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Introduction to Landiolol in Acute Cardiac Care

An overview of landiolol, a potent and cardioselective beta-blocker offering a promising addition to the armamentarium for managing acute cardiac conditions for rapid and effective rate control with minimal adverse effects.

Cardiac emergencies present complex challenges in emergency medical settings, requiring prompt and effective management to improve patient outcomes (Bezati et al. 2023). Beta-blockers have historically played a critical role in the treatment of cardiovascular emergencies (Hindricks et al. 2020; Ibáñez et al. 2015) due to their efficacy in symptom relief and long-term prognosis improvement (Rienstra et al. 2013). However, concerns about their use in acute settings have arisen due to potential negative inotropic effects, especially in patients with compromised cardiac function (Taylor et al. 1981; Waagstein 1993; Yilmaz et al. 2010). In response to these concerns, landiolol, an ultra-short-acting and highly selective beta-1 blocker, has emerged as a promising pharmacologic agent, particularly in Japanese literature, for its favourable safety profile and effectiveness in managing various acute cardiac conditions (Bezati et al. 2023)

History of Landiolol

Landiolol, developed through the chemical modification of esmolol, was designed to be more potent and cardioselective (Iguchi et al. 1992). Early clinical trials demonstrated its efficacy in rapidly controlling cardiac arrhythmias. The first clinical trial on the efficacy for the rapid control of cardiac arrhythmias showed that landiolol reduced heart rate (HR) in all patients without significant adverse effects and, more importantly, without causing any significant reduction in the peripheral blood pressure (BP) (Atarashi et al. 2000).

Pharmacological Profile of Landiolol

Landiolol's pharmacologic profile offers several advantages over other beta-blockers in acute cardiac care. Unlike other beta-blockers, landiolol's metabolism primarily occurs via plasma cholinesterase, resulting in an ultra-short half-life and minimal renal or hepatic involvement, which contributes to its rapid onset and offset of action (Bezati et al. 2023). Its increased cardioselectivity (Iguchi et al. 1992; Nasrollahi-Shirazi et al. 2016) and minimal impact on L-type calcium channels (Bezati et al. 2023) and inward rectifier potassium channels contribute to enhanced haemodynamic stability (Shibata et al. 2012). Moreover, its rapid onset of action and lack of pharmacochaperoning behaviour makes it easier to titrate and discontinue, reducing the risk of cumulative effects or rebound phenomena (Bezati et al. 2023). Additionally, in high doses, landiolol may exert partial agonist effects on beta-1 receptors, potentially conferring cardioprotective and antiarrhythmic properties (Nasrollahi-Shirazi et al. 2016; Patel et al. 2008).

Applications of Landiolol in Acute Cardiac Care

Atrial Tachyarrhythmias Management

In the setting of acute cardiac care, particularly in patients with atrial tachyarrhythmias such as atrial fibrillation (AF) or atrial flutter (AFL), landiolol offers several advantages. Clinical studies have consistently shown its efficacy in achieving rapid rate control while minimising negative inotropic effects, making it particularly suitable for patients with compromised cardiac function or haemodynamic instability (Nagai et al. 1993; Kinugawa et al. 2014). Furthermore, its ultra-short half-life and titratability facilitate precise control of heart rate, allowing for optimisation of atrioventricular synchrony and reduction of symptoms associated with rapid atrial rates.

Management of Acute Heart Failure

Landiolol has emerged as a promising agent for managing acute heart failure (AHF), especially in patients with concomitant atrial tachyarrhythmias. In this population, rapid ventricular response can exacerbate heart failure symptoms and precipitate haemodynamic compromise. By achieving prompt rate control, landiolol helps alleviate symptoms such as dyspnoea and fatigue, thereby improving patient comfort and reducing the need for intensive care interventions. Moreover, its minimal impact on myocardial contractility and relaxation makes it a preferred option over other beta-blockers, which may exacerbate heart failure symptoms by depressing cardiac function (Iwahashi et al. 2019; Matsui et al. 2019).

Management in Patients with Reduced Ejection Fraction

Patients with reduced ejection fraction (EF) represent a challenging subset in acute cardiac care, as they are predisposed to both atrial tachyarrhythmias and haemodynamic instability. Landiolol's selective beta-1 blockade provides effective rate control without compromising cardiac output, making it well-suited for this patient population. Clinical studies have demonstrated its ability to achieve target heart rates while preserving stroke volume and cardiac index, thereby mitigating the risk of hypotension and worsening heart failure symptoms (Shinohara et al. 2020).

