Vascular Reactivity during Cardiopulmonary Bypass in Patients at Punjab Institute of Cardiology & Shalamar Hospital Lahore, Pakistan

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Abstract

Background: The operative treatment of cardiac diseases remains associated with systemic inflammation and a suboptimal outcome in many patients. These inflammatory changes are manifested by systemic hypotension, myocardial failure, increased vascular permeability and consequent dysfunction of organs such as the lungs, gut and brain. In general terms, sympathetic innervations of the small arteries and arterioles allows vasoconstriction, thereby increasing resistance to blood flow, whereas innervations of the large arteries and veins decreases the volume in these vessels, resulting in the redistribution of blood volume. This study was conducted to determine the effect of vasodilator drugs on duration of vasodilatation in patients undergoing coronary artery bypass grafting (CABG) with Cardiopulmonary bypass (CPB).

Methods: We evaluated prospectively the effect of vasodilator medications before CABG surgery on hemodynamic variables and use of vasoactive drugs. We studied 30 patients with good left ventricular function allocated randomly to continue vasodilator drugs before cardiac surgery. Arterial pressure, Cardiac output, systemic vascular resistance and use of vasoactive drugs were recorded during anaesthesia, perioperative and in the early postoperative period.

Results: Patients who using vasodilator drugs before cardiac surgery had not significant relationship between vasodilator drugs and vessels reactivity (vasoconstriction & vasodilatation). However, these patients required more vasodilator drugs to control hypertension after CPB and in the early postoperative period.

Conclusion: There was no difference in hypotension at the onset of CPB or in the use of vasodilator drugs before cardiac surgery. We conclude that vasodilator drugs before cardiac surgery did not have sufficient effect to be recommended routinely.

Keywords: Cardiopulmonary Bypass, Vasodilator drugs, Coronary artery bypass grafting (CABG), Hypotension

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Introduction:

Refinements in methods of myocardial protection and operative techniques have improved the results of cardiovascular surgery. Yet, the operative treatment of cardiac diseases remains associated with systemic inflammation and a suboptimal outcome in many patients. These inflammatory changes are manifested by systemic hypotension, myocardial failure, increased vascular permeability and consequent dysfunction of organs such as the lungs, gut and brain. This is especially true when operations are performed on patients suffering acute myocardial ischemia, on patients in cardiogenic shock with reduced peripheral perfusion, or during prolonged extracorporeal perfusion.(1)

The changes in the expression and activity of both NOS and COX may affect coronary and

peripheral vasomotor tone during and after cardiac surgery. In addition to endothelial mechanisms, the regulation of coronary blood flow is determined by metabolic, autonomic, and myogenic mechanisms which are largely characteristics intrinsic to the vascular smooth muscle.

Vascular reactivity after heart surgery is mediated by the local release of vasoactive substances and increased probability active substances and increased probability of potassium channel opening, whereas myogenic mechanisms are based more on the intrinsic property of vascular smooth muscle to regulate vascular resistance in response to changes in transmural pressure. The systemic inflammatory response associated with CPB is the consequence of both ischemia-reperfusion events and blood contact with the foreign surfaces of the CPB circuit. Blood contact with the CPB circuitry has been shown to initiate humoral and cellular inflammatory responses. The sequence of events leading to this inappropriate activation of inflammatory processes has been well described and may result in an increase in vascular permeability and hemodynamic changes mediated by the liberation of pro inflammatory cytokines. Tumor necrosis factor-(TNF) and interleukin-1 (IL-1) promote vasodilatation and the expression of specific adhesion molecules such as E-selectin and intercellular adhesion molecule-1 (ICAM-1), promoting adhesion of leukocytes to endothelial cells. However, the neurologic impact of this inflammatory reaction is, as yet, not entirely understood, but it may be one of the mechanisms that lead to endothelial impairment in the brain, resulting in disruption of the brain micro vessel vasomotor tonus and a diffuse cerebral hypo perfusion.(2)

Postoperative renal function deterioration is a serious complication after cardiac surgery with cardiopulmonary bypass and is associated with increased in-hospital mortality. However, the long-term prognosis of patients with postoperative renal deterioration is not fully determined yet. Therefore, both in-hospital mortality and long-term survival were studied in patients with postoperative renal function deterioration. Included were 843 patients who underwent cardiac surgery with cardiopulmonary bypass in 1991. Postoperative renal function deterioration (increase in serum creatinine in the first postoperative week of at least 25%) occurred in 145 (17.2%) patients. In these patients, in-hospital mortality was 14.5%, *versus* 1.1% in patients without renal function deterioration ($P <$ 0.001). Multivariate analysis significantly associated in-hospital mortality with postoperative renal function deterioration, re-exploration, postoperative cerebral stroke, duration of operation, age, and diabetes. In patients who were discharged alive, during long-term follow-up (100 months), mortality was significantly increased in the patients with renal function deterioration ($n =$ 124) as compared with those without renal function deterioration (hazard ratio 1.83; 95% confidence interval 1.38 to 3.20).(3)

