Effects of Fenoldopam Mesylate Infusion on Splanchnic Perfusion After Myocardial Revascularization on Cardiopulmonary Bypass: An Ultrasound Doppler Study

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Objectives: **To measure the effects of fenoldopam mesylate infusion on splanchnic blood flow in patients undergoing myocardial revascularization with cardiopulmonary bypass.**

Design: **An experimental observational study.**

Setting: **A single-institution community hospital.**

Participants: **Eighteen patients undergoing on-pump coronary artery bypass graft surgery.**

Interventions: **Fenoldopam mesylate infusion (0.1 μg/kg/min).**

Measurements and Main Results: **Blood flow through the celiac artery, superior mesenteric artery, portal vein and hepatic artery were assessed by means of Doppler measurements. The main hemodynamic variables were measured using echocardiography. The infusion of fenoldopam significantly increased the blood flow through both celiac and superior mesenteric arteries by decreasing vascular resistance. The percentage of cardiac output directed to these 2 vessels increased significantly; the increase through the superior mesenteric artery was greater compared with the celiac artery. Portal vein and hepatic artery blood flow also consistently increased. No significant variations were observed with respect to hemodynamic variables.**

Conclusions: **The infusion of fenoldopam increased the flow through the celiac artery and superior mesenteric artery; the effect was higher for the latter. These changes did not affect the hemodynamic variables.**

KEY WORDS: splanchnic perfusion, fenoldopam, myocardial revascularization, Doppler

PATIENTS UNDERGOING cardiac surgery are at an increased risk of gut ischemia and gastrointestinal complications. Gastrointestinal integrity during the perioperative period is now recognized as an important factor for the outcome of cardiac surgery procedures.[1] In animal models, mucosal hypoperfusion of the jejunum and the ileum during both hypothermia[2] and normothermia[3] has been shown during cardiopulmonary bypass (CPB). Consistently, hypoperfusion of the gastric mucosa during CPB with[4] or without hypothermia[5] has been reported, even in humans.

The gastric intramucosal acidosis, increase of gastric-arterial PCO_2 gradient,[6] and increased lactate levels[7] seen postoperatively up to 24 hours[8] after uncomplicated cardiac surgery are manifestations of a mismatch between metabolic demand and blood flow in the gastrointestinal tract occurring during and after CPB. The use of inotropic agents to improve systemic as well as regional perfusion after cardiac surgery is common practice.

Dopamine, dopexamine, and dobutamine showed the ability to increase global splanchnic blood flow in proportion to the increase in cardiac output in patients undergoing cardiac surgery.[9-12] Transabdominal Duplex ultrasound, recognized as a valuable tool for the assessment of blood flow in many vascular territories, provides a noninvasive and accurate assessment of the splanchnic circulation; moreover, blood flow measures correlate with dye-elimination techniques and contrast angiography.[13,14]

Fenoldopam mesylate is a benzazepine derivative that is a potent short-acting dopamine A1-receptor agonist that decreases systemic vascular resistances while, at the same time, increases renal and splanchnic blood flow.[15] The aim of this study was to assess the changes in splanchnic blood flow induced by fenoldopam mesylate infusion in patients treated with coronary artery bypass graft surgery with CPB support.

METHODS

The study protocol was approved by the ethics committee of the authors' institution, and all enrolled patients provided their written informed consent to participate. The study was conducted in accordance with the ethical standards of human investigation and with the Declaration of Helsinki (1975, revised 1983).

Patients undergoing myocardial revascularization were asked to participate in the current study. All patients had preserved presurgical cardiac function, normal creatinine values, and age <75 years without concomitant major diseases. On arrival at the intensive care unit, after volume normalization, patients considered hemodynamically stable with no need of inotropic substances or mechanical supports were included. All patients were sedated with propofol (0.5 mg/kg/h) and mechanically ventilated (F_IO_2 = 0.5, tidal volume = 7 mL/kg, positive end-expiratory pressure = 5 cm/H_2O, 10 breaths/min).

After hemodynamic stabilization, mivacurium (0.1 mg/kg) was administered, and a probe for transesophageal echocardiography was inserted (5-MHz probe, Omniplane II; Hewlett Packard, Andover, MA).

