# HEMODYNAMIC EFFECTS OF DIRECT INFUSION OF NITROGLYCERIN, SODIUM NITROPRUSSIDE INTO THE PULMONARY ARTERY, AND PULMONARY VENTING IN VALVULAR HEART SURGERY(*)

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***Pulmonary hypertension is a serious problem that has deleterious effects on cardiac surgical patients, especially during the period of weaning from cardiopulmonary bypass (CPB). Pulmonary hypertension may continue to persist in spite of adequate correction of the cardiac lesions which cause pulmonary hypertension. There have been various methods to reduce the fatal effects of pulmonary hypertension in open heart surgery. Diuretics, various vasodilator agents, pulmonary artery balloon counterpulsation, or mechanical pulmonary artery venting are some of these. Recent studies have demonstrated that direct infusion of nitroglycerin into the pulmonary artery may be an effective measure in advanced pulmonary hypertension.***

***The authors performed a prospective study to compare the three methods of reducing pulmonary vasculary ressistance in three groups of pulmonary hypertensive patients who undergone open valvular heart surgery. Each group consisted of twenty patients who were selected to have similiar properties as much as possible in the meaning of age, sex distribution, preoperative clinical and hemodynamic status, valvular disease, operative procedure, etc. In***

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*the first group, a bolus of 5 mcg/kg of nitroglycerin (Glycerol trinitrate) was injected first, and continued to infuse at a rate of 2 mcg/kg/min into the pulmonary artery immediately before weaning from CPB. The infusion was continued for 15 minutes after weaning from CPB. In the second group, pulmonary artery venting was performed immediately before weaning from CPB and continued for the same time period. In the third group, 2 mcg/kg/min. Sodium nitroprusside infused into the pulmonary artery immediately before weaning from CPB and continued for the same period.*

*Seventeen early and late postoperative parameters were compared by statistical analysis between the three groups.*

*The significant decrease in mean arterial pressure has been found in the third group, the others. The increase in cardiac output, cardiac index, stroke work index and decrease in left atrial pressure, pulmonary capillary wedge pressure, total pulmonary vascular ressistance, the need for inotropic support and intraaortic balloon counterpulsation have been found statistically significant in the first group than the others. Significant decrease in systemic vascular ressistance has been found in the third group.*

*In conclusion, direct infusion of nitroglycerin into the pulmonary artery is than the most effective method of decreasing pulmonary vascular ressistance. The authors think that this method should be the first choice in preventing and overcoming the postoperative low cardiac output syndrome due to right heart failure and pulmonary hypertension.*

*Key words: Valvular heart surgery, pulmonary hypertension, nitroglycerin.*

Pulmonary hypertension is a serious problem that has deleterious effects on cardiac surgical patients, especially during the period of weaning from CPB. In other words low cardiac output due to pulmonary hypertension is an important determinant of prognosis especially in open valvular heart surgery[1]. It is often expected that pulmonary hypertension secondary to valvular heart disease should be reduced after correcting the underlying valvular lesion(s)[2,3]. However, pulmonary hypertension may continue to persist in spite of adequate correction of the cardiac lesions which cause pulmonary hypertension[1]. There have been various methods to reduce the fatal effects of pulmonary hypertension in open heart surgery. Diuretics[4,5], inotropic agents[6-10], various vasodilator agents[11-15], intraaortic balloon counterpulsation[16], pulmonary artery balloon counterpulsation[17-20], mechanical pulmonary artery venting[21,22] are some of these. Recent studies have demonstrated that direct infusion of nitroglycerin into the pulmonary artery may be an effective measure to reduce pulmonary vasculary resistance (PVR)[23,24].

## Materials and Methods

A prospective clinical study was done to compare three methods of reducing PVR in 60 pulmonary hypertensive patients who undergone open valvular heart surgery. Patients were divided into three groups each of consisted of 20 patients. It was considered to have similiar properties in the groups as much as possible in the meaning of age, sex distribution, preoperative clinical and hemodynamic findings, valvular lesion(s), operative procedure, etc. These findings in each group are shown in Tables I, II, and III. There was no significant difference between these findings in each group. Valvular lesions were in rheumatic origin in all patients. No patient had concomitant coronary or congenital heart disease and systemic disorders such as diabetes mellitus, etc.

