

Is there a place for levosimendan in the intensive care unit?

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TO THE EDITOR: We read with great interest the article by Delaney and colleagues on the role of levosimendan in the intensive care unit.¹ Although we agree that two large trials, REVIVE² and SURVIVE,³ failed to show any survival difference between dobutamine and levosimendan in acute heart failure, we disagree with their conclusion that there is no place for levosimendan in the ICU.

It is dangerous to extrapolate the results of the SURVIVE study, as it targeted only patients with decompensated left ventricular failure. It did not include patients with right ventricular dysfunction, septic shock or acute respiratory distress syndrome.

Powell and De Keulenaer recently published a short case series of the use of levosimendan as a rescue therapy in patients with septic shock.⁴ Despite a high predicted 28-day mortality of 60%, all but one of these patients survived. Morelli and colleagues showed that, in patients with sepsis-related myocardial depression unresponsive to dobutamine, levosimendan exerts beneficial inotropic effects.⁵ In our experience, levosimendan as a continuous infusion (at a rate of 0.2 µg/kg per min), without a bolus injection, is safe and does not cause the ventricular arrhythmias seen with dobutamine. In another study by Morelli and colleagues,⁶ the use of levosimendan in patients with early acute respiratory distress syndrome improved right ventricular function by decreasing pulmonary vascular resistance.

Although all the above trials involved small numbers of patients, and hence conclusions could not be drawn, they should not be ignored. We believe levosimendan can play a role in patients with severe pulmonary hypertension and septic shock.

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IN REPLY: We thank De Keulenaer and Jenkins for their interest in our article on the role of levosimendan in the intensive care unit. It may help put our article into context to state that it arose from the proceedings of a Joint Faculty of Intensive Care Medicine meeting, where we were invited to participate on the "con" side in a pro-con debate on the utility of levosimendan in intensive care.

With that in mind, we believe our conclusion — that "the best evidence currently available suggests that levosimendan does not improve survival for patients with acute severe heart failure" — remains founded on the available evidence. Our focus was to assess briefly the evidence for the use of levosimendan as a treatment for acute or decompensated heart failure. Multiple clinical

trials have examined the effectiveness of levosimendan in this context. While a high-quality systematic review would help put all the available evidence into context, it is clear from the largest available randomised clinical trial, SURVIVE,¹ that there is little evidence for the efficacy of levosimendan in this particular population of patients.

As noted by De Keulenaer and Jenkins, there may be a role for levosimendan in other conditions. While some caution is needed in applying non-randomised studies because of the potential for bias in results,² it remains possible that levosimendan will have a role in particular conditions, such as acute respiratory distress syndrome,³ right ventricular failure⁴ and peripartum cardiomyopathy.⁵ We support the search for further evidence regarding the use of levosimendan in these conditions.