Unloading Effects of Vasodilators on Peripheral Circulation and Cardiac Hemodynamics in Patients with Acute Myocardial Infarction

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SUMMARY

Effects of three representative vasodilators on peripheral and cardiac hemodynamics were studied in 20 patients with heart failure due to acute myocardial infarction (PCWP > 18 mmHg, CI > 2.20 L/min/m²) using venous occlusion plethysmography and a Swan-Ganz catheter. Sublingual isosorbide dinitrate (ISDN) significantly increased calf venous capacitance (CVC) from 5 to 60 min ($p < 0.01$) and calf blood flow (CBF) in the initial 15 min ($p < 0.05$), while simultaneously lowering PCWP ($p < 0.05$) and central venous pressure ($p < 0.05$). Calf vascular resistance (CVR), cardiac index, blood pressure, and total systemic peripheral resistance (TSPR) were not affected significantly. Nitroglycerin ointment (NGO) significantly decreased CVR ($p < 0.05$) and increased CVC ($p < 0.05$) from 60 to 240 min, simultaneously with lowering of PCWP ($p < 0.01$), central venous pressure ($p < 0.05$), and TSPR ($p < 0.05$). Oral prazosin (Pz) increased CBF ($p < 0.01$) and CVC ($p < 0.05$) from 60 to 240 min, simultaneously with significant lowering of PCWP ($p < 0.01$) and TSPR ($p < 0.05$), resulting in increased stroke work index ($p < 0.05$). These data confirm that ISDN predominantly causes capacitance vessel dilatation and reduce excessive venous return, while Pz and NGO dilate not only capacitance vessels but also resistance vessels, consequently reducing systemic vascular re-

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sistance and resulting in increased peripheral blood flow and cardiac performance. It was observed that the higher the base-line calf vascular resistance rose, the better the response to the vasodilator treatment appeared in terms of a decrease in calf vascular resistance.

Additional Indexing Words:

Isosorbide dinitrate Nitroglycerin ointment Prazosin Venous occlusion plethysmography Heart failure

IN chronic heart failure both peripheral resistance vessels and capacitance vessels constrict to maintain circulatory homeostasis, i.e., to maintain tissue perfusion and redistribute reduced cardiac output away from peripheral extremities and improve central venous return.¹⁾⁻⁵⁾

While the mechanism of vasoconstriction in acute myocardial infarction may share features in common with those operative in chronic heart failure,^{6),7)} there are also probably important differences, since there is little time to develop and regulate identical compensatory mechanisms because of the sudden onset and rapid aggravation of hemodynamics in acute myocardial infarction. A vicious cycle might be easily provoked in acute myocardial infarction. Thus the compensatory mechanisms might not be entirely beneficial but somewhat overactive in terms of peripheral vascular resistance being higher and cardiac output lower than the most salutary levels. Correspondingly, systemic venoconstriction might also be excessive, thereby resulting in a greater increase of left ventricular filling pressure than is required relative to cardiac output on the flattened ventricular function curve of impaired contractility.

Unloading treatment has been advocated in recent years, since vasodilators possess the ability to interrupt this vicious cycle by partially counteracting compensatory mechanisms.⁸⁾ To analyze the mechanism of unloading effects of vasodilators, not only cardiac but also peripheral hemodynamics should be measured simultaneously and sequentially.⁹⁾

Accordingly, the present study was carried out to qualify the primary effects of isosorbide dinitrate, nitroglycerin ointment, and prazosin on the peripheral circulation and the resulting cardiac hemodynamic modifications in patients with acute myocardial infarction.

PATIENTS AND METHODS

Twenty patients (13 males, 7 females, mean age 56, range 41-72 years) were studied in the first 72 hours after the onset of acute myocardial infarction

in the Coronary Care Unit of Nippon Medical School. All patients had acute transmural myocardial infarction complicated by heart failure, confirmed by serial electrocardiographic changes, enzyme determinations and hemodynamic monitoring (PCWP > 18 mmHg). This study was explained to each patient or his or her family and written informed consent obtained.

