BRIEF REPORT

NIFEDIPINE TREATMENT FOR PULMONARY HYPERTENSION IN A PATIENT WITH SYSTEMIC SCLEROSIS

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The etiology of scleroderma remains unknown. However, it is believed that the vascular lesions found in involved organs have a pathogenesis related to endothelial cell injury (1).

Pulmonary hypertension is the most common cause of acute dyspnea in patients with systemic sclerosis and is thought to indicate pulmonary vascular involvement with proliferative lesions of scleroderma. Therapy with glucocorticoids has been effective in some patients, when pulmonary hypertension occurs without pulmonary interstitial fibrosis. When the two coexist, however, the pulmonary hypertension has usually been refractory to treatment (2).

Calcium entry blocking drugs are potent vasodilators which have been used to treat Raynaud's phenomenon (3,4) and primary pulmonary hypertension (5) with some success. Recently, in a patient with systemic sclerosis and pulmonary hypertension, we documented the efficacy of one of these drugs—nifedipine.

Case report. VC, a 62-year-old man with a history of systemic hypertension and diabetes mellitus, was first admitted to the Bronx Municipal Hospital Center, Albert Einstein College of Medicine, in November 1981 for chest pain. He had a 4-year history of Raynaud's phenomenon complicated by digital infarctions. On his first symptomatic presentation to another medical provider, in August 1981, a ventilation-perfusion lung scan was reported as negative for pulmonary emboli, and pulmonary function studies demonstrated mild restrictive lung disease. A cardiac catheterization performed in October 1981 for angina pectoris revealed triple vessel coronary artery disease and pulmonary hypertension. His left ventriculogram revealed inferoapical akinesis.

On admission his electrocardiogram (ECG) revealed rapid atrial fibrillation, incomplete right bundle branch block, right axis deviation, and Q waves in the inferior leads. Despite normal cardiac enzymes his course was complicated by pulmonary edema, bradyarrhythmias with high degree of atrioventricular block, and severe systemic hypertension. He was treated with digoxin, diuretics, nitrates, prazosin, quinidine, and a permanent pacemaker. Laboratory studies performed in January 1982 showed an erythrocyte sedimentation rate of 30 mm/hour, antinuclear antibodies 2+, positive antihistone antibody and direct Coombs. His rheumatoid factor was negative, and anti-DNA antibody titer and total hemolytic complement were normal.

He required multiple admissions because of worsening fatigue and exertional dyspnea, despite treatment. A gated radionuclide left ventricular ejection fraction performed in April 1982 was 65%. He also had right ventricular dilatation.

He was readmitted in May 1982 because of a syncopal episode. On admission he had a pulse of 92, a blood pressure of 130/80, jugular venous distention with a prominent A wave, and clear lungs. His cardiac

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Table 1. Cardiopulmonary findings after administration of various vasodilating drugs*

Drug	P	BP	RA	PA	$\overline{PA}$	PCW	CO	PVR	SVR
Baseline	89	110/66	5	78/25	40	2	5.14	591	1183
Phentolamine, 5 mg IV	93	122/70	4	81/26	43	3	5.82	550	1141
Baseline	88	118/70	5	76/24	40	1	5.17	603	1253
Captopril, 12.5 mg PO	97	100/60	6	83/28	46	3	4.85	709	1105
Baseline	84	104/66	5	77/23	39	2	5.44	544	1088
Verapamil, 10 mg IV	86	92/60	9	56/19	29	0	4.74	489	1046
Baseline	90	110/70	4	73/23	40	2	5.45	558	1160
Nifedipine, 20 mg PO	93	100/62	10	61/22	35	2	6.19	426	840

* P = pulse, beats per minute; BP = blood pressure, mmHg; RA = mean right atrial pressure, mmHg; PA = pulmonary artery pressure, mmHg; $\overline{PA}$ = mean pulmonary artery pressure, mmHg; PCW = pulmonary capillary wedge pressure, mmHg; CO = cardiac output, liters per minute; PVR = pulmonary vascular resistance, dynes sec cm^{-5}; SVR = systemic vascular resistance, dynes sec cm^{-5}; IV = intravenous; PO = orally.

