Use of inotropic agents in open heart surgery

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Inotropic drugs, particularly sympathomimetic agents, which are primarily used in the management of sudden pump failure, increase the velocity and force of ventricular contraction. This action is observed in isolated cardiac muscle preparations, in intact animal studies, and by measuring various indices of contractility in man. For example, careful measurement of ventricular dimensions during infusion of dopamine reveals a reduced end-diastolic volume, increased velocity of wall movement during systole, and a decreased end-systolic volume.

All inotropic drugs exert some peripheral vascular actions that make it difficult to evaluate the effects of a pure inotropic intervention. Even if pure inotropic agents were available it would be difficult to isolate their inotropic effects from reflex circulatory effects that may occur. For example, any increase in stroke volume generated by more forceful ventricular contraction would lead to a change in arterial blood pressure, which in awake or lightly anesthetized man, secondarily leads to reflex changes in cardiac performance and a decrease in peripheral resistance due to stimulation of baroreceptors.

Inotropic drugs in normal man increase coronary blood flow in proportion to the increase in myocardial oxygen consumption associated with increased

contractility, increased cardiac work, increased heart rate, and increased metabolic rate associated with the use of these agents. In patients with acute coronary artery occlusion and myocardial infarction, the use of inotropic agents to support acute heart failure is associated with increased risk of extension of the size of infarction because of increased myocardial oxygen demands. The rationale for their use is based upon the fact that improved ventricular performance and increased arterial blood pressure may restore coronary flow and oxygen supply.

The initial evaluation of the patient intraoperatively and in the perioperative period, when impaired cardiac performance is associated with arterial hypotension, should be addressed to determination of the adequacy of blood volume replacement, since hypovolemia is a frequent cause of impaired cardiac performance and low cardiac output. Adequate volume replacement is a prerequisite before any therapeutic intervention with positive inotropic agents. Volume expansion is indicated for patients with hypotension and low or normal ventricular filling pressures (below 8 mm Hg). When these conditions exist, measures to correct hypoventilation; hypoxemia; alkalosis secondary to hyperventilation; metabolic acidosis; and electrolyte abnormalities, especially hyperkalemia and hypokalemia may be more important in restoring ventricular function during and after heart surgery than use of inotropic drugs.

Epinephrine

Epinephrine is an endogenous sympathomimetic with both alpha- and beta-receptor-stimulating properties. Epinephrine stimulates cardiac beta-receptors causing an increase in heart rate and myocardial contractility and enhanced excitability of pacemaker tissue not only at the sinoatrial node but also at secondary pacemaker sites. The latter effect of epinephrine may cause complications because of increased ventricular irritability and ventricular arrhythmias. The effect of epinephrine on peripheral vascular resistance is the result of its effects on both alpha- and beta-receptors in various vascular beds. In general, low-dose infusion of epinephrine may be associated with a decrease in arterial blood pressure and increase in pulse pressure due to cardiac stimulation and peripheral vasodilation associated with the drug's beta-receptor stimulating properties. At higher doses (usually >2 μg/min) the predominant circulatory effects of epinephrine are cardiac stimulation and increased peripheral vascular resistance resulting in increased arterial blood pressure because of alpha- and beta-receptor stimulation. Epinephrine, although useful in the treatment of acute cardiac failure, has been used less frequently in many cardiac surgery centers because of the ventricular arrhythmias associated with its use.

Norepinephrine

Norepinephrine is the neurotransmitter stored in and released from sympathetic adrenergic postganglionic nerves. Norepinephrine acts principally on alpha-receptors and has a much weaker beta-receptor-stimulating action. However, norepinephrine has relatively strong cardiac beta-receptor ($beta_1$-adrenergic receptor) stimulating actions causing an increase in myocardial contractility and an increase in cardiac output at low doses (<2 μg/min). However, at higher doses (>3 μg/min), norepinephrine infusion is usually associated with decreased cardiac output and increased peripheral vascular resistance because of its strong alpha-receptor

stimulating actions. In patients with oliguria or pulmonary hypertension, therapy of low cardiac output states with norepinephrine may result in a worsening of the hemodynamic situation due to the potent alpha constriction properties of this drug.

Isoproterenol

Isoproterenol is a drug with pure beta-receptor-stimulating properties. This drug will produce increases in heart rate, contractility, and cardiac output while arterial blood pressure may remain unchanged or decreased because of its peripheral dilator properties. Isoproterenol may be useful in treatment of patients with right ventricular dysfunction associated with pulmonary hypertension because of its ability to lower pulmonary vascular resistance as well as its cardiac stimulating properties. Isoproterenol may be particularly useful in patients with slow heart rates associated with low cardiac output states and may be infused at rates of 1 to 2 μg/min. The major disadvantage of isoproterenol in patients with ischemic heart disease is the tendency of some patients to develop tachycardia and ventricular arrhythmias, which may contribute to any hypotension already present.