Five to 10 mg of isosorbide dinitrate (ISDN) were administered sublingually to 7 patients, 0.5 mg/Kg BW of nitroglycerin ointment (NGO) were applied to the epigastric area with occlusive dressing technic in 7 patients, and 1 to 2 mg of prazosin were administered orally to 6 patients.

The patients were grouped according to the Killip classification¹⁰⁾; in the ISDN group all 7 patients were in class II, in the NGO group 4 were in class II, and 3 were in class III, and in the Pz group 2 were in class II and 4 were in class III. No patients received cardiotoxic agents, diuretics or other drugs influencing the peripheral circulation except for oxygenation through a nasal cannula or face mask during the study period.

Peripheral and cardiac hemodynamic measurements were done simultaneously and sequentially. Peripheral hemodynamic measurements were performed at the calf using a pneumatic plethysmograph (EDI, pneumoplethysmograph Winsor "Vasograph") with the patient supine as described previously.¹¹⁾⁻¹⁴⁾ Venous occlusion technic was used for the measurement of calf blood flow. The plethysmographic cuff was placed around the mid-calf. The second cuff was applied just above the knee which allowed an immediate pressure increase by sudden inflation to 30 mmHg. Calf blood flow was calculated from the rate of change in volume during venous occlusion and expressed in unit of ml/100 ml/min. During recording, blood flow to the foot was occluded by the use of the third cuff inflated to a suprasystolic level of pressure (usually 200-250 mmHg) for at least 1 min before determination of blood flow. Calf venous capacitance was measured by equilibration method.¹⁵⁾ The venous occlusion cuff was suddenly inflated to 30 mmHg and then venous pressure and limb circumference were permitted to equilibrate for more than 2 min. Calf venous capacitance was calculated from the increments in volume and expressed in unit of ml/100 ml. During measurements, the calf was elevated to the level of heart. Calf vascular resistance was defined as mean arterial pressure measured at the popliteal artery by Korotkoff's method divided by calf blood flow and expressed in unit of mmHg/ml/100 ml/min. Mean blood pressure (BPM) was calculated by using the formula $BPM = \text{diastolic blood pressure} + 1/3 (\text{systolic} - \text{diastolic pressure})$. The room temperature of the Coronary Care Unit was maintained at $24 \pm 1^\circ\text{C}$ to prevent effects on the peripheral circulation.

A Swan-Ganz thermodilution catheter was passed from the antecubital

vein to the pulmonary artery with the aid of electrocardiographic and pressure monitoring. Pulmonary artery pressure, pulmonary capillary wedge pressure (PCWP), obtained by balloon inflation, and central venous pressure were recorded. Cardiac output (CO) was determined by the thermodilution technic using an Edwards' Model 9520A Cardiac Output Computer. Mean blood pressure (BPm) was measured using a #19 Teflon cannula inserted in a radial or a femoral artery, or by Korotkoff's method at the right brachial artery. In addition, the following cardiac hemodynamic parameters were calculated:

$$\text{Cardiac index (CI)} = \frac{\text{CO}}{\text{Body Surface Area}} \quad (\text{L/min/m}^2)$$

Stroke volume index (SVI)

$$= \frac{\text{CO} \times 1000}{\text{Body Surface Area} \times \text{Heart Rate}} \quad (\text{ml/beat/m}^2)$$

$$\text{Stroke work index (SWI)} = \text{SVI} \times (\text{BPm} - \text{PCWP}) \times 0.0136 \quad (\text{Gm} \cdot \text{m/beat/m}^2)$$

Total systemic peripheral resistance (TSPR)

$$= \frac{(\text{BPm} - \text{CVP})}{\text{CI}} \times 79.9 \quad (\text{dyne} \cdot \text{sec} \cdot \text{cm}^{-5}/\text{m}^2).$$

All hemodynamic measurements were performed before the administration of each drug as basal control and at 5, 15, 30, and 60 min after the sublingual administration of ISDN, at 15, 30, 60, 90, 120, 240 min after applying NGO on the epigastric region, and at 30, 60, 90, 120, 180, 240 min after the oral administration of Pz.

