Relief by intracoronary glyceryl trinitrate of coronary artery spasm resistant to sublingual route of administration ★

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SUMMARY Inappropriate percutaneous transluminal coronary angioplasty of the anterior descending artery was avoided in a 52-year-old woman when the intracoronary administration of glyceryl trinitrate immediately before the angioplasty disclosed the organic component of the supposedly fixed, critical (80%) stenosis to be less than 50% of the lumen diameter. The spastic component of the stenosis had not been unmasked by the sublingual administration of two 0.4 mg tablets of glyceryl trinitrate during diagnostic angiography two weeks earlier. Intracoronary glyceryl trinitrate is indicated when suspected coronary spasm persists after the sublingual administration of this drug in potential candidates for percutaneous transluminal coronary angioplasty or coronary bypass surgery.

This report describes a patient about to undergo percutaneous transluminal coronary angioplasty in whom focal coronary spasm persisted after sublingual administration of glyceryl trinitrate, thereby simulating a purely organic stenosis. It suggests means for avoiding the danger of an inappropriate intervention.

Case Report

A 52-year-old nurse with unstable angina pectoris was scheduled for coronary angioplasty.

She was found to have essential hypertension in 1967, and adult onset diabetes mellitus in 1978. There was no family history of coronary artery disease and she was a non-smoker. In December 1978 she developed typical effort angina; this was soon followed by an attack of severe pain at rest and she was admitted to a local hospital on New Year's Eve. Myocardial infarction did not develop and she was discharged after one week taking isosorbide dinitrate 5 mg four times a day. Three weeks later the attacks recurred, mostly at night, and culminated on 16 April 1979 in five attacks in succession, each relieved by glyceryl trinitrate. She was readmitted to hospital and then transferred to the Medical College of Pennsylvania for cardiac catheterisation. At this time

she was receiving, in addition to glyceryl trinitrate and isosorbide dinitrate, digoxin 0.25 mg, methyldopa 2.0 g, propranolol 360 mg, frusemide 80 mg, potassium chloride 16 mEq, and chlorpropamide 750 mg every day.

On her admission to the Medical College of Pennsylvania physical examination was normal and her blood pressure was 150/90 mmHg. Her chest x-ray and laboratory tests, including total cholesterol, were normal. The triglycerides were raised at 2.77 mmol/l (245 mg/100 ml) (upper limit of normal 2.03 mmol/l (180 mg/dl)). The electrocardiogram showed a biphasic T wave in aVF associated with a mean frontal plane QRS axis of +30 degrees. Glyceryl trinitrate paste 1 cm was added to her regimen at bedtime and led rapidly to the disappearance of anginal attacks.

Cardiac catheterisation was carried out on 30 April 1979. The aortic pressure was 194/102 mmHg and the left ventricular pressure 194/23 (post-'a') mmHg. The left ventriculogram was normal and the ejection fraction 0.80. The dominant right, left main, and circumflex arteries were free of disease. The anterior descending artery had a proximal, localised, concentric, noncalcified 80% stenosis with good vessel quality distal to the obstruction. The stenosis persisted on angiograms repeated after the administration of a total of 0.8 mg sublingual glyceryl trinitrate (Fig. 1) and was deemed amenable to percutaneous trans-

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Fig. 1 (A) 30 April 1979 Left coronary artery (LCA) in the 15° right anterior oblique (RAO) projection after the sublingual administration of 0.8 mg glyceryl trinitrate. The anterior descending artery has a proximal, focal, critical stenosis (80% reduction of lumen diameter). (B) 60° LAO projection with 30° craniocaudal rotation of the same artery after sublingual glyceryl trinitrate. In this view the stenosis appears to be even more severe.

luminal coronary angioplasty. Accordingly she was discharged on the same treatment to be readmitted for a stress test with 201 thallium perfusion scan followed by elective percutaneous transluminal coronary angioplasty. She became exhausted during stage 3 of the Bruce protocol at a heart rate of 103/minute without chest pain or ST segment changes. The 201 thallium scan was equivocal. On the day scheduled for angioplasty a preliminary coronary angiogram confirmed the presence of an 80 per cent stenosis of the anterior descending artery. When, however, angiography was repeated after the intracoronary injection of 40 μ g sterile solution of glyceryl trinitrate in normal saline the stenosis was found to have decreased to 50% or less of the lumen diameter, not severe enough to justify dilatation (Fig. 2). She was discharged on 17 May 1979 on a coronary vasodilator regimen which included isosorbide dinitrate and

nifedipine both in initial doses of 10 mg four times a day. At follow-up on 21 September 1979 she remained symptom free.

Discussion

Percutaneous transluminal coronary angioplasty is now employed in several centres.¹ Because the procedure carries some risks every effort should be made to exclude patients who are unsuitable. Unfortunately the geometry of organic coronary artery stenosis which is suitable for dilatation (proximal, isolated, concentric, and uncalcified) is mimicked by coronary spasm, and this must be ruled out before angioplasty is attempted. According to recent experience sublingual glyceryl trinitrate is very effective in relieving coronary spasm²⁻⁴; the persistence of stenosis after administration of the drug by

Fig. 2 (A) 15 May 1979: Left coronary artery in the same projection as in Fig. 1A after the intracoronary administration of 40 μ g glyceryl trinitrate. The stenosis has decreased to less than 50% of the lumen diameter. (B) The reduced severity of the stenosis is evident also in the LAO – craniocaudal projection.

this route is taken as solid evidence of its organic nature. It has also been thought to be reliable in eliminating, and thereby unmasking, the spastic component of a subcritical organic obstruction.³⁻⁵ There is at least one recorded case, however, in which the failure of sublingual glyceryl trinitrate to relieve coronary spasm is documented,³ and one of us has had a similar experience. It is possible, moreover, that in a patient with left main coronary artery stenosis who died suddenly two months after percutaneous transluminal coronary angioplasty and in whom necropsy disclosed little evidence of atherosclerosis of this vessel,¹ that spasm was the cause of death. This patient had received sublingual glyceryl trinitrate both before and during the procedure. Because of this danger one of the authors (LGB) now gives up to 100 µg intracoronary glyceryl trinitrate when indicated during diagnostic coronary angiography, and also for the relief of ergonovine-induced spasm in patients with histories compatible with variant angina who have normal control arteriograms. There have been no side effects or complications in over 50 cases.

The complete mechanism by which intracoronary glyceryl trinitrate relieves spasm resistant to the drug given sublingually can only be speculated upon. But two advantages are obvious. Firstly, all question of variable absorption is eliminated⁶ so that the effective dose can be exact. Secondly, this quantity, since it is delivered directly to the coronary artery, can be quite large and locally very potent,* but has little or no systemic and in particular no hypotensive action. The differences may explain in part the observations made in the case being discussed.

This case report illustrates that intracoronary glyceryl trinitrate is safe and highly effective in relieving

coronary artery spasm. We recommend that it should be given routinely to patients who appear to be candidates for percutaneous transluminal coronary angioplasty because of an apparently fixed coronary stenosis. This route of administration is also advisable when sublingual glyceryl trinitrate is ineffective in relieving suspected coronary spasm, and it may help to avoid inappropriate coronary artery bypass surgery in some cases.

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* If one assumes complete absorption of sublingual glyceryl trinitrate, negligible inactivation within the blood, a similar partition coefficient among body tissues, a coronary blood flow of 5% of cardiac output, and a six to four apportionment of coronary flow between left and right coronary artery, respectively,⁷ the former would be expected to have received at most 12 µg from a sublingually administered 400 µg dose of glyceryl trinitrate by the time its tissue uptake was completed.