Phentolamine

Use in Congestive Heart Failure

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SUMMARY

Two patients (group 1) with relatively normal left ventricles who had never been in left ventricular failure, and 4 patients (group 2) with abnormal left ventricles who had previously been in left ventricular failure, underwent right and left heart catheterization. Cardiac pressures and cardiac output were measured before and at various time intervals during the continuous administration of 0.3 mg. per min. of phentolamine.

Among the subjects in group 1, phentolamine produced only minimal changes in the measured hemodynamic parameters. Among the subjects in group 2, phentolamine produced marked increases in the cardiac index and stroke index. A striking fall in the pulmonary artery pressure and left ventricular end-diastolic pressure was also observed.

Phentolamine is ideally suited for the treatment of patients in left ventricular failure. It is very effective, rapid in action, devoid of side effects and produces no arrhythmias.

Additional Indexing Words :

Cardiac catheterization Inotropic drug

IT has recently been demonstrated that phentolamine has a positive inotropic action.¹⁾ This drug can produce an increase in the force of contraction utilizing the Walton Brodie strain gauge arch in dogs, as well as a marked increase in the left ventricular dp/dt in humans. An increase in the systemic pressures and in the cardiac output, and a decrease in the left ventricular end-diastolic pressure and in the pulmonary artery pressure will ensue when phentolamine is administered intravenously for 20 min. at a rate of 0.3 mg./min. to patients with abnormal left ventricles.

The present study was performed in order to determine if the administration of phenotolamine for periods up to 90 min. could produce these favorable hemodynamic effects without complications.

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METHODS

Two patients (group 1) with relatively normal left ventricles, who had never been in left ventricular failure, and 4 patients (group 2) with abnormal left ventricles, who had previously been in left ventricular failure, underwent right and left heart catheterization. Of the 2 patients in group 1, one had mitral stenosis while the other was

Table I. Patient 1—

	Control	Phentolamine Infusion							
		2 min.	3 min.	4 min.	5 min.	17 min.	18 min.	20 min.	24 min.
Brachial Artery Pressure (mm.Hg)	$\frac{110}{62}$	$\frac{120}{70}$	$\frac{120}{65}$	$\frac{120}{65}$	$\frac{125}{70}$	$\frac{125}{72}$			
Left Ventricular Pressure (mm.Hg)	$\frac{100}{0}$				$\frac{110}{0}$		$\frac{110}{0}$		
Pulmonary Artery Pressure (mm.Hg)	$\frac{30}{15}$							$\frac{32}{15}$	
Pulse Rate (beats/min.)	83	86	86	86	86	67	67	65	63
Cardiac Index (L./min./M. ²)	3.82								4.38
Stroke Index (ml./beat/M. ²)	46								70
Arteriovenous Oxygen Difference (Vol. %)	3.6								3.4
Oxygen Consumption (ml./min./M. ²)	132								149

Table I. Patient 2—

	Control	Phentolamine								
		2 min.	3 min.	4 min.	5 min.	10 min.	15 min.	20 min.	25 min.	30 min.
Brachial Artery Pressure (mm.Hg)	$\frac{127}{68}$		$\frac{148}{80}$	$\frac{148}{80}$	$\frac{142}{80}$	$\frac{132}{68}$	$\frac{132}{65}$	$\frac{133}{68}$	$\frac{130}{70}$	$\frac{130}{70}$
Pulmonary Artery Pressure (mm.Hg)	$\frac{40}{17}$	$\frac{40}{17}$			$\frac{35}{13}$	$\frac{35}{13}$	$\frac{35}{13}$	$\frac{32}{12}$	$\frac{33}{12}$	$\frac{33}{14}$
Pulse Rate (beats/min.)	65	67	67	67	67	67	68	67	67	67
Cardiac Index (L./min./M. ²)	2.56						2.22			
Stroke Index (ml./beat/M. ²)	39						33			
Arteriovenous Oxygen Difference (Vol. %)	5.4						5.9			
Oxygen Consumption (ml./min./M. ²)	138						132			

subject to bouts of paroxysmal atrial fibrillation. This latter subject had been cardioverted 1 day prior to the procedure, and he was clinically felt to be devoid of heart disease. Three of the patients in group 2 had primary myocardial disease and the fourth patient had the carcinoid syndrome with the valvular lesions of pulmonic stenosis, tricuspid insufficiency, and mitral insufficiency. All the patients were in sinus rhythm. Patients number 3, 4 and 5 were taking digoxin. The rest were not taking any medications. Catheterization of the left ventricle was performed through