All data were expressed as the mean $\pm$ standard deviation and statistical

Table I. Isosorbide Dinitrate

	Before	5 min	15 min	30 min	60 min
BPm (mmHg)	100.7 $\pm$ 20.3	98.5 $\pm$ 17.8	92.4 $\pm$ 16.2	93.1 $\pm$ 16.6	94.4 $\pm$ 12.7
HR (beats/min)	98.9 $\pm$ 10.2	98.4 $\pm$ 14.6	96.4 $\pm$ 11.8	94.6 $\pm$ 9.2	95.6 $\pm$ 9.2
PCWP (mmHg)	24.3 $\pm$ 2.2	17.1 $\pm$ 5.4**	14.6 $\pm$ 4.5**	16.2 $\pm$ 4.9**	17.1 $\pm$ 6.9
CVP (cmH ₂ O)	9.0 $\pm$ 2.8	6.4 $\pm$ 2.7*	5.7 $\pm$ 3.0*	5.5 $\pm$ 3.5*	5.9 $\pm$ 2.9*
CI (L/min/m ²)	3.28 $\pm$ 0.16	3.0 $\pm$ 0.4	3.5 $\pm$ 0.4	3.27 $\pm$ 0.28	3.15 $\pm$ 0.16
SVI (ml/beat/m ²)	33.5 $\pm$ 2.9	31.1 $\pm$ 5.2	33.1 $\pm$ 5.3	34.5 $\pm$ 3.6	33.3 $\pm$ 3.5
SWI (Gm-m/beat/m ²)	34.6 $\pm$ 8.9	33.4 $\pm$ 8.8	34.3 $\pm$ 5.9	33.6 $\pm$ 5.1	33.5 $\pm$ 4.2
TSPR (dyne-sec-cm ⁻⁵ /m ²)	2190.9 $\pm$ 518.9	2520.6 $\pm$ 585.3	2205.1 $\pm$ 463.0	2036.8 $\pm$ 445.2	2179.7 $\pm$ 372.2
CBF (ml/100 ml/min)	1.19 $\pm$ 0.49	1.83 $\pm$ 0.98*	1.40 $\pm$ 0.63*	1.26 $\pm$ 0.57	1.34 $\pm$ 0.75
CVC (ml/100 ml)	0.42 $\pm$ 0.19	0.61 $\pm$ 0.26*	0.66 $\pm$ 0.24**	0.65 $\pm$ 0.21**	0.68 $\pm$ 0.24**
CVR (mmHg/ml/100 ml/min)	103.7 $\pm$ 63.9	13.8 $\pm$ 28.5	73.3 $\pm$ 27.8	81.7 $\pm$ 31.8	88.7 $\pm$ 47.4

CBF=calf blood flow; CVC=calf venous capacitance; CVR=calf vascular resistance.

mean $\pm$ standard deviation, paired t-test, n=7.

* p<0.05, ** p<0.01.

analyses were performed using Student's t-test for paired data, comparing each value to its corresponding basal control.

RESULTS

Hemodynamic effects of ISDN (n=7)

For the purpose of analyses, hemodynamic data measured simultane-

Fig. 1. Hemodynamic effects of sublingual isosorbide dinitrate (ISDN) on peripheral circulation and cardiac hemodynamics: drafted on percent changes. Calf venous capacitance increased significantly from 5 to 60 min and calf blood flow increased significantly in the initial 15 min. Corresponding to these peripheral hemodynamic changes, PCWP and CVP decreased significantly from 5 to 30 min and CVP decreased significantly from 5 to 60 min after the administration.

ously and sequentially are shown in Table I, and the percent changes in Fig. 1. Calf venous capacitance increased significantly from 5 to 60 min (0.42 ± 0.19 to 0.68 ± 0.24 ml/100 ml, $p < 0.01$) and calf blood flow rose in the initial 15 min (1.29 ± 0.49 to 1.83 ± 0.98 ml/100 ml/min, $p < 0.05$) after the administration. Concomitant with these peripheral hemodynamic changes, PCWP decreased significantly from 5 to 30 min (24.3 ± 2.2 to 14.6 ± 4.5 mmHg, $p < 0.01$) and CVP decreased (9.0 ± 2.8 to 5.5 ± 3.5 cm H₂O, $p < 0.05$) from 5 to 60 min. Calf vascular resistance, BPm, CI, HR, SVI, and TSPR were not affected significantly. PCWP showed a tendency of reelevation 60 min after the administration, indicating that the duration of action of ISDN was short (about 30 to 60 min).

