Title: CONTINUATION OR WITHDRAWAL OF NIFEDIPINE THERAPY: THE NEED FOR VASODILATOR OR INOTROPIC INTERVENTION POST BYPASS.

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Introduction The calcium antagonist nifedipine is commonly used for the treatment of angina pectoris. It decreases peripheral (and coronary) vascular resistance as well as myocardial contractility; these properties are the basis of its beneficial effect in relieving ischemic myocardial pain[1]. We gained the clinical impression that some patients presenting for coronary artery bypass grafting, maintained on nifedipine therapy until the time of surgery, presented certain problems with the termination of cardio-pulmonary bypass. We therefore studied the necessity for inotropic or vasodilator intervention during and after the termination of bypass in 3 groups of patients: (1) Patients maintained on nifedipine until the day of surgery, (2) Patients in whom nifedipine had been withdrawn at least 24 hours prior to surgery and, (3) A control group of patients who had never received calcium antagonists pre-operatively.

Methods 90 patients undergoing coronary artery bypass grafting were studied. Left ventricular function was assessed pre-operatively during cardiac catheterisation and angio-cardiography. Poor left ventricular function was defined as a resting left ventricular end-diastolic pressure of greater than 20 mmHg in the presence of large dyskinetic or akinetic areas in the wall of the left ventricle. Table I summarises the age, weight and sex distribution, concurrent medication (which was always continued up to the day of surgery), left ventricular function, and bypass and aortic clamp times in the 3 groups. Data has been expressed as Mean (SD).

Table I

	(1)	(2)	(3)
Total	37	24	29
Male	34	23	29
Female	3	1	0
Age(years)	55.5(5.9)	51.7(10.8)	50.6(9.0)
Weight(kg)	71.1(10.6)	76.7(11.5)	75.2(11.3)
Medication:			
β Blockers	12	5	7
Nitrates	8	6	4
β Blockers and Nitrates	10	6	11
Ventricular function	Good 25 Poor 12	Good 15 Poor 9	Good 18 Poor 11
Bypass time	91.4(26.6)	97.2(27.4)	88.1(20.3)
Aortic clamp time (mins)	47.2(16.8)	52.8(19.3)	46.8(13.8)

All patients were premedicated with diamorphine (5-7.5 mg) or papaveretum (15-20 mg) with hyoscine (0.3-0.4 mg) intramuscularly 1 hour prior to induction of anesthesia with intravenous diamorphine (0.5 mg/kg) and fentanyl (30 μg/kg) plus a small dose of hypnotic if necessary (up to 25 mg of methohexital or 5 mg of etomidate). Muscle relaxation was provided by a mixture of pancuronium 4 mg and tubocurarine 15 mg and patients were intubated and ventilated to maintain normocapnia with at least 50% oxygen plus nitrous oxide. Low (< 0.4%) concentrations of enflurane were used in order to maintain stable cardiovascular parameters. Continuous direct measurements of arterial blood pressure and central venous pressure were displayed. Prior to the commencement of cardio-pulmonary bypass the patients were given a further 5-10 μg/kg of fentanyl. During bypass all the patients were cooled to a core temperature of 27°C and the coronary arteries were flushed with 1 litre of cold cardioplegia solution. After rewarming and the termination of bypass, inotropic support was instituted if the systolic arterial blood pressure was less than 80 mmHg in the presence of an adequate left atrial filling pressure (10-14 mmHg) and stable cardiac rhythm; vasodilator treatment was instituted if the systolic arterial blood pressure was greater than 130 mmHg associated with a rising trend and not responding to a low concentration of enflurane (< 0.6%). The need for either inotropic or vasodilator intervention was recorded during the termination of bypass, in the post bypass period and for 2 hours whilst the patients were ventilated post-operatively.

Results. The results are summarised in table II.

Table II

	(1)	(2)	(3)
Total	37	24	29
Vasodilators	5	14	7
Inotropes	23	4	14
Collapse	3	2	0

Collapse was defined as a sudden massive fall in arterial blood pressure to < 40 mmHg. The results were analysed for statistical significance with Fisher's exact test. Vasodilator therapy was needed in a significantly greater number of cases where nifedipine had been withdrawn than in those where treatment was continued ($p < 0.001$) and in those who had never received treatment ($p < 0.05$). Those patients in whom nifedipine had been discontinued were significantly less likely to need inotropic support than those who continued on nifedipine ($p < 0.001$) and also those patients who had never received a calcium antagonist ($p < 0.005$). However, compared to the control group, the patients maintained on nifedipine were not significantly more likely to require inotropic support.

Discussion. In the post bypass period a low cardiac output, in the presence of an adequate filling pressure (preload) and stable cardiac rhythm, usually indicates reduced myocardial contractility and is an indication for inotropic support. We have demonstrated that, compared to a control group who have never received calcium antagonists, patients on nifedipine are no more likely to need inotropic support post bypass. Although nifedipine withdrawal made patients significantly less likely to need inotropes than either the treated or the control group, this must be balanced against the significantly increased need for vasodilators. Although this study was not specifically designed to assess changes in systemic vascular resistance following withdrawal of nifedipine, these results suggest that it may be increased for some time after the drug is discontinued, thus increasing myocardial oxygen demand. Overall, our results suggest that patients on long term nifedipine therapy should continue their medication up to the time of surgery.

References.

1. MacLEAN D, FEELY J. Calcium antagonists, nitrates and new anti-anginal drugs. Br Med J 286:1127-1130. 1983.