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Effect of Selective Blockade of α_2-Adrenoceptor Subtypes on Cardiovascular System in Rats

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Selective blockade of various α_2-adrenoceptors exerts various effects on the cardiovascular system in rats. Blockade of $\alpha_{2A/D}$-adrenoceptors in experimental animals decelerates and then accelerates HR. Blockade of α_{2B}-adrenoceptors produces a negative chronotropic effect; blockade of α_{2C}-adrenoceptors has a positive chronotropic effect. Administration of selective blockers of $\alpha_{2A/D}$- and α_{2B}-adrenoceptors causes hypotension, while selective blockade of α_{2C}-adrenoceptors increases BP.

Key Words: *heart; chronotropy; blood pressure; rat*

α_2-Adrenoreceptors (α_2-AR) are located in the vasomotor center in the medulla oblongata, on presynaptic membranes of adrenergic fibers, and on postsynaptic membranes of different cells including cardiomyocytes [5,6,9]. Molecular genetic studies have identified three α_2-AR subtypes: α_{2A} (α_{2D} in rats), α_{2B}, and α_{2C} [3,4,7]. However, understanding the role of individual receptor subtypes in regulating specific physiological functions was perplexed for a long time due to lack of subtype-specific ligands.

It was shown that α_2-AR are present in vascular smooth muscles. Inhibiting sympathetic regulatory influences, α_2-AR can reduce systemic BP [11]. The dominant role of α_{2A}-AR in the regulation of the cardiovascular system is confirmed by studies demonstrating elevation of BP and HR after elimination of the gene encoding α_{2A}-AR [2]. Presynaptic α_{2A}- and α_{2C}-AR regulate norepinephrine release in cardiac sympathetic nerve endings [10], while their knockout leads to heart hypertrophy and failure due to chronic increase in norepinephrine release in the heart and increased secretion of epinephrine from the adrenal glands [1,8]. α_{2B}-AR are located mainly on the postsynaptic membrane [10] and are possibly involved in the development of acute coronary pathology [12]. Further studies of α_2-AR subtypes will help to clarify their role in the regulation of body functions and develop drugs blocking or activating different α_2-AR subtypes.

Here we studied the effect of selective blockade of α_2-AR subtypes on heart chronotropy and BP in adult rats.

MATERIALS AND METHODS

The study was carried out on 20-week-old white outbred rats (n=40). The animals were narcotized with 25% urethane (800 mg/kg body weight intraperitoneally). α_2-AR antagonist (yohimbine, 1 mg/kg; Sigma), selective $\alpha_{2A/D}$-AR antagonist (RX 821002; 0.1 mg/kg), α_{2B}-AR blocker (imiloxan hydrochloride; 1 mg/kg), and α_{2C}-AR blocker (JP-1302; 0.3 mg/kg) were injected into the right femoral vein; all blockers were from Tocris. ECG was recorded and processed on a computer continuously throughout the experiment. BP was measured using SDK-1 device for non-invasive evaluation of systolic BP. The data were transferred from the device to the computer and processed using LGraf soft.

The obtained data were statistically processed using Student's t test and nonparametric Wilcoxon's test.

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