Table II. Nitroglycerin

	Before	15 min	30 min
BPm (mmHg)	102.4 ± 13.9	95.4 ± 18.1	95.4 ± 18.1
HR (beats/min)	100.7 ± 11.2	101.6 ± 11.6	100.1 ± 9.1
PCWP (mmHg)	28.9 ± 6.8	24.1 ± 6.3	$16.9 \pm 4.4^{**}$
CVP (cmH ₂ O)	13.4 ± 6.8	$10.3 \pm 6.5^*$	$7.9 \pm 5.8^{**}$
CI (L/min/m ²)	2.22 ± 0.74	2.17 ± 0.72	2.22 ± 0.77
SVI (ml/beat/m ²)	22.5 ± 8.4	21.9 ± 9.3	22.6 ± 9.3
SWI (Gm-m/beat/m ²)	22.8 ± 9.3	21.6 ± 10.2	24.1 ± 11.2
TSPR (dyne-sec-cm ⁻⁵ /m ²)	3573.6 ± 889.3	3439.5 ± 779.6	3636.2 ± 1618.3
CBF (ml/100 ml/min)	1.30 ± 0.76	1.37 ± 0.78	1.68 ± 1.23
CVC (ml/100 ml)	0.49 ± 0.22	0.57 ± 0.20	0.60 ± 0.21
CVR (mmHg/ml/100 ml/min)	111.7 ± 72.65	90.48 ± 36.20	$86.10 \pm 57.37^*$

Mean $\pm$ standard deviation, paired t-test, * $p < 0.05$, ** $p < 0.01$, N=7. CBF=calf blood flow;

Table III.

	Before	30 min	60 min
BPm (mmHg)	112.6 ± 18.6	$102.7 \pm 18.4^*$	103.2 ± 21.4
HR (beats/min)	90.5 ± 16.2	99.2 ± 12.0	94.5 ± 18.7
PCWP (mmHg)	25.3 ± 2.2	$17.7 \pm 4.8^{**}$	$16.8 \pm 4.9^{**}$
CVP (cmH ₂ O)	8.4 ± 4.1	6.4 ± 3.7	5.7 ± 3.0
CI (L/min/m ²)	2.36 ± 0.71	2.36 ± 0.70	2.58 ± 0.89
SVI (ml/beat/m ²)	25.8 ± 9.1	25.8 ± 9.3	2.81 ± 14.8
SWI (Gm-m/beat/m ²)	31.1 ± 15.5	32.3 ± 16.0	36.6 ± 27.8
TSPR (dyne-sec-cm ⁻⁵ /m ²)	4065.2 ± 1817.6	$2426.7 \pm 1124.6^*$	3427.8 ± 1370.1
CBF (ml/100 ml/min)	0.86 ± 0.42	$0.91 \pm 0.33^*$	$1.16 \pm 0.31^*$
CVC (ml/100 ml)	0.36 ± 0.13	$0.51 \pm 0.13^*$	$0.50 \pm 0.13^*$
CVR (mmHg/ml/100 ml/min)	164.3 ± 102.9	$124.9 \pm 36.1^*$	$94.2 \pm 36.1^*$

Mean $\pm$ standard deviation, paired t-test, * $p < 0.05$, ** $p < 0.01$, N=7. CBF=calf blood flow;

Hemodynamic effects of NGO (n=7)

