NEW ASPECTS IN INOTROPIC DRUG THERAPY

Prof. Roland Demeyere M.D., Ph.D.
University Hospital Gasthuisberg, Leuven, Belgium

Traditionally, beta-receptor agonists, the catecholamines including dobutamine, dopamine, epinephrine, norepinephrine and isoproterenol have been used as inotropic support in the perioperative period. Dopamine is still often used as a first-choice vasoactive drug with dopaminergic and - and -adrenergic effects. These effects are believed to be dose dependent and vary considerably between patients. Dobutamine is a -adrenergic agonist with positive inotropic and peripheral vasodilator properties and this drug is now considered as a first-line therapeutic choice. However, in the presence of beta-blockade, where higher than usual doses are necessary, phosphodiesterase III-inhibitors seem to have an advantage in comparison to dobutamine. Dopexamine might be the ideal drug to protect perfusion to the hepatosplanchnic and renal organs. Epinephrine is occasionally useful during the immediate postoperative period when high systemic blood pressures are sought While phosphodiesterase III inhibitors (milrinone, enoximone) increase myocardial contractility without excessive tachycardia or increasing myocardial oxygen demand, this class of drugs is also associated with distinct clinical disadvantages (arrhythmia, and sometimes excessive vasodilation).

The search for the “ideal positive inotropic drug” has continued and recently, a new class of agents, the calcium sensitizers, and specifically levosimendan, a member of this new class of drugs, was found to offer substantial clinical advantages over traditional beta-receptor agonists and phosphodiesterase inhibitors by increasing myocardial contractility without initiating tachycardia or arrhythmia nor increasing myocardial oxygen demand or excessive systemic vasodilation.

Endothelin receptor antagonism is also an attractive mechanism for potential treatment in heart failure, but a recent study with tezosentan was stopped because of disappointing interim results.

Glucose-insulin-potassium (GIK) infusions have been studied as metabolic adjuvants to enhance myocardial glucose uptake and oxidation. Glucagon-like-peptide-1 (GLP-1) with both insulinomimetic and insulinotropic actions has been shown to be also effective.