

USE OF LEVOSIMENDAN IN CARDIAC SURGERY PATIENTS WITH LOW EJECTION FRACTION

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1. Introduction: Cardiac surgery patients with a left ventricular ejection fraction (LVEF) of less than 30-35% represent a cohort of extremely high surgical risk. The physiological stress of cardiopulmonary bypass (CPB), ischemia-reperfusion injury, and the direct surgical trauma often precipitate postoperative low cardiac output syndrome (LCOS). LCOS is a leading cause of morbidity and mortality in this population, characterized by inadequate tissue perfusion despite satisfactory intravascular volume. Traditional inotropic agents, such as beta-adrenergic agonists (e.g., dobutamine), carry significant drawbacks, including increased myocardial oxygen consumption, arrhythmogenicity, and potential exacerbation of ischemic injury. Therefore, the development of alternative therapeutic strategies that provide effective inotropic support while protecting the myocardium is a paramount goal in modern cardiac surgery.

2. Unique Dual Mechanism of Action Levosimendan's efficacy stems from its novel, dual mechanism of action, which distinguishes it from conventional inotropes:

Calcium Sensitization: Levosimendan enhances myocardial contractility by binding to cardiac troponin C in a calcium-dependent manner. This stabilizes the calcium-induced conformational change, improving the efficiency of the contractile apparatus without increasing intracellular calcium concentration. This avoids the detrimental effects of calcium overload, such as increased energy consumption, diastolic dysfunction, and pro-arrhythmic potential.

Vasodilation and Cardioprotection: Through the opening of ATP-sensitive potassium (KATP) channels in vascular smooth muscle cells, Levosimendan induces systemic, pulmonary, and coronary vasodilation. This reduces preload and afterload, improving coronary blood flow and reducing myocardial workload. Furthermore, the opening of mitochondrial KATP channels is believed to mediate a potent preconditioning-like effect, protecting cardiomyocytes from ischemia-reperfusion injury.

3. Prophylactic Strategy and Improved Clinical Outcomes. A paradigm shift in the use of Levosimendan involves its prophylactic or preemptive administration in

high-risk patients, rather than as a rescue therapy for established LCOS. Numerous meta-analyses and randomized controlled trials (e.g., the CHEETAH, LEVO-CTS studies) have demonstrated that initiating Levosimendan before or during surgery in patients with low LVEF leads to:

- A significant reduction in the incidence of severe LCOS.

- A lower requirement for postoperative mechanical circulatory support (e.g., Intra-Aortic Balloon Pump - IABP).

- A trend towards reduced 30-day and long-term mortality.

- A decrease in the duration of mechanical ventilation and intensive care unit (ICU) stay.

4. Hemodynamic and Organ-Specific Benefits.

The hemodynamic profile of Levosimendan is particularly favorable in the context of post-cardiac surgery:

- Improved Cardiac Performance:** It produces a significant increase in cardiac output (CO) and stroke volume (SV).

- Optimal Unloading:** It reduces pulmonary capillary wedge pressure (PCWP) and systemic vascular resistance (SVR), effectively "unloading" the failing ventricle.

- Renal and Splanchnic Perfusion:** The combined effect of improved CO and vasodilation can enhance blood flow to vital organs, potentially reducing the risk of postoperative acute kidney injury (AKI) and splanchnic ischemia.

5. The Pharmacological Advantage of a Long-Acting Metabolite.

After a 24-hour infusion, the hemodynamic effects of Levosimendan persist for up to 7-9 days. This is attributed to its active metabolite, OR-1896, which has a prolonged half-life. This "pharmacological bridge" covers the most critical postoperative period (days 1-3), when the risk of LCOS is highest, without the need for continuous, high-dose inotropic infusion.

6. Conclusion and Clinical Implications.

Levosimendan has established itself as a cornerstone in the perioperative management of high-risk cardiac surgery patients. Its unique mechanism of action, which provides inotropic support without increasing myocardial oxygen demand, coupled with its vasodilatory and cardioprotective properties, offers a significant clinical advantage over traditional catecholamines. The strategy of prophylactic use in patients with severely impaired LVEF is evidence-based and should be integrated into standardized Enhanced Recovery After Surgery (ERAS) protocols for cardiac surgery. This approach not only improves survival and clinical outcomes but also contributes to more efficient use of healthcare resources by reducing the incidence of costly complications.

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USE OF PREGABALIN FOR CHRONIC SURGICAL PATHOLOGY

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Chronic post-surgical pain (CPSP) remains a significant clinical problem, developing in 10-20% of patients, which reduces quality of life and complicates rehabilitation. In the perioperative period, pregabalin can be used as a means of preventive analgesia to reduce acute pain and potentially decrease the incidence of pain chronicity, as well as to reduce opioid requirements and prevent the development of CPSP.