Dopamine

Dopamine is an endogenous catecholamine and is the immediate precursor of norepinephrine in its biosynthetic pathway. Dopamine has both alpha- and beta-receptor-stimulating properties. Cardiac beta-receptor stimulation by this drug results in an increase in heart rate, myocardial contractility, and cardiac output. This drug also has the ability to release norepinephrine from myocardial storage sites. The effect of dopamine on peripheral vascular beds may be primarily beta or alpha, depending on the dosage and vascular bed. In addition, a non-beta vasodilator effect occurs at low dosage in the renal, mesenteric, coronary, and cerebral vascular beds and has been attributed to binding of the drug with dopamine receptors in these vascular beds. This effect is not blocked by atropine, propranolol, or other beta agonists or beta antagonists. At low doses (2 to 5 μg/kg/min) in normal subjects cardiac contractility, cardiac output, and renal blood flow increase with a slight increase or no change in heart rate and either a reduction or no change in total peripheral vascular resistance. The effect of larger doses of dopamine (>5 or 6 μg/kg/min) is to increase peripheral and pulmonary vascular resistance and blood pressure while reducing renal blood flow because of predominantly alpha-receptor effects at the higher doses.

Dobutamine

Dobutamine is a synthetic catecholamine that acts on cardiac beta-receptors ($beta_1$), peripheral vascular beta-receptors ($beta_2$), and on alpha-adrenergic receptors. Dobutamine increases heart rate, myocardial contractility, and cardiac output. Unlike dopamine, dobutamine does not appear to stimulate the heart indirectly by releasing endogenous norepinephrine. Dobutamine exerts a peripheral vasodilator effect that is much weaker than the peripheral vascular beta-receptor-stimulating effect of isoproterenol. Dobutamine also has an alpha-adrenergic-stimulating action that is much weaker than that exerted by norepinephrine. Doses of 5 to 10 μg/kg/min may be useful to treat low cardiac output states in patients during emergence from cardiopulmonary bypass. This drug shares some of the same

potential disadvantages associated with the use of other cardiac beta-stimulating drugs. Ventricular arrhythmias, potential for extension of acute infarctions and, in some instances, deleterious effects associated with alpha-receptor-stimulating actions have led to studies of combined inotropic-vasodilator therapy for acute cardiac failure in the perioperative period.

Combined use of inotropic and vasodilator drugs

Inotropic and vasodilator drugs work through independent mechanisms to augment stroke volume. Vasodilator drugs exert no direct effect on myocardial contractility in isolated preparations. Drugs that decrease arteriolar resistance reduce aortic outflow resistance (aortic impedance) and left ventricular end-systolic volume. For some of the vasodilator drugs these effects are partially offset by a simultaneous reduction in end-diastolic volume, which appears to be due not only to the increased stroke volume, but also to an effect of the drug on venous capacitance vessels and a reduction in central blood volume. The decreases in heart size and aortic impedance result in decreased cardiac work and oxygen requirements. Thus the metabolic effects of inotropic drugs may be in part countered by the use of vasodilator drugs. The most commonly used direct-acting vasodilator, sodium nitroprusside, has a direct effect on vascular smooth muscle in the peripheral and pulmonary circulations resulting in unloading of both the left and right ventricles. It is usually used at infusion rates of 10 to 15 μg/min. Nitroprusside has potent effects both on arterial resistance vessels and on venous capacitance vessels, and in some patients with intractable acute heart failure when nitroprusside is used in conjunction with a potent inotropic agent such as dopamine, the combined effects of the two agents in improving ventricular function are much greater than can be achieved with either of the agents alone. Nitroglycerin has also been found to be useful alone or in conjunction with inotropic drugs in the treatment of acute heart failure. Nitroglycerin when given sublingually appears to achieve a major part of its desirable therapeutic effect and relief of angina by decreasing left ventricular filling pressure and tends to reduce preload more than afterload, although a reduction in afterload also may contribute significantly to decreased myocardial oxygen requirements. Nitroglycerin appears to exert a greater effect on venous capacitance vessels than nitroprusside. Nitroglycerin may be infused intravenously at a rate of 0.2 to 1 μg/kg/min. Hypotension and tachycardia may occur with administration of both nitroprusside and nitroglycerin, and a few patients exhibit relatively little response to one of these drugs but rarely to both of them. Phentolamine, an alpha-adrenergic blocking drug, as well as ganglionic blocking drugs have also been used as vasodilators in conjunction with the use of inotropic agents. Rapid direct-acting vasodilators are also used with some frequency to reverse acute postoperative episodes of hypertension following coronary artery surgery.