Relation of cyclic guanosine monophosphate and cyclic adenosine monophosphate in reducing the toxic effects of protamine administration

To the Editor:

We read with great interest the article by Raikar and associates[1] regarding nitric oxide inhibition to relieve the adverse effects of protamine on blood pressure. They declared that hypotension caused by protamine administration can be blocked by nitrous oxide inhibition. We would like to add our experience to their information.

Adverse effects of protamine administration on various organ systems have been known for a long time. These changes were attributed to the increased complement levels associated with an increase in thromboxane and leukotriene levels. These mediators may impair the function of organs such as the heart and lungs, although these changes are mostly clinically insignificant. We[2] documented that leukotriene and thromboxane levels increased after heparin reversal with protamine. These changes, which were associated with an increase in cyclic guanosine monophosphate (cGMP) levels and a reduction in cyclic adenosine monophosphate (cAMP) levels, adversely affected myocardial function. Monitoring cardiac output with a fast-response thermistor allowed us to calculate the ejection fraction changes in the right ventricle. After protamine administration, while right ventricular end-diastolic volume became stable, right ventricular end-systolic volume increased significantly, indicating the same degree of impairment in myocardial contractility. However, we did not observe any significant change in pulmonary artery pressure. These pressure changes were associated with a temporary defect in myocardial oxidative metabolism, as indicated by the changes in myocardial oxygen consumption and myocardial lactate extraction. Prostacyclin usage reduced the toxic mediator release and improved myocardial function. After protamine administration, we observed that protamine use decreased the cGMP level in the blood and increased the cAMP level in the blood.[2, 3] In light of this study, we hypothesized that a fall in cAMP level and a rise in cGMP level are responsible for the toxic manifestations of heparin reversal with protamine, similar to our observation during ischemic reperfusion.[4] On the basis of this information, we used aminophylline, a phosphodiesterase inhibitor, to increase the cAMP level and observed that aminophylline use reduced the toxic mediator release and preserved myocardial function.[5] Finally, adverse effects of protamine on myocardial function can be controlled with agents that increase the cAMP level.

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Reply to the Editor:

We appreciate the comments of Dr. Katircioğlu and his colleagues. As noted in their letter, the adverse effects of protamine may be mediated through a variety of mechanisms, including the complement system. In our study, we measured the serum level of cyclic guanosine monophosphate (cGMP) and found no significant change with the administration of protamine. Therefore we could not conclude that a fall in the cGMP level correlated with the adverse effects of protamine. This investigation focused on inhibition of the nitric oxide pathway, which decreased the systemic hypotension produced by protamine administration.

Attempts to attenuate the adverse effects of protamine have met with variable degrees of success. There may be several effectors of the systemic effects of protamine, and these mechanisms might be expected to cause different clinical manifestations during protamine reversal of heparin.

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Is left ventricular outflow tract obstruction really relieved on long-term follow-up?

To the Editor:

Luciani and associates[1] report good results in their article titled "One-Stage Repair of Interrupted Aortic Arch, Ventricular Septal Defect, and Subaortic Obstruction in the Neonate: A Novel Approach." However, I am unsure about the long-term results.

I treated a baby girl, not a neonate, who had a simple ventricular septal defect (VSD) associated with infundibular posterior malalignment, which caused only a 30 mm Hg pressure gradient through the left ventricular outflow tract (LVOT). Preoperative echocardiographic examination showed that she had a large perimembranous VSD with a mild pressure gradient between the left ventricle and ascending aorta, which resulted from posterior malalignment of the infundibular septum to the LVOT. Cardiac catheterization showed that the right ventricular/left ventricular pressure ratio was 0.9 and the pressure gradient through the LVOT was only 30 mm Hg. Cardiac angiography also showed that the infundibular septum significantly deviated to the LVOT and the ascending aorta was relatively small (6 mm).

The patient was treated with catecholamines for cardiac