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Verapamil Treatment of Intraoperative Coronary Artery Spasm

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Recurrent coronary artery spasm, also known as Prinzmetal's or variant angina, has been treated effectively by chronic oral administration of calcium entry blocking drugs.[1,2] Coronary spasm can occur in the perioperative period, ranging from asymptomatic ST segment changes to profound myocardial ischemia producing dysrhythmias and/or hypotension.[3,4] This diagnosis should be considered whenever ST segment changes suggestive of myocardial ischemia appear suddenly in the absence of hemodynamic changes related to increased oxygen demand or decreased supply. Treatment of perioperative coronary spasm with iv and intracoronary nitroglycerin has been unreliable.[3,5] Sublingual,[6] nasogastric,[5] and intracoronary[4] nifedipine, a calcium entry blocking drug not available in an aqueous form, has been used perioperatively with success. This is a report of the occurrence of an episode of apparent coronary vasospasm in the intraoperative period prior to cardiopulmonary bypass, in which another calcium entry blocker, verapamil, was administered iv to treat ST segment elevation that was refractory to intravenous nitroglycerin.

Report of a Case

An obese 58-year-old man with Type IV hyperlipidemia who underwent triple coronary artery bypass operation 5 years ago was scheduled for repeat operation due to the recent onset of severe angina pectoris. Chronic medications included oral nifedipine, controlled release nitroglycerin, procainamide, dipyramidole, aspirin, and topical nitroglycerin. Current cardiac catheterization revealed 100% proximal occlusion of the three arteries originally bypassed (left anterior descending, second obtuse marginal, and right) and atheromatous obstruction of all three grafts ranging from 60% to 95% of their lumens. Left ventricular ejection fraction was 0.65. Preoperative resting electrocardiogram showed sinus bradycardia at a rate of 58 bpm and nonspecific ST segment and T wave changes. Twenty-four-hour Holter monitoring revealed frequent premature ventricular beats. Treadmill exercise stress testing was performed for 18 min without chest pain or ST segment changes.

The patient received his chronic medications up until the night prior to surgery. He was premedicated with secobarbital 100 mg orally. Upon arrival in the operating room, arterial blood pressure was 150/70 mmHg and heart rate was 64 bpm. Anesthesia was induced over 10 min with iv diazepam (20 mg), fentanyl (1.75 mg), and pancuronium (10 mg). Supplemental isoflurane (1.0–1.5%) in oxygen was given to control arterial blood pressure during chest incision, sternotomy, and exposure of the heart in preparation for coronary artery bypass grafting. Ventilation was controlled to maintain Pa_{CO_2} between 36–41 mmHg, and Pa_{O_2} always was greater than 250 mmHg. Systolic blood pressure was maintained between 105–140 mmHg, while diastolic blood pressure ranged from 60 to 80 mmHg. Heart rate increased transiently during pericardial dissection to 92 without ST segment changes in any electrocardiographic lead and was treated with four incremental doses of propranolol (1 mg each) to maintain a heart rate of less than 80 beats per minute.

One hour after anesthesia had begun and 35 min after the last dose of propranolol, during an absence of surgical stimulation while the harvested vein was being prepared, ST segment elevation of 0.4 mV in lead V_5 suddenly appeared and was associated with reciprocal 0.1 mV ST segment depression in the inferior leads. Arterial blood pressure just prior to this event was 130/70 mmHg and heart rate was 75 bpm; neither changed at the time of ST segment elevation. One minute later, sinus rhythm changed suddenly to ventricular fibrillation, which reversed spontaneously, after 10 s of cardiac massage. Arterial blood pressure then was 125/65 mmHg and the electrocardiogram again showed sinus rhythm at a rate of 73 bpm, but the ST segment elevation was unchanged. The sternal retractor was removed, and the previous coronary artery bypass grafts were inspected to ensure the absence of external compression. Arterial blood gas analysis revealed a Pa_{O_2} of 276 mmHg, Pa_{CO_2} of 37 mmHg, and a pH_a of 7.40; potassium was 4.1 mEq/L.

