Efficacy of Captopril in Relieving Congestive Heart Failure Developing During Management of Hypertension
Case Report

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SUMMARY A 20-year-old woman presented with malignant hypertension, pulmonary edema, anemia, and azotemia. Blood pressure was adequately controlled only after progressively more intensive drug regimens, finally including minoxidil, nadolol, and furosemide. On these drugs, the patient developed progressive left and right heart failure, anasarca, and malnutrition. The control of hypertension, heart failure, and fluid retention, was accomplished by administration of captopril and furosemide. Captopril is a logical alternative to vasodilators in refractory hypertension complicated by congestive heart failure. (Hypertension 5: 390-393, 1983)

KEY WORDS  • hypertension  • heart failure  • vasodilator  • captopril

Captopril is efficacious in the management of both refractory hypertension1 and refractory congestive heart failure.2 However, in combined hypertension and congestive heart failure, the relative clinical benefit of captopril compared to conventional aggressive regimens has not been defined. We present a case of severe hypertension with renal insufficiency and refractory heart failure in which substitution of captopril for the combination of minoxidil and nadolol produced major clinical improvement.

Case Report

First Admission

A 20-year-old Latin American woman was admitted to the hospital in August, 1980, in acute pulmonary edema. She was in previously good health and had a normal pregnancy in February, 1980. Her illness began 2 days before admission, with increasing dyspnea progressing to frank pulmonary edema. She had no prior history of cardiovascular, renal, or hematologic disease.

Physical examination revealed an acutely ill female in respiratory distress. She weighed 103 lbs. Blood pressure was 180/120 mm Hg in both arms, pulse rate 150 bpm, temperature 99°F, and respiratory rate 40 per minute. Her jugular veins were distended. Retinal examination was normal. Auscultation of the lungs revealed diffuse bilateral rales. A sustained right ventricular impulse was palpable. The heart sounds were normal, and there was a summation gallop at the apex. The patient had no hepatomegaly, splenomegaly, ascites, or edema. Her peripheral pulses were normal, and there was no clubbing.

Electrocardiogram revealed sinus tachycardia and nonspecific ST-T wave changes. Chest x-ray showed biventricular enlargement and pulmonary edema. An arterial blood gas revealed a pH of 7.42, PO2 54 mm Hg, and PCO2 of 28 mm Hg. Hemoglobin concentration was 6.4 g/dl, hematocrit 18.6 vol%, and white blood cell count 8700/mm3 with a normal differential. The blood smear was compatible with microangiopathic hemolytic anemia. Coombs test was negative. Lactic dehydrogenase was 723 IU/liter (normal = 20–220) and total bilirubin 1.2 mg/dl (normal = 0.2–1.2). Serum BUN was 41 mg/dl (normal = 5–22) and creatinine 6.5 mg/dl (normal = 0.5–1.3). An antistreptolysin O titer was < 1:50 and ANA <1:20. Serum albumin and total proteins were reduced. Total hemolytic complement was normal. Microscopic examination of the urinary sediment revealed finely granular casts and 20–30 red blood cells per high-powered field. A 24-hour urine collection contained 5 g of protein.

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Right heart catheterization revealed a right atrial pressure of 15 mm Hg, right ventricular pressure of 60/20 mm Hg, pulmonary artery pressure of 60/44 mm Hg (mean, 46 mm Hg), a pulmonary capillary wedge pressure of 40 mm Hg, and a widened arterial-mixed venous oxygen difference of 5.3 vol%. An echocardiogram showed reduced left ventricular function and left atrial enlargement. The patient was initially treated with oxygen, nitroprusside, digoxin, and furosemide, with resolution of pulmonary edema. The hypertension was subsequently controlled with propranolol 40 mg twice daily, hydralazine 75 mg twice daily, and furosemide 20 mg four times daily. A repeat echocardiogram and radionuclide ventriculogram done when the patient was off digoxin showed normal left ventricular function.

Renal biopsy revealed fibrin thrombi in the glomerular capillaries with recent fibrinoid necrosis of the afferent arterioles, which also contained thrombi. Immunofluorescence studies showed 3+ staining with fibrin predominately in the capillary lumina. These findings were felt to be compatible with malignant hypertension, although the diagnosis of hemolytic uremic syndrome was also entertained. The patient developed progressive oliguria with the BUN rising to 107 mg/dl and creatinine to 9.7 mg/dl. She underwent hemodialysis over a 2-week period, with gradual improvement in renal function. Her creatinine decreased to 2.4 mg/dl. Subsequently, hydralazine was discontinued, and the patient’s blood pressure was well controlled with propranolol 40 mg twice daily and furosemide 20 mg twice daily.