Mitral Stenosis

			Infusion Stopped							
30 min.	40 min.	50 min.	1 min.	2 min.	3 min.	4 min.	5 min.	6 min.	9 min.	11 min.
$\frac{120}{75}$	$\frac{125}{65}$	$\frac{115}{60}$	$\frac{120}{60}$	$\frac{100}{60}$	$\frac{112}{57}$	$\frac{110}{60}$	$\frac{110}{60}$			$\frac{112}{60}$
$\frac{115}{0}$	$\frac{115}{0}$	$\frac{115}{0}$						$\frac{110}{0}$		
	$\frac{27}{15}$	$\frac{25}{15}$							$\frac{30}{15}$	
60	63	60	60	60	75	67	67	60	67	67
		3.36								
		56								
		3.3								
		101								

Probable Normal

Infusion										
40 min.	45 min.	50 min.	55 min.	60 min.	65 min.	70 min.	75 min.	80 min.	85 min.	90 min.
$\frac{132}{70}$	$\frac{130}{68}$	$\frac{133}{68}$	$\frac{138}{68}$	$\frac{140}{68}$	$\frac{132}{68}$	$\frac{128}{65}$	$\frac{140}{72}$	$\frac{150}{70}$	$\frac{140}{68}$	$\frac{145}{70}$
$\frac{35}{14}$	$\frac{35}{14}$	$\frac{32}{14}$	$\frac{33}{14}$	$\frac{35}{13}$	$\frac{33}{12}$	$\frac{32}{12}$	$\frac{33}{13}$	$\frac{32}{12}$	$\frac{32}{12}$	$\frac{33}{12}$
67	67	67	67	67	67	67	67	71	71	71
				2.05						2.56
				30						36
				5.5						5.2
				114						132

Table I. Continued

Infusion Stopped														
1 min.	2 min.	3 min.	4 min.	5 min.	10 min.	15 min.	20 min.	25 min.	30 min.	40 min.	45 min.	50 min.	55 min.	60 min.
$\frac{135}{67}$	$\frac{132}{68}$	$\frac{132}{68}$	$\frac{128}{68}$	$\frac{127}{68}$	$\frac{128}{65}$	$\frac{128}{68}$	$\frac{128}{65}$	$\frac{128}{65}$	$\frac{130}{70}$	$\frac{128}{68}$		$\frac{128}{68}$	$\frac{128}{68}$	$\frac{128}{68}$
				$\frac{35}{15}$	$\frac{33}{13}$	$\frac{30}{12}$	$\frac{33}{12}$	$\frac{35}{17}$	$\frac{35}{17}$	$\frac{35}{17}$	$\frac{38}{17}$		$\frac{35}{17}$	
67	67	67	67	67	67	67	67	67	65	65	65	65	65	65
									2.59					2.22
									40					34
									4.9					5.2
									127					115

a brachial arteriotomy. A Cournand needle was placed into the opposite brachial artery. A number 7 Goodale-Lubin catheter was placed in the pulmonary artery. Cardiac output was determined by the Fick technique. Left ventricular, pulmonary arterial and systemic arterial pressures and cardiac output were measured in the resting state. After the resting control values were recorded, phentolamine was given by constant intravenous drip (0.3 mg. per min.) for periods up to 90 min. At various time intervals after the start of the infusion, repeat pressure recordings and cardiac outputs were recorded.

Table II. Patient 4—

	Control	Phentolamine Infusion									
		1 min.	2 min.	3 min.	4 min.	5 min.	15 min.	20 min.	25 min.	30 min.	35 min.
Brachial Artery Pressure (mm.Hg)	$\frac{150}{95}$	$\frac{155}{95}$	$\frac{150}{95}$	$\frac{155}{90}$	$\frac{150}{90}$	$\frac{160}{90}$	$\frac{160}{90}$	$\frac{160}{95}$	$\frac{160}{95}$		$\frac{165}{98}$
Pulmonary Artery Pressure (mm.Hg)	$\frac{23}{9}$						$\frac{16}{7}$	$\frac{16}{7}$	$\frac{18}{9}$		$\frac{16}{7}$
Pulse Rate (beats/min.)	88	86	86	86	86	86	107	107	107	115	100
Cardiac Index (L./min./M. ²)	2.95						2.96				3.38
Stroke Index (ml./beat/M. ²)	34						28				30
Arteriovenous Oxygen Difference (Vol. %)	4.2						4.8				4.9
Oxygen Consumption (ml./min./M. ²)	124						142				165

RESULTS

Complete data on the 6 patients are presented in Tables I and II.