The peripheral and cardiac hemodynamic changes occurring after NGO application are shown in Table II and Fig. 2. Calf vascular resistance decreased significantly from 30 to 60 min (111.70 ± 72.65 to 86.10 ± 57.37 mmHg/ml/100 ml/min, $p < 0.05$) and calf venous capacitance increased significantly from 90 to 120 min (0.49 ± 0.22 to 0.67 ± 0.17 ml/100 ml, $p < 0.05$) after the application. Concomitant with these peripheral hemodynamic changes, BPm (from 60 to 180 min) and TSPR (from 120 to 180 min) decreased significantly ($p < 0.05$). Significant decreases were also noted in PCWP from 30 to 180 min (28.6 ± 6.8 to 14.4 ± 3.2 mmHg, $p < 0.01$) and in CVP from 150 to 180 min (13.4 ± 0.8 to 6.7 ± 4.9 cm H₂O, $p < 0.05$) after NGO. Calf blood flow,

Ointment

60 min	90 min	120 min	180 min
$90.3 \pm 10.5^*$	$85.2 \pm 7.7^*$	$86.6 \pm 7.9^*$	$85.7 \pm 6.9^*$
98.8 ± 11.1	96.4 ± 10.0	96.7 ± 10.3	94.7 ± 12.4
$14.8 \pm 3.2^{**}$	$15.2 \pm 3.1^{**}$	$15.4 \pm 3.8^{**}$	$14.4 \pm 3.2^{**}$
$6.7 \pm 4.9^*$	$7.1 \pm 4.7^*$	$8.5 \pm 4.3^*$	$9.2 \pm 5.1^*$
2.36 ± 0.66	2.24 ± 0.46	2.28 ± 0.45	2.54 ± 0.57
24.7 ± 9.0	23.4 ± 5.7	24.1 ± 6.7	27.6 ± 8.9
25.1 ± 9.0	22.8 ± 7.7	23.9 ± 7.4	26.7 ± 8.3
3039.4 ± 795.8	2910.8 ± 296.4	$2892.3 \pm 455.6^*$	$2584.6 \pm 591.7^*$
2.07 ± 0.84	1.81 ± 1.77	1.42 ± 0.83	1.57 ± 1.02
0.62 ± 0.24	$0.67 \pm 0.17^*$	$0.66 \pm 0.20^*$	$0.63 \pm 0.13^*$
$86.90 \pm 60.92^*$	88.7 ± 58.82	88.94 ± 54.76	89.91 ± 64.19

CVC=calf venous capacitance; CVR=calf vascular resistance.

Prazosin

90 min	120 min	180 min	240 min
101.9 ± 13.0	102.4 ± 15.6	101.0 ± 11.3	102.1 ± 13.3
97.2 ± 10.7	95.8 ± 16.1	93.3 ± 14.6	93.6 ± 14.4
$15.0 \pm 4.4^{**}$	$15.3 \pm 4.4^{**}$	$16.5 \pm 3.8^{**}$	$17.1 \pm 3.3^{**}$
5.6 ± 2.9	5.6 ± 3.6	5.4 ± 2.9	4.0 ± 1.6
2.77 ± 0.50	2.64 ± 0.42	2.66 ± 0.37	2.71 ± 0.48
29.4 ± 8.7	29.1 ± 10.3	30.0 ± 9.8	30.8 ± 10.0
$36.1 \pm 17.0^*$	$36.7 \pm 17.7^*$	35.4 ± 17.0	36.2 ± 15.7
2764.4 ± 422.4	3155.6 ± 613.2	2955.6 ± 415.7	2955.2 ± 524.1
$1.77 \pm 0.76^{**}$	$1.56 \pm 0.44^*$	$1.84 \pm 0.55^{**}$	$1.46 \pm 0.34^*$
$0.67 \pm 0.27^*$	$0.58 \pm 0.13^*$	$0.56 \pm 0.21^*$	$0.61 \pm 0.20^*$
$103.4 \pm 43.3^*$	$67.9 \pm 24.4^*$	$62.0 \pm 16.8^*$	$75.6 \pm 25.0^*$

CVC=calf venous capacitance; CVR=calf vascular resistance.

Fig. 2. Hemodynamic effects of nitroglycerin ointment (NGO) on peripheral circulation and cardiac hemodynamics: drafted on percent changes. Calf vascular resistance decreased significantly from 30 to 60 min and calf venous capacitance increased from 90 to 120 min after application. Corresponding to these peripheral hemodynamic changes, BP, TSPR, PCWP, and CVP decreased significantly, although CI, SWI, and calf blood flow did not change significantly.

