

Title : REFLEX SYMPATHETIC ACTIVATION PROVOKED BY DIHYDROPERIDINE CALCIUM CHANNEL BLOCKERS EXISTS DURING FENTANYL-BENZODIAZEPINE-N2O ANESTHESIA

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The effects of dihydropyridine calcium channel blockers in awake patients are a combination of direct negative inotropism and vasodilatation together with reflex sympathetic activation (1).

The aim of this study was to investigate whether reflex sympathetic activation exists when dihydropyridine calcium blockers are given during fentanyl - benzodiazepine anesthesia, and if it does, whether it influences hemodynamic parameters. In this double blind study patients received intraoperatively (vs placebo) a continuous infusion of nisoldipine (NISO), a calcium channel blocker very similar to nifedipine, which can be used intravenously (2).

**METHODS.** Twenty patients scheduled for carotid endarterectomy, with a history of chronic hypertension which was adequately controlled previous to surgery were studied. All gave informed consent after approval by our Ethics Committee. Patients were randomly assigned to receive either iv NISO (N group n = 10) or placebo (P group n : 10). Usual antihypertensive medications were given 2 hours before induction. Radial and pulmonary artery catheters were inserted after premedication with morphine 5 mg and scopolamine 0.5 mg. A double blind protocol was then followed : after an iv dose of 1 mcg.kg-1 N (or P) a continuous infusion of 0.2 mcg.kg-1.min-1 was started and maintained during the surgical procedure. Thirty minutes after the continuous N or P infusion was started, anesthesia was induced with fentanyl 6 mcg.kg-1, flunitrazepam 0.02 mg.kg-1, and pancuronium 0.08 mg.kg-1. After intubation, anesthesia was maintained under controlled ventilation with 60 % N2O in O2, and 2 other administrations of fentanyl 1.5 mcg.kg-1. During surgery, fluids were infused at the discretion of the anesthesiologist. Halothane was added in patients who developed intraoperative HT (SBP > 165 mmHg). Hemodynamic measurements were recorded and arterial blood for serum catecholamines and NISO plasma levels were drawn at the following times : after catheter insertion without drug infusion (CONTROL), after induction but before intubation, 15 seconds after intubation and under controlled ventilation (N2O 60 % in O2). Plasma catecholamines were quantified using a radioenzymatic assay, NISO levels by gas chromatography. Results are expressed as mean ± SEM and a two way analysis of variance was performed.

**RESULTS.** Both groups were similar in age (70 vs 65), preoperative hemodynamic parameters and catecholamines plasma levels (Table 1). The hemodynamic measurements and catecholamines and NISO plasma levels are shown in table 1. Mean arterial pressure (MAP) was similar in both groups during induction. Cardiac index (CI) decreased after induction only in the placebo group, this value being significantly lower than that of the N group. While the epinephrine (E) plasma level decreased significantly in both groups at induction, norepi-

nephrine (NE) decreased significantly only in the P group, this value being significantly lower than that of the N group. Fluid administration was not significantly different between the two groups. An increase in SBP (> 165 mmHg) in response to the surgical stress led to halothane administration in 8 patients in the P group and in 2 patients in the N group (p<0.05).

**DISCUSSION.** NE plasma levels significantly decreased under anesthesia only in the P group. These levels are significantly higher in the N group, this suggesting that reflex sympathetic activation in response to nisoldipine infusion exists under fentanyl - benzodiazepine - N2O anesthesia. MAP is similar in both groups at the time of induction and incision. CI and SV decreased significantly in the P group, while they remained unchanged in the N group. No hypotension and a lower incidence of increased SBP was observed intraoperatively in the N group. Thus, the drug interaction between NISO and fentanyl - benzodiazepine - N2O anesthesia, appears to be more beneficial than deleterious. The reflex sympathetic activation observed in patients receiving NISO, may have played a role in the maintenance of blood pressure and in the differences demonstrated between the two groups in CI and heart rate.

		CONTROL	INDUCTION	INTUBATION	N2O 60 %
MAP mmHg	P	96 ± 5	74 ± 4*	89 ± 5	68 ± 5*
	N	94 ± 4	70 ± 2*	89 ± 5	70 ± 4*
HR b/min	P	74 ± 4	69 ± 9	69 ± 4	62 ± 2*
	N	76 ± 4	76 ± 4	82 ± 5	70 ± 4
CI L/min/m2	P	3.6 ± 0.2	2.7 ± 0.1*	2.7 ± 0.1*	2.5 ± 0.2*
	N	3.7 ± 0.2	3.6 ± 0.1	3.8 ± 0.1	3.3 ± 0.1
NOREPI pg/ml	P	314 ± 40	197 ± 25*	201 ± 28*	129 ± 19*
	N	290 ± 35	222 ± 47	340 ± 68	233 ± 44
EPI pg/ml	P	132 ± 30	29 ± 4*	46 ± 9*	21 ± 3*
	N	113 ± 26	25 ± 4*	35 ± 6*	34 ± 12*
NISO	N	-	3.9 ± 1	4.5 ± 2	4.4 ± 2

p < 0.05 : \* vs control ; ● N vs P

#### REFERENCES

- 1 - KIEWSKI W. et al. : Acute and chronic sympathetic reflex activation and antihypertensive response to nifedipine. J. Am. Coll. Cardiol. 7 : 344-348, 1986
- 2 - SERRUYS PW et al. : Acute effects of intravenous nisoldipine on left ventricular function and coronary hemodynamics. Am. J. Cardiol. 56 : 140-146, 1985.