Phentolamine initially produced a small increase in the pulse rate and brachial artery pressure in the group 1 patients. With the continued adminis-

Table II. Patient 3—Primary Myocardial Disease

	Control	Phentolamine Infusion						Post Infusion
		4 min.	9 min.	17 min.	20 min.	37 min.	40 min.	15 min.
Brachial Artery Pressure (mm.Hg)	$\frac{140}{88}$	$\frac{143}{85}$		$\frac{138}{85}$		$\frac{105}{70}$		$\frac{135}{82}$
Left Ventricular Pressure (mm.Hg)	$\frac{130}{23}$		$\frac{145}{13}$	$\frac{125}{5}$		$\frac{105}{0}$		$\frac{125}{5}$
Pulmonary Artery Pressure (mm.Hg)	$\frac{45}{20}$		$\frac{30}{18}$		$\frac{22}{12}$			$\frac{26}{14}$
Pulse Rate (beats/min.)	88	100	100	107	107	90	94	98
Cardiac Index (L./min./M. ²)	2.64				2.97		4.25	
Stroke Index (ml./beat/M. ²)	30				28		45	
Arteriovenous Oxygen Difference (Vol. %)	5.7				5.9		4.6	
Oxygen Consumption (ml./min./M. ²)	151				175		196	

Primary Myocardial Disease

[illegible]

tration of the drug, there was a small decrease in the pulmonary artery pressure and cardiac output. In general, only minimal hemodynamic changes occurred in this group. With the cessation of the drug, the hemodynamic parameters rapidly returned to the control values.

Table II. Patient 5—

	Control	Phentolamine					
		2 min.	3 min.	5 min.	10 min.	15 min.	20 min.
Brachial Artery Pressure (mm.Hg)	$\frac{165}{110}$	$\frac{170}{110}$	$\frac{165}{105}$	$\frac{170}{105}$		$\frac{170}{100}$	
Left Ventricular Pressure (mm.Hg)	$\frac{155}{32}$			$\frac{165}{15}$	$\frac{160}{17}$		$\frac{150}{17}$
Pulmonary Artery Pressure (mm.Hg)	$\frac{85}{42}$				$\frac{75}{40}$		$\frac{75}{40}$
Pulse Rate (beats/min.)	115	120	120	120	120	115	115
Cardiac Index (L./min./M. ²)	2.73						5.15
Stroke Index (ml./beat/M. ²)	24						45
Arteriovenous Oxygen Difference (Vol. %)	7.0						4.5
Oxygen Consumption (ml./min./M. ²)	190						232

Table II. Patient 6—Carcinoid Syndrome, Mitral

	Control	Phentolamine					
		4 min.	5 min.	6 min.	8 min.	12 min.	14 min.
Brachial Artery Pressure (mm.Hg)	$\frac{155}{90}$	$\frac{175}{95}$	$\frac{170}{90}$			$\frac{165}{85}$	
Left Ventricular Pressure (mm.Hg)	$\frac{135}{3}$			$\frac{158}{2}$		$\frac{150}{2}$	
Pulmonary Artery Pressure (mm.Hg)	$\frac{20}{10}$				$\frac{20}{6}$		$\frac{18}{6}$
Pulse Rate (beats/min.)	83	86	86	86	86	86	86
Cardiac Index (L./min./M. ²)	3.0						
Stroke Index (ml./beat/M. ²)	36						
Arteriovenous Oxygen Difference (Vol. %)	4.6						
Oxygen Consumption (ml./min./M. ²)	138						

Among the subjects in group 2, with abnormal left ventricles, phentolamine produced marked increases in the cardiac index and stroke index. A striking fall in the pulmonary artery pressure and left ventricular end-diastolic pressure was also observed. The left ventricular and brachial artery systolic