HR, CI, SVI, and SWI were not influenced significantly.

Hemodynamic effects of Pz (n=6)

Hemodynamic changes after the oral administration of Pz are shown in Table III and Fig. 3. Calf venous capacitance (0.36 ± 0.13 to 0.67 ± 0.27 ml/

Fig. 3. In patients treated with prazosin (Pz) calf venous capacitance and calf blood flow increased significantly from 30 to 240 min, and calf vascular resistance decreased significantly from 60 to 240 min. Concomitant with these peripheral hemodynamic changes, PCWP was lowered from 30 to 240 min and SWI increased from 90 to 120 min. CI and SVI showed a tendency to increase, although not significantly.

100 ml, $p < 0.05$) and calf blood flow (0.86 ± 0.42 to 1.84 ± 0.55 ml/100 ml/min, $p < 0.05$) increased significantly from 30 to 240 min, while calf vascular resistance decreased significantly from 60 to 240 min (164.3 ± 102.9 to 62.0 ± 16.8 mmHg/ml/100 ml/min, $p < 0.05$) after the administration. Concomitant with these significant peripheral hemodynamic changes, PCWP was lowered significantly from 30 to 240 min (25.3 ± 2.2 to 15.0 ± 4.4 mmHg, $p < 0.01$) and SWI increased from 90 to 120 min (31.1 ± 5.5 to 36.7 ± 17.7 Gm·m/beat/m², $p < 0.05$). BPm and TSPR decreased significantly 30 min after the administration. CI and SVI tended to increase and CVP tended to decrease; however

these changes did not reach levels of statistical significance.

DISCUSSION

The hemodynamic effects of the three drugs are compared in Table IV.

We demonstrated that ISDN resulted in a decrease in PCWP and CVP associated with an increase in calf venous capacitance, whereas there were no significant changes in cardiac output, BPm, systemic peripheral resistance and calf vascular resistance. As reported previously¹⁶⁾⁻²¹⁾ the predominant hemodynamic effect of ISDN was a reduction in preload, resulting from dilation of peripheral capacitance vessels. Our results reconfirmed these effects and additionally demonstrated an initial increase in calf blood flow; this may suggest that ISDN may produce transient arteriolar dilatation. Franciosa et al^{19),20)} reported similar findings, i.e., an increase in cardiac output, with 40 mg doses of oral ISDN in patients with chronic heart failure. Leier et al¹⁸⁾ also reported a mild increase in cardiac output after the administration of 20 mg of ISDN in patients with low cardiac output congestive heart failure. These studies suggested that changes in cardiac output induced by vasodilators would be dependent on base-line hemodynamic status.¹⁸⁾⁻²⁰⁾ In the present study, smaller doses (5-10 mg) of ISDN were administered sublingually in patients with hemodynamic subsets (PCWP > 18 mmHg, CI > 2.2 L/min/m²) complicated only by backward failure,^{22),23)} which might be related to the lack of a further increase in cardiac output.

The present study proved that NGO affected not only capacitance vessels

Table IV.

	ISDN subl. (n=7)	NGO (n=7)	Prazosin (n=6)
Peripheral hemodynamics			
Calf blood flow	↑ (5-15 min)	NS	↑ (30-240 min)
Calf vascular resistance	NS	↓ (30-60 min)	↓ (60-180 min)
Calf venous capacitance	↑ (5-60 min)	↑ (90-180 min)	↑ (30-240 min)
Cardiac hemodynamics			
Mean BP	NS	↓ (60-180 min)	↓ (30 min)
HR	NS	NS	NS
PCWP	↓ (5-30 min)	↓ (30-240 min)	↓ (30-240 min)
CVP	↓ (5-60 min)	↓ (15-240 min)	NS
CI	NS	NS	NS
SVI	NS	NS	NS
SWI	NS	NS	↑ (90-120 min)
TSPR	NS	↓ (120-180 min)	↓ (30 min)

to increase peripheral venous pooling and lower elevated preload, but also resistance vessels to reduce systemic and calf vascular resistance. However, the expected increases in cardiac index or calf blood flow were not proven statistically.

