

Can we believe in levosimendan?

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Acute cardiac decompensation in patients with a pre-existing chronic heart failure is frequent, but its optimal management remains a controversial issue. Treatment depends on the precipitating cause, such as myocardial ischemia, arrhythmias, noncompliance with drug prescriptions, or concomitant noncardiac disorders. Dosage adaptation of standard heart failure drugs, in particular of loop diuretics and vasodilators is often a successful first step. Problems arise if symptoms persist and signs of hemodynamic deterioration occur. In such situations, the responsible physician is facing the following dilemma: should an inotropic agent be administered to increase cardiac output and improve organ perfusion? If the answer is yes, which inotropic agent would be the best choice? Several clinical studies indicate that dobutamine, still the first-line drug in many intensive care units; dopamine; or phosphodiesterase inhibitors (milrinone, enoximone) may worsen survival despite initial hemodynamic improvement¹⁻⁵. Increasing myocardial oxygen requirements and cardiac arrhythmias are the usual explanations for unfavorable outcomes. In view of such potential adverse events, many cardiologists are against the use of inotropic drugs in acute heart failure.

However, the introduction of the calcium sensitizer levosimendan could change this negative attitude. This new agent combines inotropic action with peripheral and coronary vasodilation and does not increase intracellular calcium and cyclic AMP concentrations. It is thus devoid of some of the disadvantages of sympathomimetic drugs.

In a direct comparison of levosimendan with dobutamine in a double-blind study (LIDO) in patients with severe low-output heart failure, the calcium sensitizer showed superior hemodynamic efficacy and better clinical outcome after up to 6 months⁶. The drug was also effective and well tolerated in patients with left ventricular failure following acute myocardial infarction⁷.

Now the BELIEF study, results published in the current issue of this journal⁸, included patients with decompensated heart failure who were treated in Brazilian centers, and it seems

to fully confirm the positive European experience, even in patients not responding to dobutamine infusions. Overall, 76.4% of patients could be classified as responders according to predefined clinical criteria. The drug was also well tolerated: no tendency to severe hypotension during levosimendan infusion and no increase in ventricular or supraventricular arrhythmias occurred. Nevertheless, it is clear that levosimendan will not save all patients with acute decompensation. Of the 182 patients, 27 (14.8%) died during hospitalization, mainly due to cardiogenic shock or severe hypotension on admission. As in other surveys, mortality of such acute complications of heart failure remains high, despite all modern therapeutic possibilities⁹.

A limitation of the BELIEF study⁸ is its observational nature without a comparative treatment group not using levosimendan. Although similar positive results during routine clinical use have been reported in a multicenter postmarketing study in Portugal¹⁰, the disappointing outcome of the recently published SURVIVE trial¹¹ will reduce the acceptance of levosimendan in those centers having no or only little experience with the drug. It should be realized, however, that in SURVIVE, several important safety aspects of an optimized levosimendan administration have not been observed: high and uniform loading and maintenance doses were given to all severely ill and intensively pretreated patients without hemodynamic monitoring. Therefore, overdosage together with unrecognized and uncorrected hypovolemia probably contributed to the high incidence of hypotension, supraventricular arrhythmias, and a lack of improvement in mortality compared with dobutamine. In contrast, in the BELIEF⁸ study, the initial infusion rate was only 0.1 mcg/kg/min, and loading doses were not given in about 20% of patients. Hypovolemia and hypokalemia were also excluded before levosimendan infusions were started.

The Brazilian experience confirms that under adequate conditions levosimendan is a very useful addition to the therapeutic armamentarium in patients with acutely decompensated congestive heart failure. Cardiologists and intensive care doctors who know how and when to use levosimendan will continue to believe in this new drug.

Key words

Levosimendan; Cardiotonic agents; Cardiac output, low; Heart failure congestive

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