Different Vasoactive Mechanisms of Various Pulmonary Vasodilators

To the Editor:

We read with appreciation and interest the ACCP Consensus Statement "Primary Pulmonary Hypertension" by Rubin, which appeared in the July 1993 issue of Chest. In the section of therapy, the author states that many vasodilators such as prostacyclin, calcium channel blockers, nitrates, and others are currently available for treatment of primary pulmonary hypertension. About a fourth of patients, however, are felt to have "fixed" vascular disease, and vasodilator therapy is contraindicated. He also mentioned the advantage of prostacyclin to determine the potential and magnitude of vasoactivity and the use of prostaglandin E1 (PGE1) as an alternative in this setting. It is a comprehensive and useful guideline. Nevertheless, the vasoactive mechanisms of these various agents on pulmonary arteries (PA) are not discussed. Are they all acting on the same site and through the same mechanism? Or do they cause the same degree of vasodilation?

Recently, we have conducted a series of investigations to study the direct vasoactive effects of various agents on isolated rabbit PAs. We used vessel rings precontracted with either norepinephrine or potassium chloride to determine the vasodilatory mechanism. Is it the result of the effect of Ca++ flux across the cellular membrane or release/reuptake of Ca++ from the sarcoplasmic reticulum (SR)? At the concentration of 10-6 M, norepinephrine-precontracted PA rings, PGE1 caused about 26 percent relaxation, nitroprusside (NTP) 70 percent, diltiazem (DTZ) 12 percent, and verapamil (VMP) 4 percent. On KCl-precontracted vessels, PGE1 produced 3 percent relaxation, NTP 20 percent, DTZ 55 percent, and VMP 22 percent. In summary, we have found that PGE1 and NTP act more on inhibiting Ca++ release from SR whereas DTZ and VMP on blocking Ca++ influx as expected. They cause different magnitude of vasodilation, which may be affected by the baseline sympathetic tone.

Is there any advantage in combined therapy? Should we base on prostacyclin only to determine the vasoactivity? Before we can effectively and comfortably treat pulmonary hypertension, we need more information about the pharmacology of these pulmonary vasodilators.

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