examination revealed an apical S4 gallop, and a loud pulmonic component of the second heart sound. In addition, hepatosplenomegaly, sclerodactyly, telangiectasias, and digital ulcerations were found. Adenopathy was absent. Except for the presence of sinus rhythm and more marked ST-T wave abnormalities, his ECG was unchanged from previous tracings. His chest roentgenogram showed cardiomegaly and mild interstitial fibrosis at both lung bases. Hand films showed digital soft tissue calcification. Hematocrit was 35%, blood urea nitrogen 17 mg/dl, and creatinine 1.5 mg/dl. Anticentromere antibodies were positive. A 2-dimensional echocardiogram demonstrated left ventricular hypertrophy with good function, normal mitral valve and left atrium, right atrial and right ventricular dilation, and a suggestion of pulmonary hypertension. Arterial blood gas analysis demonstrated a PaO_2 of 83 (96% saturation), a $PaCO_2$ of 42, and a pH of 7.44.

On May 18, 1982 he underwent a right heart catheterization with a #7F flow-directed thermodilution catheter. Pulmonary hypertension was found (see Table 1). No oxygen step-up or valvular lesion could be detected. Following insertion of the catheter, several vasodilating drugs, including nifedipine, were administered serially in an attempt to ameliorate his pulmonary hypertension. Care was taken to insure the return of his hemodynamics to baseline before each drug was given. The effect of these agents is shown in Table 1. Throughout the study he continued to receive a constant dose of digoxin, diuretic, nitrates, prazosin, and procainamide.

Discussion. Various therapies have been used for vascular involvement in systemic sclerosis. These include sympathectomy, adrenergic blocking agents, beta-receptor agonists, captopril, prostaglandins, other vasodilators, and plasmapheresis. No therapy has met with widespread success. Prompted by reports of successful therapeutic responses to nifedipine in patients with Raynaud's phenomenon and in a patient with primary pulmonary hypertension, we looked at the response to nifedipine and other vasodilators in our patient. The presence of Raynaud's phenomenon, sclerodactyly, telangiectasias, pulmonary hypertension, and interstitial lung disease in this patient satisfies the criteria for the preliminary diagnosis of systemic sclerosis (6).

As Table 1 demonstrates, our patient had moderate pulmonary hypertension at rest, with an elevated pulmonary vascular resistance despite low to normal left ventricular filling pressures. Phentolamine, an alpha-adrenergic blocker, and captopril, an angiotensin-converting enzyme inhibitor, were unsuccessful in lowering his pulmonary artery pressure. Verapamil, a calcium entry blocker, was able to lower the pulmonary artery pressure, but this was accompanied by a depression in cardiac output. This is similar to the effect seen by Landmark et al (7) in some of their patients with primary pulmonary hypertension treated with verapamil.

However nifedipine, another calcium entry blocker which is a potent vasodilator, produced a marked salutary effect on pulmonary vascular resistance and cardiac output in a patient with primary pulmonary hypertension (5), though pulmonary artery pressures were only mildly lowered. Our results, although not as marked, show a beneficial effect of

nifedipine in our patient with secondary pulmonary hypertension. There was about a 20% decrease in pulmonary vascular resistance, with a mild decrease in mean pulmonary artery pressure and no impairment in cardiac output.

That our results are not dramatic may reflect the fact that late pulmonary hypertension secondary to systemic sclerosis could be predominantly a consequence of obliterative vascular disease, rather than potentially reversible vasoconstriction. Our patient's chest roentgenogram finding of interstitial fibrosis is consistent with this explanation. In addition, he continued to receive constant doses of nitrates, prazosin, and diuretics during the study period, which could interfere with the observed effects of nifedipine.

We report this case to point out that nifedipine, which can ameliorate Raynaud's phenomenon in some patients, may prove beneficial in selected patients with pulmonary hypertension secondary to systemic sclerosis. Of significance is the observation that various vasodilators may have differing effects on the hemodynamic parameters in these patients. Undesired effects with one agent (e.g., verapamil) do not preclude benefit with another (e.g., nifedipine).

The reports pointing to the efficacy of calcium entry blocking agents in the treatment of Raynaud's phenomenon (3,4), along with the hemodynamic response of our patient to nifedipine, give hope for the control of the vascular disease in systemic sclerosis. Clearly, further use of this class of drugs is warranted on an investigational basis for treatment of some of the manifestations of this condition. Empiric use of vasodilators without hemodynamic monitoring should be discouraged, in light of our findings of divergent effects with different drugs. The recent report by Packer et al (8) of variable response to hydralazine in patients with pulmonary hypertension further emphasizes this point.

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