Hemodynamic Effects of Pentazocine in Acute Myocardial Infarction

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SUMMARY

In 12 patients with acute myocardial infarction the hemodynamic effects of a single intravenous injection of 30 mg of pentazocine were investigated. The administration of pentazocine resulted in no significant hemodynamic changes. In particular, there was no increase in peripheral vascular resistance and no evidence of decreased left ventricular function or respiratory depression. In the occasional patients who demonstrated an elevation of pulmonary arterial pressure, it was probably due to a direct effect of the drug on the pulmonary vasculature.

Additional Indexing Words :

Coronary heart disease Left ventricular function Systolic time
intervals Pulmonary artery pressure

THE analgesic effect of pentazocine in patients with acute myocardial infarction is well accepted. However, the hemodynamic effects of this drug remain controversial, particularly in patients with coronary heart disease.

Several investigators have observed that the administration of pentazocine resulted in a marked rise in mean pulmonary arterial pressure. This increase was considered to be a result of impaired left ventricular function which occurred as a consequence of the increased peripheral vascular resistance caused by the drug.^{1),10),14)} In contrast, other investigators have observed that pentazocine promoted only a slight increase in pulmonary arterial pressure and no effect on left ventricular function.^{13),17)-19)}

In view of these conflicting reports and the obvious clinical importance of this problem, we investigated the hemodynamic effects of pentazocine under the conditions of our own coronary care unit.

METHODS

Hemodynamic studies were performed on 12 patients (11 males, 1 female). The mean age of the group was 65 years (range 52-76 years). All patients had

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suffered from myocardial infarction 8 to 48 hours (mean 39 hours) prior to the study. Myocardial infarction was diagnosed by the combination of history of chest pain, characteristic ECG changes and typical elevations of pertinent serum enzymes. The infarction was anterior in 4 cases and inferior in the remaining 8.

The clinical course was characterized by only slight to moderate left ventricular failure, no patient presented with cardiogenic shock or pulmonary edema.

Table I. Hemodynamics before and

		Pre-period mean values		0 min		5 min	
				$\bar{x}$	$\pm s$	$\bar{x}$	$\pm s$
		$\bar{x}$	$\pm s$				
HR	(min ⁻¹)	70.4	19.7	73.5	21.0	74.0	20.8
SBAP	(mmHg)	152	28	151	30	146	25
DBAP	(mmHg)	76	10	76	10	75	9
MBAP	(mmHg)	101	15	101	15	99	12
CO	(l/min)	5.17	1.10	5.20	1.16	5.14	1.20
CI	(l/min·m ²)	2.80	0.55	2.81	0.58	2.78	0.57
SV	(ml)	64.4	16.5	62.8	18.1	61.7	17.5
SVI	(ml/m ²)	34.8	8.4	33.9	9.4	33.3	9.0
PVR	(dyne·sec·cm ⁻⁵)	1,695	393	1,676	446	1,639	301
SPAP	(mmHg)	34.2	15.2	35.4	14.5	39.5	16.7
EDPAP	(mmHg)	12.4	7.1	13.2	7.3	15.5	7.8
MPAP	(mmHg)	20.0	9.4	21.1	8.9	23.7	10.1
TPR	(dyne·sec·cm ⁻⁵)	362	277	392	324	426	272
LVSWI	(Gm·m/m ²)	46.6	14.5	44.7	13.1	41.7	11.8
MSER	(ml/sec·m ²)	12,945	2,590	12,509	3,035	12,191	2,520
O ₂ a	(mmHg)	69.1	18.4	62.2	13.8	62.4	13.0
O ₂ v	(mmHg)	34.8	4.7	34.8	6.7	35.1	5.9
AVDO ₂	(mmHg)	34.2	17.7	27.3	12.7	27.2	11.0
pH		7.41	0.04	7.38	0.04	7.38	0.04
pCO ₂	(mmHg)	41.5	6.0	46.1	5.7	45.2	8.2
St. Bic.	(mVal/l)	25.4	2.9	26.0	3.3	25.5	2.4
LVET	(msec)	262	34	259	37	258	38
PEP	(msec)	89	17	90	21	90	21
Q-1	(msec)	57	10	57	10	57	10
IVCP	(msec)	32	13	33	16	33	14
rel. LVET	(%)	95.0	8.5	95.7	9.8	95.2	9.8
LVET/PEP		3.07	0.83	3.06	1.07	3.04	1.00
DBAP/IVCP	(mmHg·sec ⁻¹)	2,636	858	2,550	757	2,410	972

No statistical significance was obtained in any of the listed data.

