Title : EFFECTS OF NITROGLYCERIN ON SYSTOLIC AND DIASTOLIC BYPASS GRAFT FLOW IN HUMANS : IMPORTANCE OF A MAINTAINED CORONARY DRIVING PRESSURE

Authors : S Beloucif MD, D Bousseau MD, D Payen MD PhD, F Laborde MD*.

Affiliation : Department of Anesthesiology and Intensive Care and * Cardiac Surgery Unit Lariboisiere University Hospital, 2 rue Ambroise Pare 75010 Paris, France

Introduction: Besides the action of nitroglycerin (NTG) on the coronary vasculature, the peripheral effects of NTG are considered as an important mechanism that cause a reduction of myocardial oxygen demand[1]. However, when a systemic hypotension is induced after a vasodilator, an activation of carotid baroreceptor reflex may occur, involving a certain degree of ∝ adrenergic coronary vasoconstriction[2]. As myocardial O_2 consumption and arterial pressure may be considered as independent determinants of coronary flow[3], we conducted the present study to analyse the mean and phasic (i.e. systolic and diastolic) coronary bypass graft flows (CBGF) 6 hours after surgery in humans during a NTG infusion that would cause a significant decrease in demand despite a maintained coronary driving pressure.

Material and methods: 8 patients (59.2 ± 7 yrs SD) were studied 6 hours after the surgical procedure. Written informed consent was obtained prior to the study and the protocol was approved by the University Human Studies Committee. Criteria for inclusion were an angiographically proven proximal left anterior descending coronary artery stenosis over 85%, a preoperative ejection fraction over 45 % and a post operative hemodynamic stability without vasodilating or inotropic drugs. Anesthesia (high dose fentanyl), cardiopulmonary bypass management (partial hemodilution, moderate hypothermia, cardioplegic arrest) and saphenous graft bypass were similar for all patients. The following hemodynamic parameters were measured or calculated: heart rate (HR, ECG lead); cardiac index by thermodilution (CI, $l/min/m^2$), right atrial (RAP), pulmonary artery (PAP) and pulmonary wedge (PWP) pressures via a Swan Ganz catheter; systolic (SAP), diastolic (DAP) and mean (MAP) systemic arterial pressure (mmHg) via a radial catheter; coronary driving pressure (CDP) as MAP-RAP in mmHg; left ventricular stroke work index LVSWI as .0136xSIx(MAP-PWP) in $g.m/m^2/beat$.

CBGF study: We used laboratory miniaturized implantable flow probes secured by resorbable sutures on the adventitia of the graft at the end of the surgical procedure[4]. Probe was linked to a 8 MHz pulsed Doppler apparatus via leads coming out of the thorax through the skin and was removed 6 days later by traction, without any problem. The apparatus used provided the ability to measure vessel diameter "d" and mean cross sectional blood flow velocity "Vm". Then, CBGF can be calculated as follows : $CBGF = \pi d^2/4.Vm.60$ in ml/min.

Coronary bypass graft resistances (CVR) were calculated as the ratio CDP/CBGF in IU.

Data analysis: Instantaneous flow velocity was recorded at 100 mm/sec paper speed during at least 10 cardiac cycles. After repering systolic (Ts) and diastolic (Td) times using ECG and radial pressure, each beat was manually digitized using a graphic tablet linked to a microcomputer to obtain systolic (Qs) and diastolic (Qd) coronary bypass graft flows. Systolic (VolS) and diastolic (VolD) blood volumes (ml) supplying the myocardium were calculated using phasic flows values and systolic and diastolic times respectively : $VolS = QsxTs/60$ and $VolD = QdxTd/60$.

Protocol: Measurements were performed before (control) and 30 min after infusion of 2 successive doses (.5 and 1 µg/kg/min) of NTG (central line). Statistical study was performed using 2 way analysis of variance and Newman-Keuls test.

Results: are summarized on table (mean ± SD)

	C	.5	1	CVs1	CVs.5	.5Vs1
SAP	136.5 ± 34.2	130.5 ± 34.1	126 ± 40	NS	NS	NS
DAP	70 ± 15.2	67 ± 10.8	64 ± 14	NS	NS	NS
MAP	92.2 ± 19.8	88.2 ± 17.3	84.7 ± 22	NS	NS	NS
RAP	9.6 ± 2.6	8.8 ± 1.9	7.2 ± 2.8	<.025	NS	NS
PWP	11.2 ± 2.1	9.6 ± 2.2	9 ± 2.8	<.01	<.025	NS
CI	3 ± .48	2.73 ± .39	2.6 ± .45	<.025	<.05	NS
HR	88.2 ± 13.7	88.8 ± 14.4	89.2 ± 14.2	NS	NS	NS
SI	34.8 ± 7.6	31.2 ± 4.8	29.7 ± 5.7	<.05	NS	NS
LVSWI	37.7 ± 10.2	32.8 ± 7.4	30.2 ± 10.3	<.005	<.025	NS
CBGF	99.8 ± 72	95.4 ± 64	85.9 ± 68	NS	NS	NS
Qs	69.3 ± 78.7	59.9 ± 63	63.2 ± 68.4	NS	NS	NS
Qd	124.5 ± 66.3	115.3 ± 73	108.5 ± 87.8	NS	NS	NS
VolS	.312 ± .372	.251 ± .269	.260 ± .296	NS	NS	NS
VolD	.921 ± .548	.872 ± .622	.815 ± .724	NS	NS	NS

2 positive linear correlations were found between :

* CBGF and LVSWI values : $r = .47$; $p < .05$;
* Qs and CDP values : $r = .62$; $p < .001$.

CVR remained unchanged and no stastically significant difference could be noted between the slopes of the coronary pressure/flow relationships from C to .5, .5 to 1 or C to 1 µg/kg/min of NTG.

Discussion: As expected, NTG induced a significant decrease in RAP and PWP with a constant systemic arterial pressure. HR was unchanged, and CI decrease was due to a decrease in SI, leading to a lesser LVSWI. CBGF in contrast, as well as the volume of blood entering into the myocardium in systole (VolS) and diastole (VolD) was maintained. The unchanged coronary driving pressure contributed to maintain Qs (see the correlation between CDP and Qs), and the absence of CDP decrease while myocardial O_2 consumption was reduced strongly suggests that the absence of parallel decrease in Qd could only be interpreted as a pharmacologic vasodilation. In conclusion, this study emphasizes the major role of a maintained systemic arterial pressure in the beneficial coronary bypass graft flow response after NTG.

References:

1. Ganz W, Marcus HS : Circulation 46 : 880, 1972
2. Powell JR, Feigl EO : Circ Res 44 : 44, 1972
3. Vergroesen I, Noble MIM, Wieringa PA et al : Am J Physiol 252 : H545, 1987
4. Payen DM, Bousseau D, Laborde F et al : Circulation 74 (suppl III) : 61, 1986