

Levosimendan: clinical applications

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Patients with poor left ventricular function undergoing cardiac surgery frequently require inotropic drug support immediately after cardiopulmonary bypass. Indeed, pre-existing impaired ventricular function is further compromised by variable degrees of myocardial stunning and/or myocardial injury resulting from ischemia during aortic cross-clamping. Currently available inotropic drugs enhance myocardial contractility by increasing cyclic adenosine monophosphate concentrations which ultimately increases the myocardial concentrations of calcium. This effect is associated with an increase in myocardial oxygen consumption which may further alter the already compromised myocardial oxygen balance in patients with pre-existing ventricular dysfunction.

Levosimendan is a novel compound with a unique mechanism of action. By binding to cardiac troponin C, levosimendan enhances myofilament responsiveness to calcium, thereby increasing myocardial contraction without increasing myocardial oxygen consumption⁽³⁻⁵⁾. In addition, levosimendan activates K_{ATP} channels which are important mediators of ischemic and anesthetic cardioprotection. Levosimendan might thus have a potential benefit in patients with myocardial oxygen imbalance requiring inotropic drug support.

A potential indication for the use of levosimendan is the occurrence of postcardiotomy myocardial dysfunction. Ini-

tial reports mainly involved the administration of the drug either as last rescue therapy, compared with placebo, or as the sole therapy for low cardiac index after cardiac surgery. More recently, the effects of levosimendan were compared to milrinone treatment as inotropic support for weaning from cardiopulmonary bypass (CPB) in patients with a pre-operative ejection fraction $\leq 30\%$ undergoing elective cardiac surgery. The authors observed better maintenance of cardiac function with levosimendan, thereby endorsing the evidence that the drug is effective to support myocardial function in patients with postcardiotomy cardiac failure. In addition to its favourable hemodynamic effects, levosimendan was also suggested to have direct cardioprotective properties related to a preconditioning effect which is mediated through activation of mitochondrial K_{ATP} channels. The results of a recent study in coronary artery surgery patients suggest that this phenomenon might also be present in the clinical setting. The authors observed that a short 10 min infusion of levosimendan before the start of CPB was associated with lower postoperative troponin I concentrations and a higher cardiac index. This latter effect was not confirmed in a recent study in patients undergoing cardiac surgery.

In conclusion, the results of these studies indicate that levosimendan may provide an additional therapeutic option for inotropic support of patients with cardiac failure during surgery.