This study was aimed to determine the effect of vasodilator drugs on duration of vasodilatation in patients undergoing coronary artery bypass grafting (CABG) with Cardiopulmonary bypass(CPB).

Materials & Methods:

Study Design: This study design was prospective observational study.

Study setting: The study was approved by participating institute, and informed consent was obtained. This study was conducted at the Department of Cardiac Surgery Shalimar Hospital Lahore and Punjab Institute of Cardiology Lahore.

Study Duration: Duration of this study was 6 months from September 2016 to February 2017.

Sampling: Non-probability purposive sampling technique was used.

Sample Size: Thirty consecutive patients admitted to hospital for coronary artery bypass surgery were enrolled in study.

Inclusion Criteria:

Patient undergoing Coronary Artery Bypass Grafting (CABG) using vasodilator drugs with age between 20 to 80 years

Data Collection Procedure:

Preoperative laboratory values and medications were recorded. Blood Pressure readings after induction of anaesthesia and immediately during and after the CPB.

Statistical Analysis: Continuous numerical data will be presented as mean ± Standard deviation, the Student *t* test will be used to compare means of normally distributed data. The qualitative data will be analysed using chi square test. Statistical analysis will be performed using SPSS version16.

Results:

The total number of patients under study were 30 (21 males and 9 females), in which mean age was 53.70 ± 11.16 years, the mean height was 178.33 ± 76.70 cm, the mean weight was 73.13 ± 13.83 Kg and the mean BSA was 1.816 kg/m^2 with the standard deviation of ± 0.186. Maximum age of the patient was 74 years and minimum was 22 years.

In this study, 25(83.33%) patients were reported for Ischemic heart disease (IHD), 3 (10%) patients were valvular heart diseases and 2(6.66%) patients were other cardiac procedures. Twenty-five (83.33%) patients were reported for CABG (Coronary Artery Bypass Grafting), 3(10%) patients were Valvular heart procedures and 2(6.66%) patients were other cardiac procedures. Frequency of risk factors to cardiopulmonary bypass is presented in Table 1.

Eleven (36.67%) patients were taking ACE-Inhibitor drugs pre, 21(70%) patients were using nitrate drugs, 3 were taking angiotensin receptor blockers, 23 were taking β-blockers, 19 were taking statin therapy.

Discussion:

Vasodilators are used generally in the treatment of hypertension and heart failure, prevented the harmful effects of remodelling, and has been shown to improve the prognosis after myocardial infarction. Fluctuations in the vascular sensitivity of small arteries after cardiopulmonary bypass patients whose were taking vasodilator before the surgeries discussed in different studies.

In our study, quite different effect of pre-operative applications of vasodilator on vascular reactivity during cardiopulmonary bypass. After results analysed we had not significant that no relationship between vascular reactivity and vasodilator.

Pigott et al have determined the adverse events during coronary artery bypass graft (CABG) surgery have been described in patients receiving angiotensin converting enzyme (ACE) inhibitors, including hypotension on induction of anaesthesia and an increase in vasoconstrictor requirements after cardiopulmonary bypass (CPB). Omitting regular ACE inhibitor medication before surgery may improve cardiovascular stability during anaesthesia. In those patient where vasodilator were withdrawn, atrial pressure was greater and less vasoconstrictor was needed during CPB but more of these patients required vasodilator infusion to prevent the hypertension in early period of past operative patients (4).

In our study, totally different effect of pre-operative application of nitrates on peripheral vascular reactivity during cardiopulmonary bypass (CPB). After results, we analysed that non-significant relationship between vascular reactivity and vasodilator.

(2)Cerebrovascular impairment appears early after the onset of CPB. The specific loss of acetylcholine-induced vasodilation suggests endothelial cell dysfunction rather than impaired vascular smooth muscle response to

nitric oxide. This loss of endothelium-dependent regulatory factors after CPB may enhance vasoconstriction, impair cerebrovascular function, and contribute to neurologic injury after CPB. factors after CPB may enhance vasoconstriction, impair cerebrovascular function, and contribute to neurologic injury after CPB (2).