Abbreviations: HR=Heart rate, SBAP=Systolic brachial arterial pressure, DBAP=Diastolic brachial arterial pressure, MBAP=Mean brachial arterial pressure, CO=Cardiac output, CI=Cardiac index, SV=Stroke volume, SVI=Stroke volume index, PVR=Peripheral vascular resistance, SPAP=Systolic pulmonary arterial pressure, DPAP=Diastolic pulmonary arterial pressure, MPAP=Mean pulmonary arterial pressure, TPR=Total pulmonary resistance, LVSWI

All patients were in sinus rhythm except one who exhibited atrial fibrillation. Apart from isolated supraventricular and ventricular ectopics no other arrhythmias were observed.

All medication were discontinued at least 4 hours prior to the study except for a few cases in which previously started heparin infusion was maintained.

Under local anaesthesia a 7F thermistor Swan-Ganz catheter (Edwards Lab-

after Penta zocine

Mean ($\bar{x}$) and standard deviations ($\pm s$).

After pentazocine									
10 min		15 min		20 min		25 min		30 min	
$\bar{x}$	$\pm s$	$\bar{x}$	$\pm s$	$\bar{x}$	$\pm s$	$\bar{x}$	$\pm s$	$\bar{x}$	$\pm s$
73.0	20.9	75.2	21.0	74.3	20.9	73.1	20.7	72.6	20.7
144	24	146	26	144	23	148	22	147	24
75	10	76	10	76	9	77	9	76	11
99	13	99	13	99	12	102	12	100	14
5.28	1.18	5.09	1.16	5.14	1.11	5.12	1.12	5.21	1.11
2.85	0.56	2.75	0.53	2.78	0.52	2.77	0.52	2.81	0.53
64.6	18.3	60.7	15.9	62.5	15.8	63.3	15.9	65.4	17.6
34.9	9.6	32.8	7.9	33.8	8.1	34.2	8.2	35.3	9.2
1,598	268	1,684	317	1,652	318	1,701	300	1,645	267
39.8	16.4	39.8	17.0	40.1	15.3	40.0	16.3	39.3	14.6
16.0	7.3	15.7	7.4	15.7	7.6	15.8	7.6	15.3	7.7
24.2	10.0	24.4	10.1	24.0	9.6	24.3	10.0	23.4	9.6
423	267	434	272	422	265	438	280	412	267
43.6	12.2	41.4	11.4	42.2	12.0	44.1	12.6	45.5	13.0
12,620	2,542	12,100	2,440	12,295	2,347	12,350	2,438	12,470	2,395
62.4	13.2	63.9	12.9	63.5	12.5	64.9	13.0	65.3	14.0
35.9	5.7	36.2	5.9	35.7	6.6	35.4	6.4	35.8	6.4
26.4	11.2	27.5	11.2	27.8	10.5	29.1	11.4	30.2	11.6
		7.39	0.04			7.37	0.04		
		45.9	7.9			46.9	8.6		
		25.8	2.7			25.0	2.7		
262	40	260	37	263	36	265	40	268	39
78	25	90	22	90	21	89	22	89	23
57	11	58	12	57	10	57	9	58	12
30	19	32	15	33	15	32	17	31	19
96.1	10.0	96.3	10.0	96.8	9.5	97.0	10.0	97.5	9.8
3.37	1.68	3.12	1.26	3.08	0.95	3.16	1.05	3.24	1.18
3,334	2,379	2,727	945	2,584	963	2,914	1,526	3,139	1,480

=Left ventricular stroke work index, MSER=Mean systolic ejection rate, O_2a =Arterial O_2 tension, O_2v =Mixed venous O_2 tension, $AVDO_2$ =Arterio-venous O_2 difference, pCO_2 =Arterial CO_2 tension, St. Bic.=Standard bicarbonate, LVET=Left ventricular ejection time, PEP=Pre-ejection period, Q_{-1} =Electromechanical latency, IVCP=Isovolumic contraction period, rel. LVET=LVET normalized for heart rate.

oratories, Santa Ana, California, USA) was inserted either percutaneously or by cutdown procedure into an antecubital vein and passed into the pulmonary artery. A cannula was introduced into the brachial artery (Still Infusion Cannula). For pressure recordings Statham P Db 23 pressure transducers were used, the zero reference point being set at midthoracic level. Pulmonary arterial and brachial arterial pressures were recorded simultaneously with the electrocardiogram, the external carotid pulse tracing and the phonocardiogram on a 6-channel jet inscription polygraph (Mingograph Cardirex, Siemens). Cardiac output was determined by the thermal dilution technique using a cardiac output computer (Fischer, Göttingen); the mean values from quadruplicate measurements in each instance were used. Determination of arterial and central venous oxygen tension and arterial blood gases (pH, pCO₂, standard bicarbonate) was carried out with the systems BMS 2, MK 2, and BEU 1 from Radiometer, Copenhagen. The systolic time intervals were calculated according to Blumberger^{2),3)}.

