Simultaneous Dopamine and Sodium Nitroprusside Therapy Following Open Heart Surgery

Mohammad H. NADJMABADI, M.D.,* E. AFTANDELIAN, C.R.N.A.,*
Iraj ARYANPUR KASHANI, M.D., F.A.C.C.,**
Hooshang RASTAN, M.D.,*** *and* M. BASTANFAR, M.D.*

SUMMARY

Twenty post-open heart surgery patients with low output syndrome were given dopamine, sodium nitroprusside (SNP) alone and in combination. Dopamine alone (3–4 mcg/Kg/min) caused an increase of cardiac output (CO) from 3.2 to 4.6 L/min/M^2 ($p<0.001$), SNP (1–1.5 mcg/Kg/min) raised the CO to 3.7 L/min/M^2 ($p<0.005$). While the combination of the 2 drugs elevated the CO to 5 L/min/M^2 ($p<0.001$). The mean pulmonary artery wedge pressure dropped moderately with dopamine and significantly with SNP and combined drugs. The diastolic pulmonary artery pressure fell significantly with either drug and in combination. The stroke index increased significantly with dopamine and combined therapy. All patients survivied.

It is concluded that in post-open heart surgery patients with low output syndrome substantial hemodynamic improvement results with the combined use of dopamine and SNP more than with either agent alone.

Additional Indexing Words:

Low output syndrome Catecholamine Vasodilators Afterload

LOW output syndrome following open heart surgery often necessitates the use of dopamine, the nearly ideal catecholamine.[1)–7)] We know from clinical experience, however, that since its effect may not always be adequate[2),8)–10)] this may demand increasing the dose of dopamine or the addition of another catecholamine which can result in tachycardia, ventricular arrhythmias and deleterious alterations of systemic vascular resistance. The poor survival results of increased sympathetic activity accompanying low output have been previously reported.[11)] In patients without hypotension vasodilators may be used to lower systemic vascular resistance and unload the left

From the Departments of Intensive Care* (Director M. Nadjmabadi), Pediatric Cardiology,** and Cardiovascular Surgery,*** the Cardiovascular Research Center, the Heart Hospital, Tehran, Iran.

Address for reprint: M. H. Nadjmabadi, M.D., Heart Hospital, P.O. Box 33-423, Shemiran, Tehran, Iran.

Received for publication July 6, 1979.

Manuscript revised September 5, 1979.

ventricle.[12)-16)] The successful use of dopamine to provide inotropic stimulation to the heart and the afterload reducing effect of sodium nitroprusside given simultaneously to patients with congestive heart failure has been recently reported.[17)-18)] The combined use of the 2 drugs resulted in a greater degree of augmentation of cardiac function than with either drug alone.

During the past 2 years we have used the combination of the positive inotropic agent dopamine, together with nitroprusside, an afterload reducing agent in pateints with evidence of impaired cardiac performance following a variety of intracardiac surgical procedures. Our data presented herein support the usefulness of this therapeutic combination in the postoperative cardiac patient with low output syndrome.

Materials and Methods

The study group consisted of 20 adult postoperative patients who had undergone open heart surgery. The ages ranged from 22 to 45 years (mean 35.5) and weights ranged from 42–58 Kg (mean 48 Kg). Eighteen had surgery for valvular rheumatic heart disease, one had repair of an atrial septal defect with pulmonary valvulotomy and another had coronary artery bypass (Table I). Before surgery 16 pateints were in classes II–III and 4 were in class IV of the New York Heart Association and all but 3 had congestive heart failure.

The patients were selected for study on the basis of clinical evidence of low output syndrome together with a cardiac index below 2.5 L/min/M^2 and systemic vascular resistance (SVR) more than 1500 dynes·sec·cm^{-5}. The cardiac index and SVR varied from 1.7–2.4 L/min/M^2 (mean $\pm$SEM 2.1$\pm$0.19 L/min/M^2), and 1608–2278 dynes·sec·cm^{-5} (mean $\pm$SEM 1968$\pm$285) respectively. Low output syndrome appeared in the first 24 hours after surgery in all patients. Systemic arterial pressure, ECG, pulmonary artery and wedge pressure and right atrial pressures were continuously monitored and recorded. The pulmonary artery was entered percutaneously through the left subclavian vein with a Swan-Ganz catheter.[19),20)] Cardiac output was measured by thermodilution method with duplicate injections, using an Edwards model 9520 cardiac output computer. All pressures

Table I. The Type of Surgery Performed in 20 Patients Suffering from Low Output Syndrome after Surgery

Procedures:	No. of Patients
Mitral valve replacement	6
Mitral valve repair	3
Mitral valve replacement and tricuspid repair	2
Open mitral commissurotomy	3
Aortic valve replacement	2
Aortic and mitral valve replacements	2
Pulmonary valvulotomy and repair of ASD	1
Coronary artery bypass	1

were measured using Bentley pressure transducers and recorded on a Roche model 304 recorder.