The patient was discharged on the 32nd hospital day with a blood pressure of 134/84 mm Hg.

Second Admission

Three weeks later the patient was readmitted with a 24-hour history of increasing cough and dyspnea. Blood pressure was 164/120 mm Hg, pulse 100 bpm, respiratory rate 28, and temperature 98°F. Physical findings and chest x-ray were compatible with severe biventricular failure with pulmonary edema. Arterial blood gases revealed a pH of 7.39, PO2 of 56 mm Hg, and PCO2 of 33 mm Hg. Electrocardiogram showed sinus tachycardia and T wave changes consistent with inferolateral ischemia. Hemoglobin count was 8.3 g/dl, hematocrit 23.9 vol%, reticulocyte count 2.5%, and creatinine 2.3 mg/dl. Peripheral blood smear revealed numerous red blood cell fragments. Bone marrow was normal, with adequate iron stores.

The rapid onset of pulmonary edema 1 day subsequent to an asymptomatic clinic visit was attributed to hypertension and anemia. Her blood pressure was initially controlled with nitroprusside. She subsequently required hydralazine 100 mg three times daily, propranolol 120 mg four times daily, and furosemide 40 mg twice daily. A radionuclide left ventricular ejection fraction was 39%, and the patient was begun on digoxin at a maintenance dose of 0.125 mg/day (blood level 1.5 ng/ml). The patient was discharged on the 10th hospital day with a blood pressure of 135/85 mm Hg.

Third Admission

Three months later, the patient presented with a 2-day history of progressive dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, and fatigue. On physical examination her blood pressure 225/126 mm Hg, pulse 105 bpm, and respiratory rate 20. She had bilateral early papilledema. Cardiovascular examination and chest x-ray were compatible with biventricular failure with pulmonary edema, pulmonary hypertension, and tricuspid regurgitation. Hemoglobin was 8.7 g/dl, hematocrit 26 vol%, BUN 56 mg/dl, and creatinine 3.7 mg/dl. The electrocardiogram was unchanged. The patient was again treated with nitroprusside and furosemide, with control of her hypertension and pulmonary edema. She was begun on minoxidil, which was increased to 20 mg every 6 hours, nadolol 360 mg four times daily, and furosemide 80 mg twice daily, with good control of her blood pressure. Daily weights over the next 11 days were essentially unchanged on sodium restriction. She was discharged on the 13th hospital day with a blood pressure level of 130/70 mm Hg.

Fourth Admission

Three months later the patient was readmitted because of worsening biventricular failure and severe pulmonary hypertension despite control of her systemic blood pressure. Two weeks after her previous hospital discharge she had gained 20 pounds and developed 3+ pitting edema of the legs. Over the next 2 months she noticed increasing abdominal girth and was observed to have ascites in outpatient clinic. The furosemide was gradually increased to 320 mg twice daily.

On physical examination she appeared chronically ill with severe muscle wasting, anasarca, and tense ascites. Her weight was 130 lb (39 lb greater than her previous discharge weight). Her blood pressure was 160/100 mm Hg and pulse rate 60 bpm. Carotid pulses were decreased in amplitude, and her skin was cool. Jugular venous pressure was elevated to 15 cm with a prominent V wave. She had rales at the left base and a right pleural effusion. Cardiovascular examination disclosed cardiomegaly with severe pulmonary hypertension, tricuspid regurgitation, and biventricular failure. There was tense ascites, pulsatile hepatomegaly, anasarca, and 2+ peripheral edema.

Hemoglobin was 13 g/dl, hematocrit 39 vol%, BUN 27 mg/dl, and creatinine 2.6 mg/dl. Electrocardiogram showed sinus tachycardia and right ventricular hypertrophy. Chest x-ray revealed cardiomegaly, a large right pleural effusion, and pulmonary venous congestion. Echocardiography (M mode and 2D) showed concentric left ventricular hypertrophy with reduced function. The right ventricle was enlarged and there was paradoxical septal motion. A ventilation perfusion lung scan was normal. Right heart catheterization during nitroprusside infusion (2 μg/kg/min) revealed a right atrial pressure of 12 mm Hg, right ventricular pressure 65/18 mm Hg, pulmonary artery pressure 60/40 mm Hg, and pulmonary capillary wedge pressure of 28 mm Hg. The brachial artery pressure was 150/100
mm Hg. Cardiac index was 2.1 liters/min/m². Systemic vascular resistance was 1775 dynes-sec-cm⁻⁵.

