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Pharmacodynamic and Pharmacokinetic Studies on Prizidilol and Nipradilol (K-351), Antihypertensive Drugs with Combined Vasodilator and β -Adrenoceptor Blocking Actions, in Rabbits

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Effects of prizidilol and nipradilol (K-351), β -adrenoceptor antagonists with vasodilator action, on blood pressure and heart rate were studied in normotensive conscious rabbits after i. v. administration. In addition, we investigated relationships between plasma drug concentrations and β -adrenoceptor blocking activity as estimated by the inhibition of isoproterenol-induced tachycardia and vasodilator activity as assessed by the inhibition of pressor response to angiotensin II (ANG II). Prizidilol (4 mg/kg) produced a significant and sustained fall in blood pressure and a slight increase in heart rate, while hydralazine (2 mg/kg) caused the same degree of hypotension and a marked tachycardia. Nipradilol (1 mg/kg) caused a significant reduction of resting heart rate, but had no significant effect on blood pressure. Propranolol (1 mg/kg) did not affect resting blood pressure and heart rate. Hypertensive response to ANG II was significantly attenuated only by hydralazine. Isoproterenol-induced tachycardia was significantly suppressed by prizidilol, nipradilol and propranolol. Good correlations were observed between β -adrenoceptor blocking activity and plasma drug concentrations. These data suggest that prizidilol has an advantage over hydralazine to induce less tachycardia, but still may cause a certain degree of increase in heart rate. Nipradilol has a more potent β -adrenoceptor blocking action than propranolol, while its vasodilator action is not obvious, at least in rabbits. Plasma concentrations of prizidilol and nipradilol are good indicators for β -adrenoceptor blocking activity, but not for vasodilator activity.

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