Left and right ventricular stroke work indexes (LSWI and RSWI) were calculated using the following formulas: $LSWI = 1.36(\bar{P}\text{-}PCW) \times SI/100$ and $RSWI = 1.36(PAP\text{-}CVP) \times SI/100$, where $\bar{P}$ = mean systemic arterial pressure, PCW = mean pulmonary capillary wedge pressure, SI = stroke index, PAP = mean pulmonary artery pressure, and CVP = central venous pressure.

Systemic and pulmonary vascular resistances (SVR and PVR) were calculated according to the following formulas: $(\bar{P}\text{-}RAP) \times 80/CO$ and $PVR = (PAP\text{-}PCW) \times 80/CO$, where RAP = mean right atrial pressure, CO = cardiac output in L/min/M^2, PAP = mean pulmonary artery pressure, and PCW = mean pulmonary capillary wedge pressure. Stroke index was calculated by dividing cardiac index by heart rate per minute. All measurements were done before drug infusions with a Braun microperfusor were begun. Dopamine infusion of 3–4 mcg/Kg/min was given for 30 min and measurements obtained. Nitroprusside 1–1.5 mcg/Kg/min was administered alone for 30 min and determinations again made. Then simultaneous dopamine and nitroprusside infusion at the same rates was carried out with final measurements made after 30 min of combined therapy. Washout time of 30 min was permitted before each drug infusion and the study drugs were given in reversed sequence in alternate patients.

Results

All patients survived with continuation of the treatment as required for 8–36 hours. Control cardiac output of 3.2 ± 0.21 L/min (Tables II, III, Figs. 1–3) increased slightly to 3.7 ± 0.24 L/min with SNP; rose moderately to 4.6 ± 0.28 with dopamine $p < 0.005$) and showed a striking increase to 5.0 ± 0.33 L/min ($p < 0.001$) with combined infusion. Mean systemic arterial pressure decreased from 87 ± 4.8 to 74 ± 3.2 mmHg ($p < 0.001$) with SNP, while dopamine produced little change from control pressure. Dopamine and SNP together reduced it to 77 ± 4.1 mmHg ($p < 0.005$). Heart rate remained fairly constant with the greatest change occurring with SNP which raised the rate from 95 ± 5.6 to 107 ± 10 beats/min ($p < 0.005$). Control diastolic arterial pressure of 65 ± 4.6 fell noticeably with SNP to 51 ± 4.9 mmHg and with combined therapy to 55 ± 5.2 mmHg; with equal significance ($p < 0.001$). Mean pulmonary artery pressure was little effected by either drugs. However, the control pulmonary diastolic pressure of 21 ± 2.5 mmHg fell markedly with SNP to 14 ± 3.0 mmHg ($p < 0.001$) and with simultaneous infusion to 15 ± 2.2 mmHg ($p < 0.001$). The control pulmonary capillary wedge (occluded) pressure of 17 ± 1.5 mmHg decreased to 15 ± 2.0 mmHg with dopamine ($p < 0.001$), showing further and equal reductions with SNP and combination therapy to 13 ± 1.8 mmHg and 13 ± 1.9, respectively ($p < 0.001$).

Mean right atrial pressure showed insignificant changes with either drug

Table II. Measured Hemodynamic Values (Means±SEM) before and after Administration of Dopamine 3-4 mcg/Kg/min and Sodium Nitroprusside 1-1.5 mcg/Kg/min alone and in Combination in 20 Patients

	Control	Dopamine 3-4 mcg/Kg/min	SNP 1-1.5 mcg/Kg/min	Dopamine SNP
Cardiac output (L/min)	3.2±0.21	4.6±0.28*	3.7±0.24+	5.0±0.33*
Heart rate (beats/min)	95±5.6	101±7.1	107±10++	99±8.5
Mean arterial blood pressure (mmHg)	87±4.8	84±5.2+	74±3.2*	77±4.1+
Diastolic arterial pressure (mmHg)	65±4.6	62±3.5*	51±4.9*	55±5.2*
Pul. arterial pressure (mmHg)				
Systolic	47±3.8	52±4.5	49±3.4	50±4.1
Diastolic	21±2.5	19±1.8	14±3.0*	15±2.2*
Mean	33±4.1	32±3.2	29±2.9*	29±3.0+
Occluded (wedge)	17±1.5	15±2.0*	13±1.8*	13±1.9*
Mean right atrial pressure (mmHg)	10±1.7	10±0.9	9±1.1	8±1.5