The same protocols, which are our clinic's routine methods of premedication, anesthesia, cardiopulmonary bypass, myocardial protection

**Table I.** Preoperative clinical characteristics of the groups.

| | Group I | Group II | Group III |
|---|---|---|---|
| **Age:** | | | |
| range | 13-73 | 16-71 | 17-74 |
| mean (± SD) | 38.6 ± 6 | 39.1 ± 7 | 38.4±6 |
| **Sex:** Male/female | 8/12 | 7/13 | 9/11 |
| CCF (No) | 9 | 10 | 9 |
| C/T (mean %) | 63 ± 2 % | 62.8 | 64 ± 1 |
| **Rythm:** Sinus | 11 | 10 | 9 |
| AF | 9 | 10 | 11 |
| **Valvular Lesion(s)** | | | |
| Mitral(M) | 13 | 12 | 15 |
| Aort(A) | 1 | 2 | — |
| Double(M+A) | 2 | 1 | 1 |
| M+Tricuspid | 3 | 4 | 2 |
| Triple | 1 | 1 | 2 |

Group I: Nitroglycerin group, Group II: Pulmonary venting group, Group III: Sodium nitroprusside group. SD: Standard deviation, CCF: Congestive cardiac failure, C/T: Cardiothoracic ratio, AF: Atrial fibrillation,

were used in all patients. Premedication was done with Flunitrazepam 1 mgr. p.o. at the night of the operation, and 0.3 mgr/kg Diazepam I.M. before the operation. All of the patients were ventilated by a Drager-Tiberius 12 anesthesia device during anesthesia. Induction was done with 60 mgr/kg Fentanyl and 20 mgr/kg Flunitrazepam I.V., and muscle relaxation was obtained with Pancronium Bromide 100 mgr/kg I.V. Anesthesia was continued with 100% oxygen inhalation and Fentanyl administration of 8 mgr/kg/hour. All of the anesthetic administrations were stopped at the begining of CPB and began after weaning from CPB.

CPB was instituted by aortic and double venous cannulation via the right atrium to superior and inferior venae cavae. CPB was maintained by Biomedicus centrifugal pump in all patients. Left heart venting was estabilished by a vent catheter inserted into the left atrium via left upper pulmonary vein.Myocardial protection was obtained by moderate systemic hypothermia to 26°C, topical hypothermia with ice slush. Cardiac arrest was obtained by cold blood cardioplegia, and maintained by intermittant cold St. Thomas II crystalloid cardioplegia infusions. Warm blood cardioplegia (hot shot) infusion was given before reperfusion.

Systemic arterial pressure was monitored via the radial artery, and central venous pressure via right internal jugulary vein. Pulmonary artery pressure, pulmonary capillary wedge pressure were monitored by a thermodilution catheter via the right internal jugulary vein. Left atrial pressure was monitored by the vent catheter used for left heart venting. Cardiac output (CO), cardiac index (CI), stroke work index (SWI), systemic vasculary ressistance (SVR), and pulmonary vasculary ressistance (PVR) were calculated by "Gould P 23 ID, B-21268" cardiac output monitor.

In the first group, a bolus of 5 mcg/kg of nitroglycerin (glycerol trinitrate) was injected first and continued at a infusion rate of 2 mcg/kg/min. into the pulmonary artery via the thermodilution catheter immediately before weaning from CPB, and continued for 15 minutes after weaning from CPB.

In the second group, pulmonary artery venting was done by a roller pump via a vent catheter placed into the main pulmonary trunk with a rate of 1500 ml/min. Venting was begun immediately before weaning from CPB, and continued for 15 minutes after weaning from CPB.

In the third group, 2 mcg/kg/min. of Sodium nitroprusside was begun to infuse into the pulmonary artery via the thermodilution catheter immediately before weaning from CPB and continued for the same time period.

The measurements of heart rate (HR), mean systemic arterial pressure (MSAP), mean pulmonary artery pressure (MPAP), pulmonary capillary wedge pressure (PCWP), left atrial

**Table II.** Preoperative hemodynamic characteristics of the groups.

| | Group I | Group II | Group III |
|---|---|---|---|
| SAP (S/D/M) (mmHg) (±SD) | 110±12/72±9/91±11 | 107±10/69±8/89±10 | 118±6/71±9/86±13 |
| PAP (S/D/M) (mmHg) (±SD) | 53±6/21±8/34±8 | 52±4/23±9/36±4 | 56±9/20±5/37±8 |
| PCWP (mmHg) (± SD) | 24±11 | 23±14 | 22±13 |
| CVP (mmHg) ( ± SD) | 12±3 | 11±4 | 13±4 |
| CO (lt/min) ( ± SD) | 5.3±1.2 | 5.1±1.8 | 5.6±09 |
| CI (lt/min/$m^2$) (± SD) | 3.2±1.4 | 3.2±1 | 3.3±1.2 |