Primary Myocardial Disease

Infusion			Infusion Stopped							
30 min.	45 min.	60 min.	2 min.	3 min.	4 min.	5 min.	10 min.	20 min.	25 min.	30 min.
$\frac{170}{100}$	$\frac{150}{85}$	$\frac{145}{80}$	$\frac{150}{85}$	$\frac{150}{85}$	$\frac{145}{85}$	$\frac{150}{85}$	$\frac{150}{85}$	$\frac{145}{85}$		
$\frac{155}{18}$		$\frac{140}{15}$					$\frac{140}{17}$	$\frac{140}{15}$		$\frac{140}{17}$
$\frac{75}{40}$	$\frac{65}{35}$	$\frac{55}{25}$					$\frac{55}{25}$	$\frac{55}{25}$		
107	100	95	95	95	95	95	95	95	100	95
		4.34							4.14	
		46							42	
		5.0							4.7	
		217							195	

and Tricuspid Insufficiency, Pulmonic Stenosis

Infusion						Post Infusion		
18 min.	19 min.	20 min.	30 min.	36 min.	40 min.	1 min.	5 min.	6 min.
	$\frac{165}{85}$		$\frac{165}{85}$		$\frac{165}{85}$	$\frac{165}{85}$	$\frac{165}{85}$	
$\frac{152}{2}$			$\frac{153}{1}$	$\frac{168}{0}$				$\frac{165}{0}$
	$\frac{18}{6}$		$\frac{18}{6}$	$\frac{20}{6}$				$\frac{22}{8}$
90	86	88	86	86	88	86	86	86
		3.24			4.13			
		37			47			
		4.8			3.5			
		156			145			

pressures rose with the administration of the drug. However, in patients number 3 and 5 with the abnormally increased end-diastolic pressure, the continued administration of phentolamine produced a decline in the left ventricular and brachial artery systolic pressures. No patient complained of any symptoms due to the infusion of the drug. No arrhythmia was noted, and no patient developed chest pain.

DISCUSSION

We previously administered phentolamine for 20 min. to 5 patients with relatively normal ventricles who had never been in left ventricular failure, and to 13 patients with abnormal left ventricles, who had previously been in left ventricular failure.¹⁾ The administration of phentolamine to the 5 normal patients produced little or no change in the heart rate, cardiac pressures, cardiac output or left ventricular volume. Among the subjects with abnormal left ventricles, phentolamine produced a marked increase in the cardiac output with moderate increases in the brachial artery systolic pressure and pulse rate. The left ventricular dp/dt , which is a measure of contractility, increased in all patients.

In our present and previous study, the 2 groups of patients responded hemodynamically in a similar fashion. It was interesting to observe that in patients number 3 and 5 with the increased left ventricular end-diastolic pressure, the administration of phentolamine initially produced an increase in the left ventricular and brachial artery systolic pressure. This is comparable to our previous experience in patients with abnormal left ventricles. However, as the drug was continued, a striking decline in the brachial artery and left ventricular pressures was observed due to the improvement in cardiac function. These beneficial hemodynamic effects persisted up to 30 min. after the cessation of the drug.

If the patient in congestive heart failure demonstrates a favorable clinical and hemodynamic response following the parenteral administration of phentolamine, then in those patients with pulmonary edema, phentolamine administration should also produce a rapid alleviation of this cardiovascular emergency. We have recently demonstrated this to be the case in 6 patients with pulmonary edema.²⁾ The clinical improvement in these patients was associated with a rapid decrease in the systemic blood pressure. However, it is well known that in patients with pulmonary edema, the blood pressure is usually elevated unless they are in shock. With successful treatment of this entity, the blood pressure will fall to the pre-pulmonary edema values.

The low dose of phentolamine (0.3 mg./min.) that we employed in our

study produced a rise in the systemic pressure due to the predominant inotropic action. The higher doses used by other investigators probably produced predominant vasodilatation with a resultant fall in the systemic pressure, masking the inotropic effect of the drug. This is similar to the clinical experience with isoproterenol which can initially produce a rise in the systemic pressure, due to the contractility effect. When the dose is increased, the systemic pressure falls due to the dominant vasodilatation effect.

The positive inotropic action of phentolamine may be due to a direct or an indirect cardiac mechanism. 1) Phentolamine may act like isoproterenol and directly stimulate the beta adrenergic receptor sites in the heart, 2) Phentolamine may act like morphine and produce a sympathoadrenal discharge which indirectly stimulates the beta adrenergic receptors of the myocardium.³⁾ No matter which mode of action is finally established, phentolamine is ideally suited for the treatment of patients in left ventricular failure. It is very effective, rapid in action, devoid of side effects and produces no arrhythmias.

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