

# Effects of prostaglandin E<sub>1</sub> and other vasodilator agents in pulmonary hypertension of scleroderma

Sir,  
Guadagni *et al.*<sup>1</sup> have recently reported the haemodynamic effects of prostacyclin in pulmonary hypertension. We report here the effects of prostaglandin E<sub>1</sub> (PGE<sub>1</sub>) in the treatment of pulmonary hypertension in a patient with scleroderma.

A 25 year old woman with scleroderma was admitted to hospital in February 1980 for assessment of pulmonary hypertension. An open lung biopsy in January 1979 showed distinct changes in the small to medium sized muscular pulmonary arteries, with intimal fibrosis and medial hypertrophy. Neither plexiform lesions nor parenchymal fibrosis was found. In May 1979, the pulmonary arterial pressure was raised at 80/35 mmHg (mean 54 mmHg) and the pulmonary arteriolar resistance was 650 dynes s cm<sup>-5</sup>. An intravenous infusion of nitroprusside at a dose of 6 µg/kg per min lowered pulmonary arterial pressure by 26% and pulmonary arteriolar resistance by 50%. Phentolamine, 5 mg intravenously, produced a 20% reduction in pulmonary arterial pressure and 13% reduction in pulmonary arteriolar resistance. The patient was placed on oral phentolamine 250 mg daily in divided doses but developed progressive dyspnoea.

On examination, the chest was normal. The jugular venous pressure was raised and a left parasternal heave was present. Skin over the fingers and toes was tight and bound down and multiple digital ulcerations were present. Telangiectasia were present on the face. Antinuclear factor was positive to a titre of 1/200.

Right heart catheterisation was performed with a Swan-Ganz catheter. Cardiac output was assessed with the thermodilution technique using a bedside cardiac output computer (Edwards Laboratories). Diazoxide was given by bolus injection through the right atrial port. PGE<sub>1</sub> (Upjohn Company of Canada) was infused through the right atrial port for 10 minutes out of each hour for a total of 49 infusions. The initial dose was 1 ng/kg per min for 10 minutes increasing to a maximum tolerated level of 32 ng/kg per min for 10 minutes. The haemodynamic effects of PGE<sub>1</sub> were assessed just before the final infusion of 32 ng/kg per min and immediately after completion of this infusion. Between treatment with diazoxide and

PGE<sub>1</sub>, haemodynamic measurements were allowed to return to baseline values.

The right atrial pressure was 14 mmHg. Pulmonary arterial pressure was 75/34 mmHg (mean 51 mmHg), cardiac index 2.33 l/min per m<sup>2</sup>, and stroke index 23 ml/beat per m<sup>2</sup>. The catheter tip could not be made to flow into the wedged position and thus the total pulmonary resistance index was calculated instead of pulmonary arteriolar resistance. Diazoxide produced an increase in pulmonary arterial pressure to 85/39 mmHg (mean 60 mmHg) but a 24% decrease in systemic vascular resistance. PGE<sub>1</sub> did not affect pulmonary arterial pressure, but just before the last infusion there had been a 23% increase in total pulmonary resistance index from 1751 dynes s cm<sup>-5</sup>. m<sup>-2</sup> to 2153 dynes s cm<sup>-5</sup>. m<sup>-2</sup> and a fall in stroke index of 22%.

The failure of intravenous diazoxide to reduce pulmonary arterial pressure suggests progression to fixed pulmonary hypertension and may explain the lack of response to PGE<sub>1</sub>. This differs from the previous reports suggesting that prostaglandins may ameliorate haemodynamic measurements in pulmonary hypertension.<sup>1-4</sup> On the other hand, studies in normal humans have also been variable, with PGE<sub>1</sub> producing either a slight rise<sup>5</sup> or fall<sup>6</sup> in pulmonary arterial pressure or resistance. These results suggest that the effect of PGE<sub>1</sub> on the pulmonary circulation in man remains to be clarified.

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## References

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This letter was shown to Dr Ikram who replies as follows.

Sir,

The authors conclude that PGE<sub>1</sub> infusion in their case produced no reduction in pulmonary arterial pressure and an increase in pulmonary resistance. Unfortunately their data are complicated by the prior administration of diazoxide and though they claim that the haemodynamic status had returned to baseline levels, this is clearly not the case at the start of the PGE<sub>1</sub> infusion. If the haemodynamic measurements immediately before the PGE<sub>1</sub> at 32 ng level are taken as control, then there is a small fall in systemic and pulmonary vascular resistance and a rise in cardiac output with consequently no

change in pulmonary pressure. PGE<sub>1</sub> is not as potent a vasodilator as PG<sub>12</sub> (prostacyclin) and there are patients who respond minimally even to this, the most potent naturally occurring pulmonary vasodilator.

The general experience with all vasodilator therapy in pulmonary hypertension is that responses tend to be variable and unpredictable. The fact that the vasculature was more responsive to vasodilators previously suggests the development of obstructive changes which would not be influenced by PGE<sub>1</sub>. The authors talk about lack of "benefit". It is difficult to assess or even define what constitutes benefit in this situation. A fall in pulmonary pressure would be desirable but frequently does not occur because of increased flow. The best estimate would be regression of right ventricular hypertrophy but this is not possible in an acute study. Improvement in right ventricular function assessed by pressure and radionuclide methods would help in assessing beneficial action but was not performed.

I would certainly endorse the authors' comments that "the effect of PGE<sub>1</sub> in the pulmonary circulation in man remains to be clarified" especially in patients with pulmonary vascular disease.

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