SAP: Systemic arterial pressure, S: Systolic, D: Diastolic, M: Mean,
PAP: Pulmonary artery pressure, PCWP: Pulmonary capillary wedge pressure,
CVP: Central venous pressure, CO: Cardiac output, CI: Cardiac index.

pressure (LAP), central venous pressure (CVP), CO, CI, SWI, SVR, and PVR were recorded first immediately after discontinuation of CPB and then 30 minutes later. The average values reported as mean± standart error and the average changes (increment or decrement) in these parameters were compared between these three groups by Student's t test. Also, these three groups were compared according to urine output within 24 hours after operation, mechanical ventilation time, need for inotropic drug or IABP support, mortality and functional capacity according to NYHA classification at the second month of operation.

## Result

The average values of 11 parameters measured at two times in early postoperative period and changes between these two measurements expressed as percent in each group are shown in table IV. Postoperative urine output, mechanical ventilation time, need for inotropic

**Table III.** Operative procedures performed in each group

| Operative Procedure | Group I | Group II | Group III |
|---|---|---|---|
| MVR (Bioproshesis) | 6 | 5 | 7 |
| MVR (Mechanical) | 5 | 4 | 6 |
| Mitral reconstruction (MR) | 2 | 3 | 2 |
| AVR | 1 | 2 | — |
| MVR+AVR | 1 | 1 | 1 |
| MR+AVR | 1 | — | — |
| MVR+Tricuspid reconstruction (TR) | 2 | 3 | 2 |
| MR+TR | 1 | 1 | — |
| MVR+AVR+TR | 1 | 1 | 2 |
| ACC (mean±SD) (minute) | 71±12 | 76±10 | 78±13 |

MVR: Mitral valve replacement, AVR: Aortic valve relacement,
ACC: Aortic cross clamp time.

**Table IV.** The average valvues of eleven hemodynamic parameters at two measurements and changing expressed as percent in three groups.

| Hemodynamic parameter | Group I | | | Group II | | | Group III | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1. | 2. | % | 1. | 2. | % | 1. | 2. | % |
| HR (Beat/min) | 94±12 | 98±11 | +4±1 | 93±11 | 94±14 | +2.1±1 | 96 ± 13 | 98 ± 11 | +2±1.5 |
| MSAP (mmHg) | 63±8 | 61±11 | -5.1±2 | 64±11 | 66±12 | +3.2±1 | 62±12 | 55±11 | -10.2±2 |
| CVP (mmHg) | 6±2 | 5±2 | -16±2 | 5±3 | 4±2 | -15±1 | 6±2 | 6±3 | -9.6±2 |
| MPAP (mmHg) | 29±6 | 21±9 | -27.6±8 | 31±11 | 21±10 | -29.2±6 | 28.7±7 | 22±5 | -22.3±4 |
| PCWP (mmHg) | 13±4 | 5±3 | -61±4 | 14±3 | 8±4 | -42.6±6 | 12±4 | 9±2 | -26±6 |
| LAP(mmHg) | 11±2 | 4±2 | -51±6 | 12±2 | 8±3 | -33.3±8 | 10±3 | 8±2 | -20.6±6 |
| CO(lt/min) | 5.6±0.8 | 6.3±0.6 | +13±4 | 5.7±0.7 | 5.8±0.6 | +2.1±1.6 | 5.9±0.5 | 5.9±0.7 | +1.4±0.7 |
| CI(lt/min/$m^2$) | 3.1±0.4 | 3.7±0.6 | +16±5 | 3.3±0.4 | 3.3±0.4 | +3.2±1.4 | 3.1±0.6 | 3.2±0.4 | +3.1±1.6 |
| SWI(gm/$m^2$) | 56±7 | 68±4 | +26±7 | 57±8 | 61±6 | +4.3±5 | 57±6 | 59±8 | +2.6+6 |
| SVR (dyne/sec/$cm^{-5}$) | 1360±180 | 1240±260 | -11.2±4 | 1330±240 | 1340±160 | +1.2±1 | 1350±160 | 1100±210 | -26.3+7 |
| PVR (dyne/sec/$cm^{-5}$) | 230±51 | 180±46 | -26.4±5 | 241±64 | 221±47 | +10±4 | 238±63 | 211±54 | -13+6 |

HR: Heart rate, MSAP: Mean systemic arterial pressure, CVP: Central venous pressure,
MPAP: Mean pulmonary artery pressure, PCWP: Pulmonary capillary wedge pressure, LAP: Left atrial pressure,
CO: Cardiac output, CI: Cardiac index, SWI: Stroke work index, SVR: Systemic vascular resistance,
PVR: Pulmonary vascular resistance.

