

Levosimendan: The Next Dobutamine?

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Dobutamine, a traditional beta-receptor agonist, is perhaps the most commonly used agent in the world to increase myocardial contractility. However, distinct clinical disadvantages exist when using this class of drugs (tachycardia, arrhythmia, increased myocardial oxygen demand). While phosphodiesterase inhibitors (milrinone) increase myocardial contractility without initiating tachycardia or increasing myocardial oxygen demand, this class of drugs is also associated with distinct clinical disadvantages (arrhythmia, sometimes excessive systemic vasodilation). Levosimendan, a member of a new class of drugs – calcium sensitizers – may 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.

Traditional beta-receptor agonists increase formation of intracellular cAMP whereas phosphodiesterase inhibitors prevent cAMP breakdown. Increased intracellular cAMP (from both classes of drugs) increases calcium current into myocytes to increase myocardial contractility. In contrast, levosimendan increases the sensitivity of myofilaments to calcium (increases myocardial contractility) without alteration of intracellular calcium levels. Potential clinical benefits of levosimendan include increased myocardial contractility (without increased intracellular calcium levels), vasodilation (coronary, systemic, pulmonary), and no effects on myocardial oxygen demand nor arrhythmogenesis. The most common adverse effects are headache and mild hypotension.

Clinical research experience has been accumulating with levosimendan. In patients with severe low-output heart failure, intravenous levosimendan has improved hemodynamic performance more effectively than dobutamine (fewer serious side effects, lower mortality). Several trials have validated the safety and efficacy of levosimendan as an inotropic agent. Several promising human studies on levosimendan usage in cardiac surgery have also been published, suggesting the drug may be useful in low-output states after cardiac surgery. The available evidence suggests that levosimendan enhances cardiac performance and reduces left ventricular afterload following cardiopulmonary bypass in patients with normal preoperative left ventricular function. Also, in addition to being effective in postoperative rescue therapy for patients with difficult weaning from cardiopulmonary bypass, elective preoperative initiation of levosimendan in patients with high perioperative risk or compromised left ventricular function appears to reduce catecholamine requirements, need for mechanical circulatory support, and duration of critical care.

In summary, levosimendan is a positive inotropic drug with vasodilating properties that has been extensively investigated in experimental studies and that is also increasingly the subject of clinical trials. To date, clinical experience with the drug is encouraging because it combines several beneficial actions that differ considerably from other cardiogenic drugs.

Levosimendan increases myocardial contractility without increasing intracellular calcium concentration, does not increase myocardial oxygen demand, does not increase heart rate, does not impair myocardial relaxation, improves coronary blood flow, reduces preload and afterload, and may also exert anti-ischemic actions. Initial clinical studies have revealed beneficial effects on short- and long-term survival compared with standard inotropes. The drug is associated with a low incidence of adverse effects when used in appropriate amounts. These encouraging preliminary results with levosimendan suggest that the drug may perhaps replace the more commonly utilized traditional beta-receptor agonists and phosphodiesterase inhibitors when one wants to increase myocardial contractility.

References

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