Considerations in Severe Renal Impairment

In patients with severe renal impairment, traditional beta-blockers may pose an increased risk of drug accumulation and adverse effects due to impaired drug clearance. Landiolol, with its predominantly hepatic metabolism and minimal renal excretion, offers a safer alternative in this population. By avoiding renal

clearance pathways, landiolol reduces the risk of drug accumulation and associated adverse events, making it a preferred choice for rate control in patients with compromised renal function (Kinugawa et al. 2014).

Management in Septic Cardiomyopathy

Septic cardiomyopathy, characterised by myocardial depression and impaired contractility in the setting of severe sepsis or septic shock, represents a unique challenge in acute cardiac care. Landiolol's beta-1 selective blockade can attenuate excessive adrenergic stimulation, thereby mitigating the risk of tachyarrhythmias and haemodynamic instability (Okajima et al. 2015). While its use in septic shock requires careful consideration alongside standard measures, landiolol may offer additional benefits in improving myocardial oxygen supply-demand balance and reducing the risk of arrhythmias in this critically ill population (Kakihana et al. 2020).

Conclusion

Experts recognise landiolol's potential as a valuable therapeutic option in acute cardiac care, particularly in patients with supraventricular tachyarrhythmias and impaired cardiac function. Its favourable safety profile and reversible adverse effects make it suitable for use even in critically ill patients (Bezati et al. 2023).

"studies have consistently shown the efficacy of landilol in achieving rapid rate control while minimising negative inotropic effects, suitable for patients with compromised cardiac function or haemodynamic instability"

However, dosing adjustments and close haemodynamic monitoring are crucial, especially in patients with severely reduced EF (Wada et al. 2016; Shinohara et al. 2020; Iwahashi et al. 2019) or those with septic shock (Lescroart et al. 2022).

In conclusion, landiolol represents a promising addition to the armamentarium for managing acute cardiac conditions, offering rapid and effective rate control with minimal adverse effects. Its unique pharmacologic properties make it particularly suitable for patients with impaired cardiac function or those at risk of arrhythmias in various clinical scenarios. Continued research and clinical trials are essential to further elucidate landiolol's role in optimising outcomes in acute cardiac care and to establish clear guidelines for its use in different patient populations (Bezati et al. 2023).

Disclaimer

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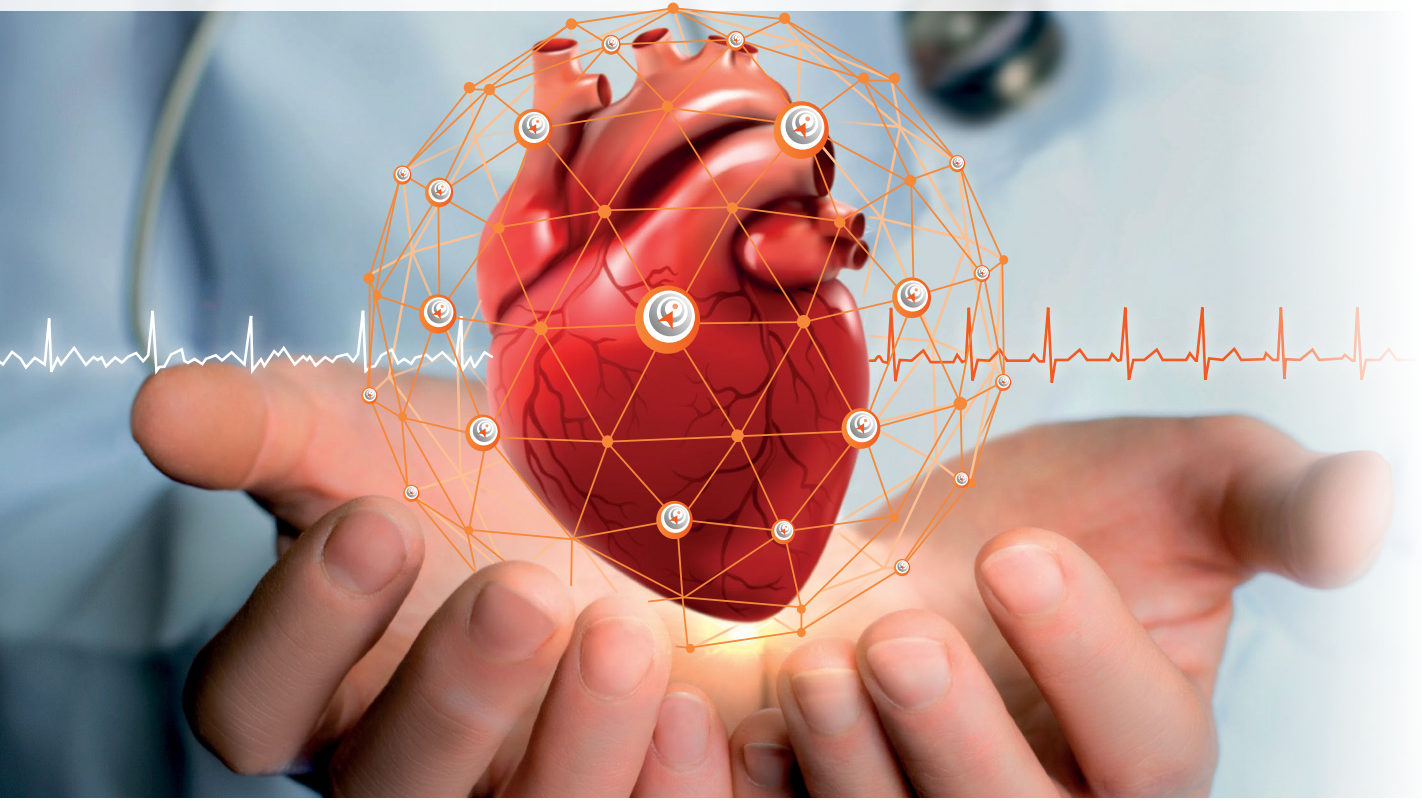
Rapibloc®
Landiolol hydrochloride