The following transesophageal views were recorded: (1) midesophageal 4 chamber, (2) midesophageal long axis, (3) transgastric mit axis, and (4) deep transgastric. Tissue Doppler imaging was measured on the lateral wall of the mitral annulus in the 4-chamber projection. All the measurements were performed by a single operator (MM). The spectral Doppler signal settings were adjusted at the lowest wall filter and at the minimum optional gain. The measurements were performed during expiration using the mean of 3 consecutive cardiac cycles.

The preload of the heart was evaluated by left ventricular end-diastolic volume, end-diastolic area, and central venous pressure (CVP), and left atrial pressure was calculated according to Nagueh et al[16] using the following formula: left atrial pressure = 2 + 1.3 (E/E'). The afterload was evaluated by (1) end-systolic meridional wall stress (ESMWS = 0.33*SAPP[ESID/ESPWT]*[1 + ESPWT/ESID], where SAP is the systolic arterial pressure, ESID is end-systolic internal diameter, and ESPWT is end-systolic posterior wall thickness); (2) left ventricular systolic wall tension (LVSWT = 1.33*SAP*(ESID/2);

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(3) aortic elastance (Ae = [0.9*SAP]*SV, where SV is stroke volume), and (4) systemic vascular resistance indexed (SVRI = MAP-CVP/CI*80, where MAP is mean arterial pressure and CI cardiac index).

The cardiac index was calculated as SV*HR/BMI, where SV is stroke volume, HR is heart rate, and BMI is body mass index; and SV was calculated as SV = TVI*AVA, where TVI (cm/s) is the time-velocity integral of the flow across the aortic valve obtained with a continuous-wave Doppler in a deep transgastric view, and AVA (cm^2) is the mean effective aortic valve area throughout the ejection phase. The cross-sectional area was calculated as π^2*r, where r represents half of the annular diameter measured immediately proximal to the point of insertion of the aortic leaflet at the time of maximal separation. The cardiac contractility was calculated by measuring the ejection fraction and the fractional diameter shortening (EDID-ESID/EDID*100, where EDID is the end-diastolic internal diameter).

A Sonos 5500 Ultrasound system (Philips Medical Systems, Andover, MA) with 8-MHz multiband transducer has been used. Using pulsed-Doppler tracing, peak systolic flow velocity, diastolic flow velocity, mean flow velocity, TVI, time-averaged mean velocity, and the diameter of each artery was recorded for the superior mesenteric artery (SMA) and celiac artery (CA). Three sets of measurements were taken and their mean values eventually considered to account for variability in insonation angles.

The portal vein was scanned longitudinally, and the sample volume placed in the middle of the portal trunk underneath the hepatic artery. Hepatic artery measurements were taken in a straight segment parallel to the portal vein. Theta "θ" angle (angle between the ultrasonic beam and the blood flow direction) was kept at below 55°. By means of pulsed-Doppler tracing, the time-averaged mean velocity, the diameter of the portal vein, and the hepatic artery were recorded. The pulsatility index (PI) was calculated using the formula PI = peak systolic flow velocity − end-diastolic volume/mean velocity. The vascular resistance of the celiac trunk and SMA (mmHg/min/L) was calculated by dividing the MAP by flow volume. Vessel flow was measured according to the following formula: flow (mL/min) = π * (½d)^2* TAVM * 60.

All data are reported as mean ± standard deviation. All categoric variables were analyzed with analysis of variance test. The categoric variables were analyzed by either the chi-square test or the exact Fisher test when possible. The normality of sample distribution was verified by applying the Kolmogorov-Smirnov test; because PI does not have a normal distribution, a logarithmic transformation was applied. A p value <0.05 was considered statistically significant.

RESULTS

Between March 2009 and September 2009, 18 patients were enrolled. Table 1 shows the general characteristics of the patient population. No severe or serious complications occurred during the study, and no patients died.

