Paradoxical acute thromboembolism
during prostacyclin administration

Paradoxical acute brain thromboembolism during prostacyclin (PGI$_2$) acute challenge for primary pulmonary hypertension (PPH) in a patient with patent foramen ovale was reported. It is claimed to be the first case of thromboembolism during acute testing with prostacyclin (PGI$_2$) due to the evoked changes in haemodynamics. No information on the source of the embolism is given, however. In primary pulmonary hypertension, acute pulmonary vasodilatation is currently sought using inhaled nitric oxide, oral calcium channel blockers or infused PGI$_2$ and PGE$_2$, to predict the long-term effects of pulmonary vasodilators which might improve the quality of life and survival in some patients. PGI$_2$ has been demonstrated — like other substances — to be safe for testing for PPH. Systemic embolization of a pre-existing thrombus via a patent foramen ovale may occur during catheterization and cannot be totally prevented either with heparin or another anticoagulant therapy, with PGI$_2$ and PGE$_2$. Systemic vasodilatation is not documented and does not necessarily result from PGI$_2$ application at a rate of 10 ng kg$^{-1}$ min$^{-1}$. PGI$_2$ contracts (tonisation) rather than dilates the venous vascular bed. The systemic embolization of a right-sided thrombus as a consequence of PGI$_2$ is thus extremely unlikely. It seems to be associated to high-risk patients, simply reflecting the prevalence of thromboembolic complications, but does not necessarily arise in such patients. If the source of the embolism is unknown, there is no single reason, from a pharmacological standpoint, to think that the thromboembolism could have been avoided by inhaling nitric oxide. If local application is considered, PGI$_2$ and PGE$_2$ could be used locally (inhaled) as well.

The conclusions drawn are thus not substantiated by the data communicated. Acute thromboembolism seems to be much more likely associated to PGI$_2$ therapy rather than causative.

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References


A reply

In response to Drs Kritz and Sinzinger, we would like to comment on our report of a case of paradoxical thromboembolism during prostacyclin (PGI$_2$) acute challenge for primary pulmonary hypertension (PPH) (EUR Heart J 1996; 17: 153–4).

1. Drs Kritz and Sinzinger will probably agree that the Swan–Ganz catheter is the most likely primary site of thrombosis in our patient. Catheter-associated thrombosis is a well known complication of central venous catheterization, especially in patients with impaired haemodynamic status. In addition, Doppler examination of the deep veins of the legs disclosed no evidence of thrombosis in our patient.

2. Regarding the responsibility of PGI$_2$ in the constitution of acute paradoxical thromboembolism, we feel that Drs Kritz and Sinzinger misunderstood our conclusions. We only stated that 'changes in pulmonary and systemic haemodynamics induced by PGI$_2$ may have promoted the systemic embolization of a right-sided thrombus'. Because intravenous PGI$_2$ acts as a non-selective vasodilator, the safety of PGI$_2$ infusion during acute testing for PPH is not related to its specific vasodilating properties but rather to its very short half-life. From a pharmacological standpoint, transient systemic vasodilatation can be encountered with PGI$_2$ as with any other non-selective vasodilator. We agree that systemic vasodilatation is not necessarily found' during PGI$_2$ acute testing for PPH. However, it is well established that haemodynamic response to vasodilators in these patients is unpredictable and highly individual. A significant number of patients undergoing acute vasodilator testing for PPH exhibit a prevailing systemic response characterized by decreased systemic vascular resistance, increased cardiac output and unchanged or increased pulmonary artery pressure as a result of 'fixed' pulmonary vascular resistance. Clearly, our patient had such a haemodynamic response to 10 ng kg$^{-1}$ min$^{-1}$ PGI$_2$ infusion. Finally, PGI$_2$ administration in our patient resulted in an eight fold increase in mean right atrial pressure and reversal in mean interatrial pressure gradient. Drs Kritz and Sinzinger will certainly agree that even a transient rise in right atrial pressure may facilitate the embolization of a right-sided intracardiac thrombus through a patent foramen ovale. Such a response would not have been observed with a vasodilator with no or minimal action on the systemic vascular bed, such as inhaled nitric oxide.

We therefore remain firmly of the opinion that our patient's individual response to PGI$_2$ infusion created a favourable haemodynamic condition for the systemic (paradoxical) embolization of a Swan–Ganz catheter-related thrombus.

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References