To simultaneously manage her heart failure and hypertension, captopril was substituted for minoxidil and nadolol. This was accomplished by discontinuation of nadolol and minoxidil and subsequent control of blood pressure by nitroprusside over the subsequent 4 days. Captopril was added at an initial dose of 12.5 mg. The dose was gradually increased to a maximum of 300 mg by the 30th hospital day. The patient was diuresed to dry weight, (75 lbs), over a 3-week period. The maximum furosemide dose was 200 mg/day. A diuretic response was obtained during concomitant administration of captopril and furosemide. The patient's course was complicated by development of acute cholecystitis on the 29th hospital day. This subsided spontaneously, but recurred 10 days later. At emergency surgery, two bilirubin stones were found in the common duct. The patient tolerated the surgical procedure well. Blood pressure was well controlled, requiring steadily reduced doses of captopril and furosemide, which at the time of discharge were 25 mg orally twice daily and 20 mg orally twice daily, respectively.

Clinical signs of congestive heart failure, pulmonary hypertension, and tricuspid regurgitation gradually subsided during captopril administration. Creatinine fluctuated between 1.1 and 1.7 throughout the hospital admission and was 1.6 at the time of discharge. The patient was discharged on the 20th hospital day with a blood pressure of 130/75 mm Hg and no signs of congestive heart failure. Over the following 8 months, good control of her blood pressure (128/80) was obtained with captopril 75 mg twice daily and furosemide 40 mg twice daily. She had no further problems with cardiac decompensation and remained edema free. She gained 33 pounds, reflecting improved nutritional status. The patient's response to antihypertensive drug therapy is summarized in figure 1.

![Figure 1](http://hyper.ahajournals.org/)

**Figure 1.** Summary of response to antihypertensive drug regimens from time of first admission to 8 months following fourth hospitalization.
Discussion

This case illustrates the efficacy of captopril in severe hypertension complicated by congestive heart failure. The patient's hypertension had been refractory to an intensive regimen consisting of furosemide, propranolol, hydralazine, and clonidine. Subsequently, blood pressure could be reasonably well controlled with high doses of minoxidil, furosemide, and nadolol. However, on the latter combination of drugs, the patient developed progressive biventricular heart failure with severe pulmonary hypertension, tricuspid insufficiency, and anasarca. Substitution of captopril for minoxidil and nadolol was effective in controlling blood pressure. Subsequently, there was complete resolution of left and right heart failure.

Clearly, the tendency to fluid retention in this patient was much greater during treatment with minoxidil and nadolol than with captopril. At equivalent levels of arterial pressure, approximately 130/80 mm Hg, the patient experienced progressive weight gain while receiving nadolol and minoxidil, despite 200 mg three times daily of furosemide. In contrast, while on captopril 50 mg three times daily, there was no tendency to fluid retention at a much reduced furosemide dose (40 mg twice daily). Therefore, when fluid retention and heart failure accompany refractory hypertension, captopril should be strongly considered as an antihypertensive agent.

The tendency to sodium retention during minoxidil administration is well recognized and may have contributed, in part, to the development of heart failure in our patient. While all the factors accounting for sodium retention during minoxidil have not been precisely defined, there is an increase in sympathetic nervous system activity, plasma renin activity, and a less marked increase in aldosterone. In contrast, during short-term administration of captopril there is a decrease in plasma angiotensin II and aldosterone. Plasma norepinephrine and epinephrine remain unchanged. In addition, captopril increases renal blood flow when administered to hypertensive patients or patients with congestive heart failure. While renal blood flow was not measured in our patient, there was a sustained reduction in serum creatinine during captopril administration, consistent with an increase in glomerular filtration rate.

The severity of this patient's heart failure was clinically striking. Cardiologic consultation at the time of her fourth admission documented signs of severely reduced cardiac output, left ventricular failure, pulmonary hypertension, and tricuspid insufficiency. The severity of her chronic illness was indicated by malnutrition as evidenced by a weight gain from 75 to 108 lbs over the 9 months after starting captopril. The increase in weight occurred subsequently to marked improvement in her cardiovascular functional status.

The therapeutic approach that was successful in this patient may be applicable to other cases of refractory hypertension with heart failure and fluid retention. The dramatic and sustained clinical improvement that accompanied substitution of captopril for minoxidil and a beta-blocking drug suggests that a therapeutic trial of this drug is justified in similar clinical settings.

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