Inhaled prostacyclin is safe, effective, and affordable in patients with pulmonary hypertension, right-heart dysfunction, and refractory hypoxemia after cardiothoracic surgery

To the Editor:

We read with interest the elegant article by De Wet and associates, who demonstrated that inhaled prostacyclin (PGI₂) prevents pulmonary hypertension, right-heart dysfunction, and refractory hypoxemia after cardiothoracic surgery. We would like to add some observations regarding the mechanisms of action that might be of interest and of possible value in the further clinical implementation of inhalational PGI₂.

First, pulmonary hypertension is associated with increased superoxide (O₂⁻) formation that is largely mediated by an upregulation of intravascular reduced nicotinamide adenine dinucleotide phosphate (NADPH) oxidase. O₂⁻ reacts with endogenous nitric oxide (NO) to form reactive nitrogen species, which effectively reduces NO bioavailability. Because NO is a vasodilator and an inhibitor of inflammation, the reduction of NO formation is considered axiomatic in pulmonary hypertension.

O₂⁻ also reduces endogenous vascular PGI₂ formation. We recently demonstrated that the PGI₂ analogue iloprost is a potent inhibitor of NADPH oxidase expression and activity in porcine pulmonary arteries and therefore of O₂⁻ formation. Therefore by reducing O₂⁻ formation, PGI₂ protects and enhances NO formation, which itself inhibits NADPH oxidase. The reduction of O₂⁻ also prevents the formation of isoprostanes, which are vasoconstrictors and promoters of NADPH oxidase expression.

One interesting facet of the effect of inhalational PGI₂ reported by De Wet and associates was that it prevented refractory hypoxemia. We found that hypoxia promotes the expression of NADPH oxidase in porcine pulmonary arteries. Hypoxemia, by promoting O₂⁻ formation, would create a self-perpetuating cascade that would worsen hypertension and further augment hypoxemia. PGI₂, by blocking the expression of NADPH oxidase, might break this cycle and protect the pulmonary vasculature during surgical intervention through this antioxidant mechanism. Inhalational PGI₂ might also prevent perioperative and postoperative intrapulmonary inflammation because PGI₂ prevents the adhesion of leukocytes and platelets to vascular walls. Similarly, the preservation of intrapulmonary NO-forming capacity would also afford protection against inflammation because NO has similar anti-inflammatory properties to PGI₂. This is of importance because leukocytes and platelets release vasoconstrictors and inflammmogens, including thromboxane A₂ and cytokines, all of which upregulate the expression of NADPH oxidase.

The beneficial effect of inhalational PGI₂ on left ventricular function reported by De Wet and associates could be related to its antioxidative effect on the lungs. There is substantial evidence that reactive oxygen species, including O₂⁻ and peroxyxinitrite, impair left ventricular function. Thus it is reasonable to suggest that the suppression of intrapulmonary oxygen free radical formation by PGI₂ might contribute to the beneficial downstream protective effect of the prostanoid on the left ventricle.

Finally, in a broader context the administration of the stable analogue iloprost in cardiac surgery might be indicated for other more long-term conditions. In particular, PGI₂ has been shown to inhibit vascular smooth muscle cell proliferation and migration, platelet and leukocyte adhesion, and metalloproteinase expression, all key components of vein graft disease. As such, iloprost might be useful in preventing vein graft failure.

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Henry T. Bahnsen, Hopkins, and harmonica

To the Editor:

Like many of Henry T. Bahnsen’s surgical peers at Johns Hopkins who were cited in the in memoriam article by Griffith, I was privileged to be a close cardiology colleague of Hank at Hopkins. My association with Hank was primarily through my work in the cardiac catheterization laboratory at Hopkins. At that time, the cardiac catheterization laboratory was under the department of surgery because the laboratory was considered as a preoperative diagnostic facility before patients, young and old, were operated on for their congenital and acquired heart diseases by Blalock and associates. I was a fellow in the respiratory laboratory of the late Dr Richard L. Riley, who arranged with Blalock to let me work 1 day a week in the cardiac catheterization laboratory because Riley knew of my interest in cardiac catheterization. I still remember the few times that I needed some advice from Hank during cardiac catheterization of babies. I asked the nurse to page H.T.B. for me. She immediately tried to correct me by saying, “Do you mean H.B.T.?” H.B.T. stood for Helen B. Taussig of the Blalock-Taussig operation, and H.T.B. stood for Henry T. Bahnsen. Because the patient was a baby, it was natural for the nurse to think I wanted to speak to Helen B. Taussig rather than to Henry T. Bahnsen.

Because Griffith’s article began and ended with a reference to Bahnsen’s harmonica, I wish to amplify a bit on Hank’s association with this musical instrument. As Griffith mentioned, The Wall Street Journal in 1999 published an article titled “Of artificial hearts and artificial harps in a Pittsburgh laboratory,” with the subtitle “Cardiac surgeon and bioengineer study a harmonica virtuoso from inside his mouth.” The reporter mentioned Hank’s application of his artificial heart experience to that of artificial harps, more commonly known as the harmonica. Because many of your readers might not be familiar with publication number 250 in Hank’s bibliography mentioned in Griffith’s article, I wish to mention that the article by Hank was published in the Journal of the Acoustical Society of America, American Institute of Physics.

References


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