Nitroglycerin, 200 μg was administered iv in four 50-μg doses over 10 min. Arterial blood pressure decreased to 110/75 mmHg and heart rate increased to 82 bpm, but the electrocardiogram did not change (fig. 1). Administration of 2.5 mg of verapamil iv resulted in no relative change in ST segment position. After two additional 2.5 mg increments of verapamil over the next 5 min to a total dose of 7.5 mg, the ST segment returned to its original isoelectric position (fig. 1). Arterial blood pressure was 125/75 mmHg and heart rate was 75 bpm after verapamil therapy. Cannulation of the aorta and right atrium and initiation of cardiopulmonary bypass were accomplished without incident. Four new aortocoronary bypass grafts were installed. No further episodes of coronary artery spasm occurred in the perioperative period.

Discussion

In awake patients, coronary spasm is characterized by sudden onset of chest pain at rest associated with ST segment elevation. Unlike effort-induced ischemia, there are no antecedent hemodynamic indications of increased myocardial oxygen demand or decreased supply. Spasm

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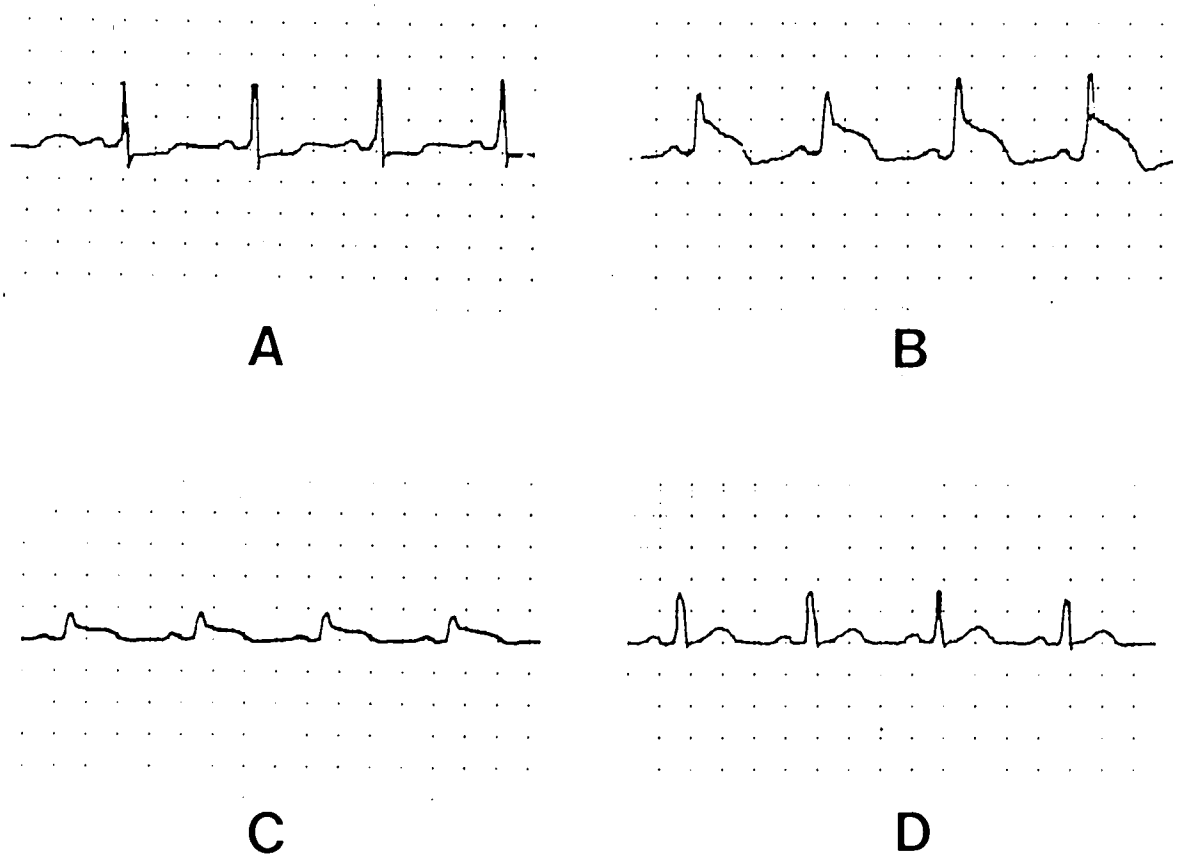

