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**Pharmacokinetics and Pharmacodynamics of Low-, Intermediate-, and High-Dose Landiolol and Esmolol During Long-Term Infusion in Healthy Whites.**

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Abstract

The pharmacokinetics, pharmacodynamics, safety, and tolerability of long-term administration of esmolol and landiolol, a new fast-acting cardioselective  $\beta$ -blocker, were compared for the first time in Caucasian subjects in a prospective clinical trial. Twelve healthy volunteers received landiolol and esmolol by continuous infusion for 24 hours in a randomized crossover study using a dose-escalation regimen. Blood concentrations of drugs and metabolites, heart rate, blood pressure, ECG parameters, and tolerability were observed for 30 hours and compared. Drug blood concentrations and areas under the curve were dose-proportional. The half life of landiolol (4.5 minutes) was significantly shorter than that of esmolol (6.9 minutes). Volume of distribution and total clearance were lower for landiolol. Heart rate reduction was faster and more pronounced with landiolol and retained throughout the administration period; effects on blood pressure were not different. Landiolol turned out to be superior to esmolol with respect to pharmacokinetic and pharmacodynamic profile and local tolerability.

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