* $p<0.001$, + $p<0.005$, ++ $p<0.05$

Table III. Derived Hemodynamic Data (Means±SEM) before and after Administration of Dopamine 3-4 mcg/Kg/min and Sodium Nitroprusside 1-1.5 mcg/Kg/min alone and in Combination in 20 Patients

	Control	Dopamine 3-4 mcg/Kg/min	SNP 1-1.5 mcg/Kg/min	Dopamine SNP
Stroke index (ml/beat/M^2)	22±2.5	29±3.0*	24±1.5++	32±3.0*
Systemic vascular resistance (dynes·sec·cm^{-5})	1968±285	1389±245*	1421±166++	1169±248+
Pulmonary vascular resistance (dynes·sec·cm^{-5})	426±101	300±151	308±89++	302±121+
Left ventricular stroke work index (Gm/beat/M^2)	21±2.1	26±2.7+	21±1.3++	28±1.7+
Right ventricular stroke work index (Gm/beat/M^2)	7.3±0.8	8.1±0.9	5.8±0.3++	9.0±0.8

* $p<0.001$, + $p<0.005$, ++ $p<0.05$

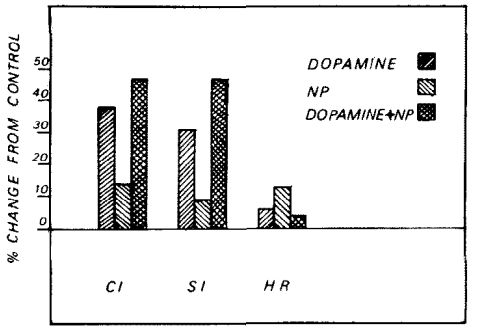

Fig. 1. Average percentile changes of cardiac index (CI), stroke index (SI), and heart rate (HR) from control values during dopamine and nitroprusside administration singly and in combination.

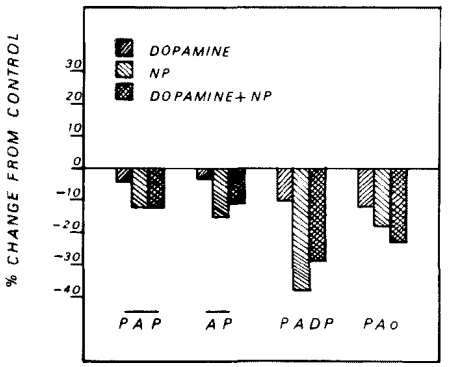

Fig. 2. Average percentile changes of mean pulmonary pressure ($\overline{PAP}$), mean systemic pressure ($\overline{AP}$), mean pulmonary arterial diastolic pressure (PADP), and mean balloon-occluded pulmonary arterial pressure ($\overline{PAo}$) from control values during dopamine and nitroprusside administration singly and in combination.

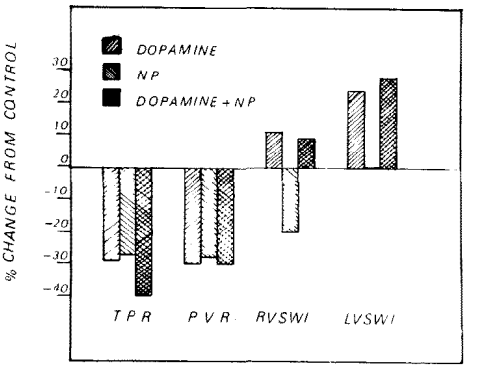

Fig. 3. Average percentile changes of systemic vascular resistance (TPR), pulmonary vascular resistance (PVR), right ventricular stroke work index (RVSWI), and left ventricular stroke work index (LVSWI) from control values after administration of dopamine, nitroprusside alone and in combination.

or the combination. Stroke index (control) of 22 ± 2.5 ml/beat/M^2 showed no significant change with SNP; rose to 29 ± 3.0 ($p<0.001$) with dopamine alone and rose further to 32 ± 3.0 ml/beat/min ($p<0.001$) with combined drugs. Nitroprusside lowered the systemic vascular resistance from 1968 ± 285 dynes·sec·cm^{-5} to 1421 ± 166 ($p<0.05$), nearly the same as dopamine at 1389 ± 245 ($p<0.001$); but the combination therapy brought about an obvious decrease to 1169 ± 248 ($p<0.005$). All drugs lowered pulmonary vascular resistance to about the same degree. Nitroprusside had little effect on left ventricular stroke work index, however dopamine alone and in combination with SNP enhanced cardiac work from 21 ± 2.1 g-m/beat/M^{-2} to 28 ± 1.7 ($p<0.005$).

