Effect of Selective Blockade of α2-Adrenoceptor Subtypes on Cardiovascular System in Rats

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Selective blockade of various α2-adrenoceptors exerts various effects on the cardiovascular system in rats. Blockade of α2A-adrenoceptors in experimental animals decelerates and then accelerates HR. Blockade of α2C-adrenoceptors produces a negative chronotrophic effect; blockade of α2B-adrenoceptors has a positive chronotrophic effect. Administration of selective blockers of α2A- and α2C-adrenoceptors causes hypotension, while selective blockade of α2B-adrenoceptors increases BP.

Key Words: heart; chronotropy; blood pressure; rats

α2-adrenoceptors (α2-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 α2-AR subtypes: α2A, α2B, and α2C [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 α2-AR are present in vascular smooth muscles. Inhibiting sympathetic regulatory influences, α2-AR can reduce systemic BP [11]. The dominant role of α2A-AR in the regulation of the cardiovascular system is confirmed by studies demonstrating elevation of BP and HR after elimination of the gene encoding α2A-AR [2]. Premature α2A- and α2B-AR regulate norepinephrine release in cardiac sympathetic nerve endings [10], while their knockout leads to heart hypertrophy and fatigue due to chronic increase in norepinephrine release in the heart and increased secretion of epinephrine from the adrenal glands [1, 8]. α2B-AR are located mainly on the post-synaptic membrane [10] and are possibly involved in the development of acute coronary pathology [12]. Further studies of α2-AR subtypes will help to clarify their role in the regulation of body functions and develop drugs blocking or activating different α2-AR subtypes.

Here we studied the effect of selective blockade of α2-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=49). The animals were narcotized with 2.5% urethane (800 mg/kg body weight intraperitoneally), α2A-AR antagonist (yohimbine, 1 mg/kg; Sigma), selective α2B-AR antagonist (RX 821007, 0.1 mg/kg), α2A-AR blocker timolol hydrochloride (1 mg/kg), and α2C-AR blocker (JP-1102, 0.3 mg/kg) were injected into the right femoral vein; all blockers were from Toeris. ECG was recorded and processed on a computer continuously throughout the experiment. BP was measured using SD-1 device for non-invasive evaluation of systolic BP. The data were transferred from the device to the computer and processed using Lirlab soft.

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

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