: Effect of captopril on hemodynamics and blood gases in chronic obstructive lung disease with pulmonary hypertension. J Respiration 49: 251-6, 1986.
11. Niarchos AP, Whitman HH, Goldstein GE, Larogh JH: Hemodynamic effects of captopril in pulmonary hypertension of collagen vascular disease. Am Heart J 104: 834-8, 1982.
12. Berkas S, Melman KL: Effect of angiotensin II blockade on hypoxic pulmonary vasoconstriction *in vitro* and *in vivo* in the cat (abstract). Clin Res 22: 231A, 1974.
13. Sada T, Koike H, Ikeda M, et al: Cytosolic free calcium of aorta in hypertensive rats. Chronic inhibition of angiotensin converting enzyme. Hypertension 16: 245-51, 1990.
14. Milledge JS, Catley DM: Renin, aldosterone and converting enzyme during exercise and acute hypoxia in humans. J Appl Physiol 52: N2; 320, 1982.
15. Slater JDH, Tuffley RE, Williams ES, et al: Control of aldosterone secretion during acclimatization to hypoxia in man. Clin Sci 37: 327-41, 1969.

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