Clinical Pharmacokinetics of Vasodilators
Part II

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Abstract

Stimulating cardiac \( \beta_1 \)-adrenoceptors with oxyfedrine causes dilatation of coronary vessels and positive inotropic effects on the myocardium. \( \beta_1 \)-adrenergic agonists increase coronary blood flow in nonstenotic and stenotic vessels.
The main indication for the use of the phosphodiesterase inhibitors pamrinone, mirinone, enoximone and piroximone is acute treatment of severe congestive heart failure. Theophylline is indicated for the treatment of asthma, chronic obstructive pulmonary disease, apnea in preterm infants ans sleep apnea syndrome.

Severe arterial occlusive disease associated with atherosclerosis can be beneficially affected by elcosanoids. These drugs must be administered parenterally and have a half-life of only a few minutes.

Sublingual or buccal preparations of nitrates are the only prompt method (within 1 or 2 min) of terminating anginal pain, except for biting nifedipine capsules. The short half-life (about 2.5 min) of nitroglycerin (glyceryl trinitrate) makes long term therapy impossible. Tolerance is a problem encountered with longer-acting nitric oxide donors.

Knowledge of the pharmacokinetic properties of vasodilating drugs can prevent a too sudden and severe blood pressure decrease in patients with chronic hypertension. In considering the administration of a second dose, or another drug, the time necessary for the initially administered drug to reach maximal efficacy should be taken into account.

In hypertensive emergencies urapidil, sodium nitroprusside, nitroglycerin, hydralazine and phentolamine are the drugs of choice, with the addition of β-blockers during catecholamine crisis or dissecting aortic aneurysm.

Childhood hypertension is most often treated with angiotensin-converting enzyme (ACE) inhibitors or calcium antagonists, primarily nifedipine. Because of the teratogenic risk involved with ACE inhibitors, extreme caution must be exercised when prescribing for adolescent females.

The propagation of health benefits to breast-fed infants, combined with more women delaying pregnancy until their fourth decade, has entailed an increase in the need for hypertension management during lactation. Low dose hydrochlorothiazide, propranolol, nifedipine and enalapril or captopril do not pose enough of a risk to preclude breastfeeding in this group.

The most frequently used antihypertensive agents during pregnancy are methyldopa, labetalol and calcium channel antagonists. Methyldopa and β-blockers are the drugs of choice for treating mild to moderate hypertension. Prazosin and hydralazine are used to treat moderate to severe hypertension and hydralazine, urapidil or labetalol are used to treat hypertensive emergencies. The use of overly aggressive antihypertensive therapy during pregnancy should be avoided so that adequate uteroplacental blood flow is maintained. Methyldopa is the only drug accepted for use during the first trimester of pregnancy.

1. α-Adrenergic and Imidazole Receptor Agents

Nonspecific α-antagonists, such as phentolamine and phenoxbenzamine block noradrenaline (norepinephrine) both pre- (α2) and post- (α1) synaptically. The double blockade inactivates the normal feedback mechanism, resulting in higher noradrenaline levels. High noradrenaline levels stimulate β-receptors in the heart, resulting in increased cardiac output which compensates for much of the blood pressure (BP) reduction achieved by vasodilation. Specific α1-antagonists such as urapidil, prazosin and its derivatives do not interfere with the normal noradrenaline feedback mechanism and noradrenaline is not increased. Peripheral vasodilation pre-