Title: CHRONIC ADMINISTRATION OF CALCIUM ENTRY BLOCKERS AND THE CARDIOVASCULAR RESPONSES TO HIGH DOSES OF FENTANYL IN MAN

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Introduction

Calcium entry blockers are widely used clinically as antianginal, antiarrhythmic and antihypertensive drugs. Nifedipine, a calcium entry blocker, inhibits the electromechanical coupling process and results in the relaxation of the muscle fiber. For the blood vessels, this causes vasodilation and for the myocardium, a negative inotropic effect. Concern that the pharmacologic properties of nifedipine may cause hemodynamic instability during induction of anesthesia prompted this study.

Methods

Seven consecutive patients scheduled for coronary artery bypass-grafting who were taking at least 80 mg/day of oral nifedipine were evaluated (Group I). Seven additional consecutive patients scheduled for the same operation but not receiving nifedipine were also evaluated and used as the control group (Group II). Nifedipine was administered until the evening prior to surgery. All patients were on beta blockers. The patients (10 males and 4 females) were premedicated with morphine (0.1 mg/kg) and scopolamine (0.4 mg). Fentanyl (50 mcg/kg) was administered intravenously over 10 minutes to induce anesthesia; metocurine iodide (0.3 mg/kg) provided muscle relaxation. Patients were ventilated with 100% O_2. Measurements were made before anesthetic induction (Phase I), after 15-20 mcg (Phase II), 25 mcg/kg (Phase III) and 50 mcg/kg (Phase) of fentanyl i.v. Measured hemodynamic variables included heart rate (HR, b/min), mean systemic arterial (MAP), mean pulmonary arterial (MPAP) and right (RVFP) and left (LVRP) filling pressures (torr) and cardiac output (L/min). Calculated variables included cardiac index (CI, L/min/m^2), stroke volume (SV) and index (SI, ml/b/m^2) and systemic (SVR) and pulmonary (PVR) vascular resistances (units). Volume requirements and vasoactive drug administration during the period of the study were also evaluated. Statistical analysis (Student's correlated t-test) were performed between Phase I vs II, Phase I vs III, and Phase I vs IV. Student's uncorrelated t-test was used between the two groups. Significance was defined as $p < 0.05$.

	Phase:		I	II	III	IV
HR	group	I	59 ± 2	52 ± 2	57 ± 2	60 ± 2
		II	62 ± 3	54 ± 2	56 ± 2	64 ± 4
MAP	group	I	90 ± 4	79 ± 4**	71 ± 3***	79 ± 4**
		II	98 ± 4	93 ± 3*	90 ± 3*	91 ± 3*
SI	group	I	42 ± 2	42 ± 2	43 ± 2	41 ± 2
		II	46 ± 4	43 ± 3	45 ± 3	43 ± 3
SVR	group	I	17 ± 1	18 ± 1	13 ± 1***	13 ± 1**
		II	16 ± 1	17 ± 1	14 ± 1*	15 ± 2

Table I *: $p < .05$, **: $p < .01$, ***: $p < .001$

Results

Results are presented as Mean ± SEM in the Table. Baseline variables were not statistically different between the two groups. However, significant differences with fentanyl were observed between the groups in MAP, LVFP, RVFP, and SVR at all phases of the study. Volume requirements during the induction period were significantly greater for patients on nifedipine (460 ± 100 ml) as compared to the control group (260 ± 60 ml) ($p < 0.05$). Five patients on nifedipine, in addition to volume administration, required phenylephrine infusion to restore arterial pressure. None of the patients in the control group required phenylephrine during the same period.

Discussion

The study suggests that chronic administration of nifedipine, a calcium entry blocker, potentiates some cardiovascular responses to high doses of fentanyl in patients undergoing coronary artery bypass grafting. Patients on large doses of nifedipine can develope severe hypotension during anesthetic induction with fentanyl.

This is of particular importance in the patient with an extremely limited myocardial reserve.