

PLENARY PRESENTATIONS

LAPPACONITINE HYDROBROMIDE (ALLAPININ): CLINICAL AND EXPERIMENTAL PROSPECTS

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Despite the widespread use of antiarrhythmic drugs, the optimal therapy for cardiac arrhythmias in patients with coronary artery disease (CAD) remains a subject of debate. Limitations regarding class IC drugs are largely based on the results of the CAST trials conducted over 30 years ago. Current experimental and clinical data suggest that certain representatives of this class may have more complex mechanisms of action and may demonstrate a favorable efficacy and safety profile when used rationally.

To evaluate the experimental mechanisms of action of lappaconitine hydrobromide and analyze its clinical efficacy in patients with CAD who underwent surgical myocardial revascularization.

The experimental part was performed using an aconitine-induced arrhythmia model in rats. Lappaconitine hydrobromide was administered prophylactically at a dose of ED₅₀, followed by evaluation of the expression of 84 cardiomyocyte target genes using real-time PCR. The clinical trial included 186 patients with coronary artery disease and tachyarrhythmias after surgical myocardial revascularization. Patients were divided into two main groups: those with atrial fibrillation (n=93) and those with high-grade ventricular extrasystoles (n=93). In each group, the efficacy of three approaches was compared: lappaconitine hydrobromide in combination with beta-blockers, amiodarone in combination with beta-blockers, and beta-blocker monotherapy. The incidence of postoperative tachyarrhythmias and the effectiveness of prophylactic antiarrhythmic therapy were assessed.

An experimental study demonstrated that lappaconitine hydrobromide affects not only sodium channels but also alters the expression of genes associated with potassium and calcium channels, as well as increases the expression of the acetylcholine transporter gene. This suggests a more complex mechanism of antiarrhythmic action than traditionally understood for class IC drugs. The clinical trial demonstrated comparability between the study groups in key clinical and surgical characteristics. The use of lappaconitine hydrobromide in combination with beta-blockers was associated with a statistically significant reduction in the incidence of postoperative atrial fibrillation and ventricular extrasystoles compared to beta-blocker monotherapy and demonstrated superiority over amiodarone therapy in several analyzed parameters. Short-term use of the drug in patients with preserved left ventricular systolic function was characterized by high clinical efficacy and a satisfactory safety profile. Current experimental data also demonstrate the potential for developing new lappaconitine hydrobromide derivatives with more pronounced activity at lower active substance concentrations. Conclusion. Lappaconitine hydrobromide exhibits a multifactorial mechanism of antiarrhythmic action that goes beyond the classic characteristics of class IC drugs. Its short-term use in combination with beta-blockers in patients with coronary artery disease after surgical myocardial revascularization and preserved left ventricular ejection fraction is an effective and safe method for preventing postoperative tachyarrhythmias. The obtained results support the rationale for further fundamental and clinical studies of the drug and its derivatives.