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Long-term treatment of pulmonary hypertension with aerosolized iloprost

To the Editor:

We are concerned about the conclusions drawn by MACHERNDL *et al.* [1] which appear to contradict the findings of HOEPER *et al.* [2] last year. The authors report on the results of nebulized iloprost therapy in 12 subjects with a dose of 100–150 μg for 3–19 months, and conclude that "inhaled iloprost in addition to conventional therapy in the presently recommended dose of 100 $\mu g \cdot day^{-1}$ delivered in 8–10 two-hour portions is not an efficient vasodilator therapy in severe pulmonary hypertension."

We agree with GALIE [3] that uncontrolled trials can be misleading because of the methodology and it is likely that the discrepancy between these two studies is explained by significantly different subject groups. While all of the subjects in the study of HOEPER *et al.* [2] had a diagnosis of primary pulmonary hypertension, nine of the 12 subjects in the study of MACHERNDL *et al.* [1] had a diagnosis of either thromboembolic or congenital heart disease. There is still no clear evidence of a beneficial long-term response to vasodilators in these two groups of patients. The best data comes from MCLAUGHLIN *et al.* [4] in an uncontrolled study of intravenous prostacyclin in 33 patients with secondary pulmonary hypertension. MCLAUGHLIN *et al.* [4] included seven subjects with congenital heart disease, one of whom died, and reported an overall improvement in haemodynamics after an average of 12.7 months therapy. Only three subjects with thromboembolic disease were also included, of whom one also died. OLSCHEWSKI *et al.* [5] did not include any subjects with congenital heart disease in their study of nebulized iloprost and only two subjects with thromboembolic disease, one of whom died. The results of the 12-week randomized controlled trial of subcutaneous uniprost, which included congenital heart disease are awaited, however those with thromboembolic disease were excluded.

Furthermore, of the three remaining patients in the study of MACHERNDL *et al.* [1], two received therapy for only 3 months. HOEPER *et al.* [2] reported a beneficial long-term effect of nebulized iloprost after treating all their patients with primary pulmonary hypertension $\geqslant$12 months. Although BARST *et al.* [6] found a significant improvement after only 12 weeks of therapy with continuous intravenous prostacyclin in primary pulmonary hypertension, this was a much larger study and comparison was made with a control group receiving conventional therapy only.

The message from the study of MACHERNDL *et al.* [1] should not be that nebulized iloprost is ineffective, but that pulmonary hypertension due to congenital heart disease and chronic thromboembolism may not respond as well to vasodilators, and the results of treatment should be analysed separately. We agree with HIGENBOTTAM and SIDDONS [7] that a verdict on this form of therapy should await the outcome of the recently completed randomized controlled trial later this year, although unfortunately those with congenital heart disease and anatomically operable thromboembolic disease were excluded.

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