Effect of Levosimendan Treatment of Myocardial Stunning and Low-Output Syndrome After Cardiac Surgery

To the Editor:

The pathophysiologic mechanisms underlying myocardial stunning, especially following heart surgery, are fascinating and optimal treatment of the condition is of fundamental importance. We therefore read the recent article by Álvarez et al[1] with great interest and we must congratulate the authors on their excellent work. Nevertheless, we would like to make the following observations.

At least 14 studies have evaluated the usefulness of levosimendan in the treatment of low cardiac output in heart surgery performed in a variety of clinical situations: adult patients with normal or depressed preoperative systolic function, emergent surgical coronary revascularization, off-pump cardiac surgery, and even congenital heart disease in children. Four of those were randomized controlled trials.[2] There are no unanimous criteria for the dose of levosimendan used and the majority, though not all, use a loading dose of between 6 and 36 μ/kg, followed by infusion of between 0.1 and 0.3 μg/kg/min for varying periods of time. All confirm the beneficial hemodynamic effects of levosimendan and at least 6 also observed a positive effect on other variables, such as successful "weaning" from cardiopulmonary bypass without the need for circulatory assistance, the requirement for catecholamines, and the length of stay in postoperative intensive care.[2]

Álvarez et al[1] mentioned that ischemia-reperfusion caused by aortic clamping leads to transient ventricular dysfunction due to depletion of high-energy phosphates, intracellular calcium overload, generation of free radicals, and abnormalities of the coronary microcirculation. We would like to add that there is also a loss of myofilaments, reduced sensitivity of myofilaments to calcium, inactivation of enzymes, and stimulation of apoptosis in cardiac myocytes. In addition, inflammatory phenomena generated by ischemia increase circulating concentrations of proinflammatory cytokines and other inflammatory mediators that contribute to an increased depression of contractility.[3]

In our opinion, the cardioprotective effects of levosimendan through opening of ATP-sensitive potassium channels,[4,5] a potential therapeutic target in such situations, are of particular interest in addition to its effects as a calcium sensitizer: activation of those channels leads to calcium efflux, hyperpolarization of cell membranes, and reduction of calcium influx, thereby shortening the duration of the transmembrane action potential. In the smooth muscle fibers of the vessel wall, those effects lead to systemic and coronary vasodilation.[6] However, in addition, K_{ATP} channels, located both in the plasma and mitochondrial membranes, play an important role linking electrical activity and cellular metabolic status[4] and are involved in ischemic preconditioning, myocardial stunning, ischemia-reperfusion injury, and apoptosis of cardiac myocytes.[7] In our opinion, these effects of levosimendan have not been sufficiently appreciated. Our group has recently demonstrated the inotropic, hemodynamic, and cardioprotective effects of levosimendan in patients with acute myocardial infarction treated by primary angioplasty who subsequently developed heart failure and cardiogenic shock.[8,9]

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