THE ROLE OF ALPHA2 AGONISTS IN ANESTHESIOLOGY

Mervyn Maze

ADRENERGIC RECEPTORS AND THEIR AGONISTS

The actions of catecholamines are mediated through the activities of agonists on two types of adrenergic receptors, alpha receptors and beta receptors. Alpha receptors are subdivided into two groups, alpha1 (alpha1A, alpha1B, and alpha1D) receptors and alpha2 (alpha2A, alpha2B, and alpha2C) receptors. While alpha receptors were initially divided into subtypes based upon the presynaptic or postsynaptic location of the receptor, this division is no longer reasonable. For example, alpha2 receptors may be located presynaptically, postsynaptically, or extrasynaptically (4). Rather, the various receptor subtypes are best characterized by molecular techniques and cloning. Beta receptors are subdivided into three groups: beta1, beta2, and beta3. These nine different adrenoreceptor subtypes mediate the variety of effects of only two physiologic agonists: epinephrine and norepinephrine.

ALPHA1 ADRENERGIC RECEPTORS

Alpha1 adrenoceptors are present in several tissues including those of the brain, heart, smooth muscle, liver, and spleen (6). Binding of alpha1 agonists at the neuro-effector junction induces a variety of physiologic effects including vasoconstriction, glycogenolysis, and increased heart rate and contractility. The various subtypes, or differences in subtype receptor density in disparate tissues, may modulate the diverse physiologic functions of alpha1 agonists.
**ALPHA 2 ADRENERGIC RECEPTORS**

Alpha2 adrenoceptors can be found in the central nervous system (CNS), peripheral nerves (somatic and autonomic), autonomic ganglia, and are ubiquitously distributed throughout the body but especially in tissues innervated by the sympathetic nervous system. Postsynaptic alpha2 adrenoceptors are also found in effector organs such as vascular smooth muscle. Activation of alpha2 receptors produces a variety of responses. Stimulation of presynaptic alpha2 receptors located in the sympathetic nerve endings inhibits the release of the neurotransmitter norepinephrine (4). Activation of postsynaptic receptors by alpha2 agonists in the CNS leads to inhibition of sympathetic activity, decreases in blood pressure and heart rate, decreased arousal, sedation, and relief of anxiety, and binding of agonists to alpha2 adrenoceptors in the spinal cord producing analgesia (4). Peripheral alpha2 receptors in blood vessels mediate vascular smooth muscle contraction (4). Thus, rapid intravenous injection of a potent alpha2 agonist can initially produce an increase in blood pressure resulting from a peripherally induced increased vascular resistance. This effect is transitory, as centrally mediated inhibition of sympathetic activity becomes dominant.

In addition, intestinal motility, salivation, and secretion of gastrointestinal fluids are partially regulated by alpha2 adrenoceptors (4). Activation of alpha2-receptors in the kidneys stimulates sodium and water excretion (4). The physiologic role of alpha2-receptors in the pancreas, adipose tissue, and platelets is incompletely understood. Studies in alpha2-adrenoceptor knockout mice have clarified the role of the various alpha2 receptor subtypes in cardiovascular regulation (7). It appears that the central hypotensive action of alpha2 agonists is due to an action mediated by alpha2A subtype receptors. Increases in systemic vascular resistance and hypertensive responses to alpha2 agonists are a result of stimulation of alpha2B receptors.

**BETA ADRENERGIC RECEPTORS**

Binding of an agonist to beta-receptor mediates a number of different effects (8). Stimulation of beta1 receptors increases the heart rate, contractility, and cardiac impulse conduction velocity. In addition, beta1