Discussion

Pre-operatively impaired and intra-operatively induced myocardial dysfunction are 2 major factors contributing to the low output state seen after cardiac surgery. The syndrome can result in significant morbidity and mortality after surgery, particularly in patients who suffer from impaired myocardial function and advanced heart disease. The traditional approach of increasing the force of contraction has consisted of using catecholamines, particularly dopamine which has recently gained wide popularity.[1)-6)] Nevertheless, in some patients with elevated systemic vascular resistance and high left ventricular end-diastolic pressure, dopamine alone cannot solve the problem. In such circumstances, the addition of a systemic vasodilator and a preload reducing agent can serve as an adjunct to dopamine.

We have clearly demonstrated the higher degree of augmentation of cardiac function when low output syndrome requires the use of fairly large doses of dopamine for improving the contractility of the left ventricle and a lowering of impedance to ejection provided by nitroprusside. The 47% improvement in cardiac output along with a 15% decrease of the mean systemic pressure is obviously advantageous. The combination of these drugs allows ideal functioning of the myocardium without the greater demand for myocardial oxygen which may occur when dopamine is employed solely for the failing heart.

Nitroprusside has been reported[21)] to increase coronary blood flow by 200% in the dose range we use with a parallel increase of myocardial venous oxygen content. However, nitroprusside cannot be safely administered to patients with hypotension and dopamine does not relieve pulmonary venous congestion or lower left ventricular end-diastolic volume. The disadvantages of the two are reciprocally compensated when they are given simultaneously which results in an increase in cardiac performance greater than can be achieved with either drug alone.

A recent study[22] has shown a 76% rise of cardiac index with nitroprusside given alone in children with low output syndrome following the repair of congenital cardiac lesions. It is of interest that nitroprusside alone in our study resulted in less remarkable effects on cardiac index. This can be explained by the presence of congestive heart failure and impaired myocardial function in the majority of our cases We believe that in such circumstances the combination of dopamine and nitroprusside is definitely superior to either agent alone. Thus, dopamine enhances myocardial contractility while nitroprusside permits more effective left ventricular emptying along with a lower arterial pressure which reduces myocardial oxygen consumption.

Miller[8] performed his study during cardiac catheterization with lightly sedated patients. The time limitation during catheterieation and the stress on the awake patient could have provided less than ideal circumstances for the effects of this drug combination to be thoroughly studied.

Our patients with low output syndrome after surgery are usually sedated with 200 mg phenobarbital as required and remain intubated until they can be weaned from both drugs with stable heart function. Furthermore, Miller's study group was given 5–7 mcg/Kg/min dopamine which increased the heart rate by 10% with greater myocardial oxygen demand. This higher dose can produce more alpha-vasoconstrictive effect than within the lower dosage range of 3–4 mcg/Kg/min. If the cardiac output remains low with nitroprusside 1–1.5 mcg/Kg/min and dopamine 3–4 mcg/Kg/min, we administer another inotropic agent such as adrenalin in very low doses. This would probably minimize the increase in myocardial oxygen demand.[2),4] The infusion rate of the additional inotropic drug is adjusted to maintain adequate arterial pressure to increase cardiac output in severe low output states.

Inadequate blood volume after surgery with impaired cardiac performance can be avoided by repeated measurements of pulmonary wedge and diastolic pressures to determine the adequacy of volume replacement. In patients without tricuspid valve disease, we maintain the pulmonary wedge pressure at 16–20 mmHg to prevent hypovolemia while giving dopamine and nitroprusside to enhance pump function as there is sufficient preload and optimal stroke volume without producing pulmonary venous congestion or edema.

The ideal inotropic agent, i.e., one which will not increase myocardial oxygen demand, vasomotor tone, heart rate or disturb rhythm is not yet available. Presently, the judicious management of postoperative cardiac patients necessitates the combined use of nitroprusside for coronary artery dilitation with afterload reduction and dopamine to stimulate left ventricular performance. Impaird myocardial contractility from a variety of causes can be

effectively augmented with the combined use of dopamine and nitroprusside while the major disadvantages of either drug are negated so as to provide favorable physiologic circumstances. We believe that this beneficial combination will gain wide usage for the impaired ventricle until a single agent is found to be optimal.

