EDITORIALS

Vasodilator Therapy in Primary Pulmonary Hypertension

Primary pulmonary hypertension (PPH) is a progressive, debilitating disease mostly affecting young women. Death usually occurs within two to ten years of onset of clinical symptoms. The exact etiology is still unknown. It seems, however, that constriction of the arteriolar lumen by medial contraction is seen in the early stage in patients with PPH. These changes lead to intimal cell proliferation in the constricted segment, glomoid formation distal to the region of constriction, poststenotic dilation, and in late stages, there is a hypertensive necrosis of the arteries proximal to the stenosis produced by the arteriolar intimal proliferation and glomoid.

It is only logical to expect that minimizing the vasospastic component by using pulmonary vasodilator agents may in some patients decrease right ventricular afterload, and thus, augment emptying and improve symptoms of low cardiac output and congestive right ventricular failure. In fact, in recent years numerous reports have indicated that various vasodilator agents can be beneficial for the treatment of patients with PPH. The data are, however, limited, and more studies will be needed in order to answer important questions such as: How many patients with PPH will respond to vasodilator therapy? Can a favorable versus unfavorable response be predicted? Which agent should be selected for a given patient? Can therapy alter the natural progression of the disease?

In this issue of Chest (see page 292), Lupi Herrerra and coworkers describe the results of isoproterenol therapy in a relatively large group of patients with PPH. Isoproterenol is known as an active pulmonary vasodilator,2,3 and when administered orally or intravenously, has been shown to lower pulmonary vascular resistance in patients with PPH.4 Recent reports have demonstrated long-term improvement of symptoms upon reduction of both pulmonary vascular resistance and pressures.5 At the same time, other data showed increased cardiac output and pulmonary pressure following isoproterenol administration in a patient with fixed pulmonary vascular resistance which was followed by tremulousness and anginal chest pain.6 Perhaps the most interesting finding of Lupi-Herrerra et al is the observation that isoproterenol was effective in patients with only a moderate increase in pulmonary resistance while patients with a severe increase remained unresponsive. Daoud et al7 also found that isoproterenol was not uniformly useful in all their patients with PPH. The response however, did not correlate well with the baseline hemodynamic findings. Pulmonary pressure increased after isoproterenol in some of the patients in whom the inotropic and chronotropic effects of the drug were probably more significant than its pulmonary vasodilatory action. Considering the fact that the grade of vascular pathology found in PPH correlates well with the severity of pulmonary hypertension measured clinically,1 increase of pulmonary pressure in some patients following isoproterenol could be harmful and may even accelerate progression of the underlying disease. It seems, therefore, that isoproterenol therapy for patients with PPH should be initiated in small doses and under hemodynamic monitoring.

Two recent reports have shown that diazoxide, a potent vasodilator used for the treatment of systemic hypertension, is also capable of lowering pulmonary vascular resistance and causing longstanding improvement of symptoms in patients with PPH.8,9 We have recently treated a 39-year-old man having PPH with diazoxide following the protocol suggested by Wang et al.8 Administration of 45 mg and 90 mg of the drug into the pulmonary artery was followed by no significant hemodynamic changes. The injection of 180 mg resulted in a small fall in systemic blood pressure and no change in pulmonary artery pressure or heart rate. The next dose (300 mg), however, was followed by profound hypotension (systemic blood pressure of 64/44 mm Hg) which was associated with only a mild decrease of pulmonary pressure. The ECG showed sinus tachycardia initially and then supraventricular tachycardia of 160 beats per minute, which was

253
controlled only after repeated doses of intravenous digoxin and propranolol.

Ruskin and Hutter reported an improvement in exercise tolerance in one patient with PPH treated with oral phentolamine. Although the drug produced only minor hemodynamic changes at rest, it prevented the significant increase in pulmonary resistance with exercise which was seen during control state prior to initiation of therapy. The mechanism of action of phentolamine may be at least partially explained by its ability to block the sympathetic nervous activity and to antagonize circulating catecholamines. The drug, therefore, may be more effective during exercise when there is an augmentation of sympathetic activity accompanied by an increase in pulmonary arteriolar tone.

Oral hydralazine has also been added to the list of vasodilator agents used for the treatment of PPH. Rubin and Peter have treated four severe PPH patients with 200 mg oral hydralazine daily and showed significant fall of pulmonary vascular resistance and enhancement of cardiac output, both at rest and during exercise. Hydralazine, which has a direct relaxing effect on smooth muscle, mainly of the systemic arteriolar circulation, appears to have a similar action on the pulmonary vessels. Our experience in one patient with severe PPH has been somewhat at variance with that of Rubin and Peter. We administered hydralazine to a 48-year-old woman with an 11-year history of PPH in increasing doses up to 400 mg daily with no hemodynamic response. The administration of 5 mg of oral prazosin, however, was followed by a moderate but consistent fall in pulmonary resistance and pressure accompanied by an enhancement of cardiac output. These findings suggest that prazosin, a vasodilator whose cardiocirculatory action is mainly attributable to alpha adrenergic receptor blockade, may warrant a clinical trial in patients with PPH.

In summary, vasodilator agents such as isoproterenol, phentolamine, diazoxide, hydralazine and prazosin appear to have beneficial effects on the hemodynamic profile and symptoms in some patients with PPH. More information in larger groups of patients should lead us to a refinement of our ability to optimize the usage of this therapeutic option in patients with the progressive and fatal syndrome called PPH.

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References


Incentive Spirometry

The Answer Is Blowing in the Wind

Soon after the call was raised to banish the IPPB machine to the storeroom, their place at the bedside of the postoperative patient was taken by the incentive spirometer. It may be premature to denounce the incentive spirometer, but clearly its widespread current use is disproportionate to the scanty evidence supporting its efficacy in preventing postoperative complications. Early papers by Bartlett et al showed that its use encouraged large tidal volumes and improved arterial oxygenation. These studies implied but did not demonstrate that use of the incentive spirometer would minimize postoperative atelectasis.

Jung and colleagues (Chest 1980; 78:31-35) confirm earlier disappointing reports;4-7 incentive spirometry is no better than IPPB or blow bottles in preventing postoperative atelectasis. In one study where there was overall superiority of the incentive spirometer over physiotherapy, this difference did