Rapid Rate Control with Myocardial Protection.[1]



Rapid control of ventricular rate in patients with SVTs and AF[1]

First-line for patients with cardiac dysfunction[2]

- **Limited effect** on blood pressure and inotropy[3]
- **Favourable safety profile for patients with renal and hepatic comorbidities** due to inactive metabolites and hydrolysis by plasma esterases[1,4]
- **Compatible with pulmonary disorder patients** due to highest cardioselectivity (β1/β2-selectivity = 255:1) among β1-blockers[5]
- **Limited rebound and tolerance effect** due to lack of pharmacochaperoning activity[6]

Rapibloc® 300 mg: Rapibloc® 300 mg powder for solution for infusion. **Composition:** A vial of 50 mL contains 300 mg landiolol hydrochloride which is equivalent to 280 mg landiolol. After reconstitution each mL contains 6 mg landiolol hydrochloride (6 mg/mL). Excipients with known effect: Mannitol E421, sodium hydroxide (for pH adjustment). **Therapeutic Indication:** Landiolol hydrochloride is indicated for supraventricular tachycardia and for the rapid control of ventricular rate in patients with atrial fibrillation or atrial flutter in perioperative, postoperative, or other circumstances where short-term control of the ventricular rate with a short acting agent is desirable. Landiolol hydrochloride is also indicated for non-compensatory sinus tachycardia where, in the physician's judgment the rapid heart rate requires specific intervention. Landiolol is not intended for use in chronic settings. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients, severe bradycardia (less than 50 beats per minute), sick sinus syndrome, severe atrioventricular (AV) nodal conductance disorders (without pacemaker): 2nd or 3rd degree AV block, cardiogenic shock, severe hypotension, decompensated heart failure when considered not related to the arrhythmia, pulmonary hypertension, non-treated phaeochromocytoma, acute asthmatic attack, severe, uncorrectable metabolic acidosis. For further information on warnings and precautions for use, interaction with other medicinal products and other forms of interaction, fertility, pregnancy, lactation, effects on ability to drive and use machines, unsiderable effects, and habituation effects, please refer to the published SmPC **Prescription only/available only from pharmacy. Date of revision of the text:** 09/2021. **Marketing authorization holder:** Amomed Pharma GmbH, Leopold-Ungar-Platz 2, 1190 Vienna, Austria

1 Summary of Rapibloc® Product Characteristics, current version. – **2** Hindriks G., et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). European Heart Journal (2020) 00, 1-126. – **3** Shibata et al. Direct Effects of Esmolol and Landiolol on Cardiac Function, Coronary Vasoactivity, and Ventricular Electrophysiology in Guinea-Pig Hearts. J Pharmacol Sci 118, 255 – 265 (2012). – **4** Yokoyama H. (2016) Stabilization in Off-Pump Coronary Artety Bypass. Springer Tokyo Heidelberg New York Dordrecht London © Springer Japan. – **5** European Heart Journal Supplements (2018) 20 (Supplement A), A1-A24. – **6** Nasrollahi-Shirazi S et al. Comparison of the b-adrenergic receptor antagonists landiolol and esmolol: receptor selectivity, partial agonism, and pharmacochaperoning actions. J Pharmacol Exp Ther 2016; 359:73–81

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