References

1. Goldberg LI: Drug therapy. Dopamine-Clinical uses of an endogenous catecholamine. N Engl J Med **291**: 707, 1974
2. Nadjmabadi MH, Purschke R, Tarbiat S, Lennartz H, Bircks W: Comparing studies on the influence of dopamine and orciprenaline and renal function of patients after cardiac surgery. Thoraxchirurgie **23**: 552, 1975
3. Nadjmabadi MH, Koch M: Influence of dopamine on the pulmonary pressure and shunt volume after cardiac surgery. Anaesthesist **25**: 274, 1976
4. McNay JL, Goldberg LI: Comparison of the effects of dopamine, isoproterenol, norepinephrine and bradykinin on canine renal and femoral blood flow. J Pharmacol Exp Ther **151**: 23, 1966
5. Ramdohr B, Schuren KP, Biamino G, Schroder R: Der Einfluß von Dopamin auf Hämodynamik und Nierenfunktion bei der schweren Herzinsuffizienz des Menschen. Klin Wschr **51**: 549, 1972
6. Ramdohr B, Biamino G, Warda H, Schroder R: Vergleichende Untersuchungen über die Wirkung von Dopamin und Orciprenalin am gesunden menschen; Einfluß von Hämodynamik und Herzkontraktilitat. Z Kreisl-Forsch **61**: 326, 1972
7. Goldberg LI: Use of sympathomimetic amines in heart failure. Am J Cardiol **22**: 177, 1968
8. Nadjmabadi MH, Lennartz R, Purschke R, Bircks W, Baum H, Tarbiat S: Einfluß von Dopamin bzw Orciprenalin auf Herz- und Nierenfunktion nach kardio-chirurgischen Eingriffen. Med Welt **26**: 554, 1975
9. McCannel KL: Hemodynamic responses to dopamine and isoproterenol following acute myocardial injury. Canad J Physiol Pharmacol **47**: 25, 1967
10. McNay JL, Goldberg LI: Hemodynamic effects of dopamine in the dog, before and after alpha-adrenergic blockade. Circulat Res **18** (Suppl I): 110, 1966
11. Dietzman RH, Ersek RA, Lillehei CW, Castaneda AR, Lillehei RA: Low output syndrome. Recognition and treatment. J Thorac Cardiovasc Surg **57**: 138, 1969
12. Franciosa JA, Guiha NH, Limas CJ, Rodriguera E, Cohn JN: Improved left ventricular function during nitroprusside infusion in acute infarction. Lancet **1**: 650, 1972
13. Chatterjee K: Vasodilator therapy for heart failure. Ann Int Med **83**: 421, 1975
14. Chatterjee K, Swan HJC, Kaushik VS, Jobin G, Magnusson A, Forrester JS: Effects of vasodilator therapy for severe pump failure in acute myocardial infarction on short-term and late prognosis. Circulation **53**: 797, 1976
15. Rowe GG, Henderson RH: Systemic and coronary hemodynamic effects of sodium nitroprusside. Am Heart J **87**: 83, 1974
16. Miller RR, Vismara L, Zelis R, Amsterdam E, Mason DT: Clinical use of sodium nitroprusside in chronic ischemic heart disease. Effects on peripheral vascular resistance and venous tone and on ventricular volume, pump and mechanical performance. Circulation **51**: 328, 1975
17. Goldberg LI, Hsieh YY, Resnekov L: Newer catecholamines for treatment of heart failure and shock. An update on dopamine and a first look at dobutamine. Prog Cardiovasc Dis **19**: 327, 1977
18. Miller RR, Awan NA, Joye JA, Maxwell KS, DeMaria AN, Amsterdam EA, Mason DT:

Combined dopamine and nitroprusside therapy in congestive heart failure. Circulation **55**: 881, 1977

19. Nadjmabadi MH, Rastan H: Subclavian approach for cardiac catheterization with balloon-tipped pulmonary arterial catheter. Am J Cardiol **39**: 471, 1977
20. Swan HJC, Ganz W, Forrester J, Marcus H, Diamond D, Chonette D: Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med **283**: 447, 1970
21. Hess W, Tarnow J, Patschke D, Bruckner JB: Hämodynamik und Sauerstoffversorgung des Herzens bei kontrollierter Hypotension mit Natriumnitroprusside und Trimethaphan. Eine tierexperimentelle Untersuchung. Anaesthesist **25**: 27, 1976
22. Benzing G III, Helmsworth SA, Schrieber JT, Laggie J, Kaplan S: Nitroprusside after open heart surgery. Circulation **54**: 467, 1976