Table 1. Patient Characteristics

Sex (%)	
Male	11 (56)
Female	7 (34)
Age (y)	66 ± 4
Number of grafted vessels	3 ± 1
CPB time (min)	55 ± 9
ACC time (min)	35 ± 7
Minimum reached core temperature (°C)	36 ± 0.6
β-Blockers	9 (50)
ACE inhibitors (%)	10 (55)
Diuretics (%)	12 (66)
Nitrates (%)	14 (77)

Table 2. Indices of Preload, Afterload, and Ventricular Contractility at Basal Conditions and During Fenoldopam Mesylate Infusion

	Basal	Fenoldopam
Left atrial pressure (mmHg)	12.40 ± 3.1	13.16 ± 3.1
End-diastolic area (cm^2)	15.6 ± 4.1	15.2 ± 4.6
LVEDV (mL)	77.9 ± 10.2	81.4 ± 9.2
EDID (cm)	4.2 ± 0.4	4.1 ± 0.4
ESID (cm)	2.9 ± 0.2	2.9 ± 0.1
CVP (mm/Hg)	9.5 ± 1.6	9.7 ± 1.2
SAP (mmHg)	131 ± 15	127 ± 15
DAP (mmHg)	74 ± 8	72 ± 8
MAP (mmHg)	92 ± 9	89 ± 10
EDPWT (cm)	1.3 ± 0.3	1.25 ± 0.2
ESPWT (cm)	1.66 ± 0.1	1.70 ± 0.2
LVSWT (*10^3 dynes/cm^2)	256.84 ± 90.8	258.12 ± 79.3
ESMWS (*10^3 dynes/cm^2)	119.37 ± 29.7	115.37 ± 25.5
Aortic elastance (mmHg/mL)	1.7 ± 0.3	1.6 ± 0.4
SVRI (dynes · s · cm^{-5})	2,594 ± 505	2,356 ± 506
Aortic diameter (cm)	1.98 ± 0.05	1.98 ± 0.05
Time velocity integral (cm/s)	24 ± 4.4	25.4 ± 4
Cardiac index (mL/min/m^2)	2,950 ± 730	3,100 ± 770
Ejection fraction (%)	61.02 ± 5.1	61.17 ± 7.6
FDS (%)	28.94 ± 14	28.71 ± 10
Heart rate	69 ± 9	71 ± 9
E′ wave (cm/s)	6.8 ± 1.5	8.5 ± 1.3*
Deceleration time (cm/s^2)	205.77 ± 63.2	191.52 ± 53.4
E wave (cm/s)	62.5 ± 23.4	68 ± 26.1

Abbreviations: LVEDV, left ventricle end-diastolic volume; EDID, end-diastolic internal diameter; ESID, end-systolic internal diameter; CVP, central venous pressure; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; EDPWT, end-diastolic posterior wall thickness; ESPWT, end-systolic posterior wall thickness; LVSWT, left ventricle systolic wall tension; ESMWS, end-systolic meridional wall stress; SVRI, indexed vascular resistance; FDS, fractional diameter shortening.

*$p < 0.05$.

Table 2 shows the hemodynamic indices at baseline and during fenoldopam mesylate infusion at 0.1 μg/kg/min. Preload parameters did not change significantly during fenoldopam mesylate infusion. None of the variables used to evaluate the hemodynamic status of the patients before and during fenoldopam infusion showed any significant variation; no changes in terms of systemic arterial blood pressure, heart rate, and cardiac index have been recorded. Preload as well as afterload indexes were not affected by fenoldopam infusion. Overall, none of the variables indicative of a possible reduction of the resistances induced by fenoldopam showed any significant change (Table 2).

At the level of the CA, systolic, diastolic, and mean velocities significantly increased during the infusion of fenoldopam (Table 3). Even the time-average mean velocity was increased significantly (Table 3). The flow of the CA was increased significantly (Table 3 and Fig 1) as well as vascular resistance in this district was decreased significantly (Table 3 and Fig 2). The percentage of cardiac output directed to the CA increased significantly (Fig 1). At the level of the SMA, systolic, diastolic, and mean velocities are increased significantly during fenoldopam infusion (Table 3).

The flow of the SMA was increased significantly (Table 3