In our study, pre-operative applications of B-blockers on peripheral vascular reactivity was quite parallel to different studies. After results, we analysed that no significant relationship between vasodilator and vessels reactivity during CPB. (5)The differences in the systemic vascular effects of thiopentone, etomidate and Propofol in our study and in those in which they were used to induce anaesthesia may be related to the circumstances pertaining during CPB. In particular, the use of non-pulsatile flow and hypothermia may have altered the sensitivity of vascular smooth muscle to the vasodilating effects of these drugs. The decrease in SVR produced by droperidol is of longer duration during non-pulsatile flow compared with pulsatile flow. All three drugs are moderately to highly bound to plasma proteins: thiopentone 80-84%, etomidate 70-75%, Propofol 98%. Thus, haemodilution during CPB results in an increase in the free fraction of unbound drug, with a corresponding increase in pharmacological effect. The free fraction of Propofol increases 1.5-3 folds during bypass. The use of heparin during CPB, by increasing non-esterified fatty acids, may further decrease the binding of drug to plasma proteins. All our patients were taking p-adrenoceptor antagonists and calcium entry blockers. These drugs may have influenced the results.(5).

Conclusion:

There was no difference in hypotension at the onset of CPB or in the use of vasodilator drugs before cardiac surgery. We conclude that vasodilator drugs before cardiac surgery did not have sufficient effect to be recommended routinely.

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Table 1. Risk Factors of Cardiopulmonary Bypass

Risk Factors	Present	Absent
Hypertension (HTN)	20(66.7%)	10(33.3%)
Diabetes mellitus (DM)	15(50%)	15(50%)
Smoking	9(30%)	21(70%)
IHD	25(83.3%)	5(16.7%)
Hyperlipidaemia	6(20%)	24(80%)
Percutaneous Coronary Interventions (PCI)	2(6.7%)	28(93.3%)
Family History	8(26.7%)	22(73.3)
COPD	1(3.3%)	29(96.7%)

on vasodilator drugs

Table 2. Vascular Activity among patients

Vascular activity time on CPB start	Patients on Vasodilator Drugs		
	Yes	No	Total
30-60 seconds	3	5	8
	27.3%	26.3%	26.7%
60-90 seconds	5	12	17
	45.5%	63.2%	56.7%
>90 seconds	3	2	5
	27.3%	10.5%	16.7%

Supplementary File 1:

Questionnaire

Vascular Reactivity during Cardiopulmonary Bypass (CPB)

Name: Age: Gender: DOA:
D.O.OPERATION: Registered # Diagnosis:
Operation Type: Weight: Height: BSA: Flow Rate: EF:

Preoperative Variables:

HTN: Y N DM: Y N Smoker: Y N IHD: Y N

HLP: Y N PCS: Y N Renal Failure: Y N PVD: Y N

IABP inserted: Y N COPD: Y N Family History: Y N PCI: Y N

Preoperative Medications:

ACE Inhibitors: Y N Dose: Duration:

Calcium Blockers: Y N Dose: Duration:

ARBs: Y N Dose: Duration:

Nitrates: Y N Dose: Duration:

B-blockers: Y N Dose: Duration:

Anticoagulants: Y N Dose: Duration:

Antiplatelets: Y N Dose: Duration:

Ionotropics: Y N Dose: Duration:

Steroids: Y N Dose: Duration:

Statin Therapy: Y N Dose: Duration:

Preoperative Laboratory:

HB mg/dl	RBCs	WBCs	Platelets	Neutrophils %	Urea mg/dl	Creatinine mg/dl	BSR mg/dl

Operative Data:

CPB TIME	CLAMP TIME	LOWEST TEMP AT CPB	HIGHEST TEMP AT CPB	WHOLE BLOOD	PACKED CELLS	FFP

Blood Pressure Recordings:

PARAMETERS	TIME DURATION (MINUTES)	SYSTOLIC B.P (MMHG)	DIASYSTOLIC B.P (MMHG)	MEAN B.P (MMHG)
Induction				
20 minutes after Induction				
Pre- CPB				
CPB-On (Lowest Pressure at time)				
Stable Perfusion Pressure (P/P)				
Max Perfusion Pressure(P/P)				
Lowest Perfusion Pressure(P/P)				
Off-CPB				
Supportive Drugs(Ionotropes,Vasodilators, Vasoconstrictors)				
Stay in O.T after CPB-Off				

Postoperative Data:

Re-CPB: Y N