**Table V.** Postoperative functional status of the patients in three groups.

| | Group I | Group II | Group III |
|---|---|---|---|
| Urine output ml/hour | 90 ± 12 | 84 ± 13 | 12 ± 14 |
| Mechanical ventilation time (hr.) | 8.6 ± 2 | 9.3 ± 2 | 9 ± 4 |
| Need for inotropic drug support (n) | 3 | 7<br>2 | 9<br>2 |
| Need for IABP support (n) | — | 1 | — |
| Mortality (n) | — | | |
| Postoperative NYHA Class | | | |
| I | 16 | 12 | 11 |
| II | 3 | 4 | 6 |
| III | 1 | 3 | 3 |
| IV | 0 | 0 | 0 |

drug and IABP support, mortality and postoperative functional class at the second month of operation in each group are shown in Table V.

There was no significant change in heart rate in the three groups. MSAP reduced mostly in the third group (Nitroprusside group). There was also no significant change in CVP between the three groups. MPAP reduced almost equally in each group. PCWP, LAP reduced much more in the first group (Nitroglycerin group) than the others. Also increments in CO, CI, SWI were much more in the first group. SVR reduced much more in the third group while PVR in the first group.

There were not significant differences between the three groups in urine output and mechanical ventilation time. Three patients in the first group, 7 in the second and 9 in the third group needed inotropic drug support at postbypass period. Two patients in the second group and 2 in the third group needed IABP support while no patient needed in the first group. There was only 1 early death in the whole population and it was in the second group. According to the functional status of the patients at the second postoperative month, the patients in the first group were better than the others.

## Discussion

Pulmonary hypertension is a grave consequence of valvular heart disease that influences the outcome of the cardiac surgical patient in a negative manner[1]. While weaning the patient from CPB, pulmonary hypertension might be a fatal factor on the outcome[1,25]. Various methods have been used in managing the pulmonary hypertensive patients subjected to open heart surgery. Diuretics[4,5], various inotropic agents[6-10], various vasodilators[11-15,26], IABP[16], pulmonary artery balloon counterpulsation [17-20], mechanical pulmonary artery venting [21-22] are some of these interventions. These methods could be used separetely or in combination. The advantages and disadvantages of these methods over each other are still controversy[27-32].

It has been reported recently that vasodilator agents have a significant effect in the treatment of low cardiac output syndrome[14,13,30,33,34]. It has been documented that nitroglycerin has also a positive inotropic effect besides decreasing the preload and afterload[35,36]. The increase in cardiac contractility by nitroglycerin administration is much more evident than other vasodilator agents[37,38]. It has been shown in this study that nitroglycerin augments the CO and myocardial contractility much more evidently in pulmonary hypertensive patients who undergone open valvular heart surgery, compared with the pulmonary artery venting technique or infusion of nitroprusside. Parenteral administration of nitroglycerin in cardiac surgery is more practical, the effect is seen in a short time, the dosage could be regulated more easily and the effect dissapears rapidly after discontinuation of the administration[36].

Unlike most other vasodilators, nitrates, especially nitroglycerin are metabolized also in the vascular wall, other than liver[39,40]. Therefore, direct administration of nitroglycerin into the vascular bed which is desired to dilate is more effective while systemic effects are lesser. We've preferred to infuse nitroglycerin directly into the pulmonary artery via the thermodilution catheter and by this route achieved a significant decrease on left ventricular preload (decrease in LAP, PCWP and PVR in our results)compared with the other systemic effects.

It has been stated that, intermittant bolus injection of nitroglycerin had the hazard of reflex vasomotor spasm at the interval between the injections. Therefore, by continuous infusion after a bolus injection, constant plasma levels could be maintained and vasodilator effect could be achieved more easily and more stable[24].

As it could be seen in our results, cardiac performance at early and late postoperative period is better by nitroglycerin administration in pulmonary hypertensive patients who undergone valvular heart surgery. In this study, there were not seen any complications related to direct infusion of nitroglycerin into the pulmonary artery.

## Conclusion

The authors have found that direct infusion of nitroglycerin into the pulmonary artery is a more effective method of decreasing PVR, increasing CO and cardiac contractility than the other two methods those infusing sodium nitroprusside into the pulmonary artery and mechanical pulmonary artery venting. So, they think that this method should be the first choice in preventing and overcoming the postoperative low cardiac output syndrome especially caused by pulmonary hypertension in open heart surgery.

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