FIG. 1. Electrocardiogram at four times (calibration in each frame: 1 mV = 13 mm): *A*. Preinduction. *B*. During episode of coronary artery spasm after treatment with intravenous nitroglycerin, but before intravenous verapamil. *C*. After the first 2.5-mg increment of verapamil (note decreased amplitude of R wave at same calibration, no explanation was apparent). *D*. After the total verapamil dose of 7.5 mg.

is known to occur in the presence of variable degrees of coronary atherosclerosis and can contribute to myocardial ischemia in patients with fixed obstructive coronary artery disease.[7] In our patient, the absence of any increase in heart rate or arterial blood pressure prior to sudden ST segment elevation supports the diagnosis of coronary spasm. The occurrence of this problem in the perioperative period, although rare, has been implicated as a precipitating factor in acute myocardial infarction[7] and in sudden circulatory arrest and death.[3,6]

Prophylactic use of long-acting nitrates has not reliably decreased the frequency of variant angina attacks in awake patients. In addition, treatment of perioperative episodes of coronary artery spasm with iv and intracoronary nitroglycerin has not consistently resolved ST segment changes, hypotension, or arrhythmias.[3,5] The known arterial vasodilating properties of the calcium entry blocking drugs suggest their efficacy in the treatment of variant angina. *In vitro* investigations in isolated K^+ depolarized coronary strips have shown that the coronary dilation produced by calcium entry blockers differs from that produced by nitrates in several ways: 1) onset of action is more rapid with nitrates; 2) relaxation is less complete with nitrates; and 3) nitrate relaxation is transient even in the continued presence of the drug.[8]

Nifedipine has been used successfully in the treatment of acute clinical manifestations of coronary vasospasm in the perioperative period.[4-6] Since nifedipine is not available in an aqueous form, methods of administration to the anesthetized patient include the sublingual[6] and nasogastric[5] route, which may result in slow or unreliable absorption. It occasionally has been intravascularly administered,[4] but preparation of the drug for this use is hampered by the fact that nifedipine in solution is extremely light sensitive; it is currently available only as a capsulized gel. Verapamil is the only calcium entry blocking drug now provided in an aqueous form suitable for intravascular injection. While 10 times less potent than nifedipine for *in vitro* coronary vasodilation,[8] this drug has similar efficacy in the chronic therapy of coronary artery spasm.[2] Effective blood levels can be achieved with rapidity, ease, and consistency via the intravenous route. Thus, iv verapamil was chosen to treat this episode of suspected coronary arterial spasm that was refractory to nitroglycerin. Resolution of ST segment changes after intravenous verapamil in our

patient was dramatic. Intracoronary injection might have been utilized but would have required injection into multiple obstructed grafts with unreliable placement.

Clinical experience with the calcium entry blocking drugs has suggested that they may be safely continued through the morning of surgery.[9] It is predictable from pharmacokinetic studies that their effects would persist for at least 5 h after the time of last oral administration.[10] Effects of calcium entry blockers administered preoperatively to patients undergoing aortocoronary bypass surgery have been demonstrated through the period prior to cardiopulmonary bypass.[9] Abrupt cessation of these drugs may be associated with new ischemic events.[11] Our patient received his last dose of oral nifedipine on the evening prior to surgery. Continuation of oral therapy through the morning of operation might have prevented the event.

In summary, this is a description of the successful treatment of apparent intraoperative coronary vasospasm with iv verapamil. Because of the established efficacy of the calcium entry blocking drugs, the advantages of availability, ease of administration, and rapid and consistent absorption, iv verapamil may be the preferred drug for perioperative coronary artery spasm.

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