Taylor et al²⁴⁾ examined cardiac and peripheral hemodynamic effects of NGO in congestive heart failure for the first time. They demonstrated a decrease in PCWP and an increase in cardiac output with a concomitant decrease in peripheral vascular resistance and an increase in peripheral venous capacitance. Our results were similar to their report except for lack of the increase in cardiac index. The reason for this discrepancy might be in a difference in the base-line hemodynamic values of cardiac index, i.e., in their study mean cardiac index was lower (1.7 L/min/m²) than that in the present study (2.2 L/min/m²). Other previous studies^{25)–27)} have also demonstrated a decrease in systemic and forearm vascular resistance in addition to the predominant effect of preload reduction with nitroglycerin.

In contrast to the short duration of action of ISDN, percutaneously absorbed NGO showed a more prolonged influence on hemodynamic parameters and an afterload reduction effect.

Although all three drugs reduced PCWP with a concomitant increase in calf venous capacitance and NGO showed a significant decrease in systemic and calf vascular resistance, only prazosin (Pz) significantly improved stroke work index.

Several studies have been done concerning this point, i.e., the pre- and afterload reduction effects of Pz in the treatment of heart failure.^{27)–29)} Awan et al^{28),30)} initially reported the effects of Pz on cardiac hemodynamics and peripheral circulation in patients with congestive heart failure. They demonstrated that Pz induced peripheral venodilatation to lower excessive preload, and peripheral arteriolodilatation to augment lowered cardiac output, suggesting potential benefits of Pz for the relief of pulmonary congestion and the improvement of cardiac performance.

Our results were in agreement with their study except for lack of the increase in cardiac output. This may be due to the difference in base-line cardiac output, i.e., mean cardiac index changed from 1.95 to 2.89 L/min/m² in their study and from 2.36 to 2.77 L/min/m² in the present study.

Lopez-Sendon et al³¹⁾ employed Pz for the treatment of complicated AMI for the first time. They demonstrated that Pz alleviated pulmonary congestion and improved cardiac output by reducing LV filling pressure and aortic impedance. The present analyses of peripheral hemodynamic effects would corroborate these results.

Fig. 4. Correlation between base-line and post treatment calf vascular resistance ($n=20$, $r=0.92$, $p<0.01$). It was found that the higher the base-line calf vascular resistance, the better the effect appeared in terms of decreased calf vascular resistance.

Peripheral hemodynamic changes in relation to base-line hemodynamic values

As previously reported it is known that changes in cardiac hemodynamics are somewhat dependent on base-line hemodynamic status.^{18),20)} However, little analysis has been done concerning how the base-line peripheral hemodynamic status is related to the resulting hemodynamic changes. When relationships between base-line and posttreatment peripheral hemodynamic changes were considered (Fig. 4), highly negative correlation was noted for the calf vascular resistance, i.e., $r=-0.99$ ($p<0.01$) in patients treated with prazosin, $r=-0.87$ ($p<0.01$) in NGO treatment, $r=-0.87$ ($p<0.01$) in ISDN treatment, and $r=-0.92$ ($p<0.01$) in all 20 patients. This means that the higher the base-line calf vascular resistance, the greater was the decrease elicited by vasodilator treatment. However, the base-line calf blood flow or calf venous capacitance values showed no significant correlation to the changes in these parameters following vasodilator administration.

CONCLUSION

The present study was done to qualify the primary effects of vasodilator therapy on the peripheral vessels and resultant cardiac hemodynamic modifications in patients with acute myocardial infarction.

ISDN predominantly affected capacitance vessels to increase peripheral venous capacitance and reduce excessive venous return (PCWP and/or CVP), while Pz and NGO dilated not only capacitance vessels but also resistance vessels, thereby reducing peripheral vascular resistance and consequently in-

creasing peripheral blood flow and/or SWI. The effects of the latter two drugs lasted more than 240 min as compared to 60 min with ISDN.

Considering the relationship between base-line and posttreatment peripheral hemodynamic changes, it was observed that the higher the base-line calf vascular resistance, the better the effect appeared in terms of a decrease in calf vascular resistance.

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