From the measured parameters the following were calculated:—

Peripheral vascular resistance and total pulmonary resistance, using standard definitions, in addition left ventricular stroke work index (LVSWI) and mean systolic ejection rate (MSER) according to the following formulae:

$$\text{LVSWI} = \frac{(\text{MBAP} - \text{EDPAP}) \times \text{SVI} \times 1.36 \times 1.055}{100} \quad [\text{Gm} \times \text{m/m}^2]$$

$$\text{MSER} = \frac{\text{SVI} \times 100}{\text{LVET}} \quad [\text{ml/sec. m}^2]$$

MBAP = mean brachial arterial pressure (mmHg)

EDPAP = end diastolic pulmonary arterial pressure (mmHg)

SVI = stroke volume index (ml/m²)

LVET = left ventricular ejection time (sec), measured from the carotid pulse curve or the arterial pressure tracing.

In calculating the left ventricular stroke work index, the end diastolic pulmonary arterial pressure was used as an indirect parameter for the left ventricular filling pressure, since corresponding comparative measurements have shown a good correlation ($r=0.93$) even in acute myocardial infarction.⁸⁾

In all patients 30 mg pentazocine was injected intravenously within 2 min. Measurements were taken 15, 10, 5, and 0 min before the administration of the drug and 0, 5, 10, 15, 20, 25, and 30 min afterwards. From all values before the administration of the drug an initial mean value was calculated for each patient and compared with the values after the administration of pentazocine.

Statistical analysis was performed using Student's t-test for paired data.* ** A significant difference was assumed if the bilateral probability of error was less than 5% ($2p < 0.05$).

* CD 3105-Computer from the Computer Center of the University of the Saarland, Homburg terminal-supported by the DFG.

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RESULTS

Table I shows the hemodynamic effects of pentazocine in the 12 patients with recent myocardial infarction.

There was no change in heart rate, blood pressure, cardiac index, stroke volume, or peripheral vascular resistance.

The changes in pulmonary arterial pressure were inconsistent with the mean pulmonary arterial pressure showing an insignificant increase from 20.0 ± 9.4 to 24.4 ± 10.1 mmHg. There was no significant change in pulmonary vascular resistance. However, in isolated cases, an increase in pulmonary arterial pressure by a maximum of 18 mmHg (systolic) and 11 mmHg (diastolic) could be observed.

In view of the lack of change in measured parameters the calculated parameters LVSWI and MSER also showed no change.

Following the administration of pentazocine the arterial O_2 tension fell by a mean of 6.7 mmHg in the first 10 min. Since the mixed venous oxygen tension remained constant there was a temporary drop in $AVDO_2$. The arterial CO_2 tension tended to increase and the pH tended to fall with the standard bicarbonate remaining constant. However, none of the changes in blood gases were significant.

In a similar manner to other measurements pentazocine caused no change in systolic time intervals and in particular there was no alteration of

Table II. Hemodynamics before and after Pentazocine

	Pre-period mean values	0 min	5 min	10 min	15 min	20 min	25 min	30 min
SBAP (mmHg)	153	154	150	152	149	248	152	156
DBAP (mmHg)	74	76	76	77	75	75	79	80
MEAP (mmHg)	100	102	102	105	103	102	108	107
SVI (ml/m ²)	37.5	37.0	35.1	38.5	36.0	37.2	37.5	38.4
PVR (dyne·sec·cm ⁻⁵)	1,587	1,524	1,597	1,516	1,548	1,481	1,567	1,572
SPAP (mmHg)	32.1	36.5	42.7	46.0	46.2	45.5	45.7	43.5
EDPAP (mmHg)	11.2	13.2	16.5	18.7	18.0	17.2	18.5	18.0
MPAP (mmHg)	18.6	21.5	25.2	28.2	28.0	26.5	28.0	23.7
TPR (dyne·sec·cm ⁻⁵)	288	313	393	506	417	385	408	386
LVSWI (Gm·m/m ²)	47.8	46.6	42.8	47.6	43.4	44.8	48.0	49.1
MSER (ml/sec·m ²)	13,909	13,640	13,099	14,012	13,314	13,585	13,739	13,744
IVCP (msec)	37	36	35	31	33	36	37	34
DBAP/IVCP (mmHg·sec ⁻¹)	1,497	1,717	1,672	4,510	2,832	2,607	2,640	3,292

Patients with an increase in MPAP by >8 mmHg (N=4). Mean values, symbols as Table 1.

the DBAP/IVCP ratio.

There was a small sub-group of patients who demonstrated an increase of mean pulmonary arterial pressure greater than 8 mmHg. This group did not differ from the total group regarding changes in systemic arterial pressure, peripheral vascular resistance, LVSWI, MSER, or DBAP/IVCP ratio (Table II).

DISCUSSION

Our results confirm the findings of others^{7),16),19)} that, in patients with acute myocardial infarction, the administration of 30 mg of pentazocine resulted in no significant hemodynamic changes.

Other investigators have observed an increased pulmonary arterial pressure following the administration of pentazocine.^{1),10),14),17),19)} They have considered this increase to be a primary effect on the pulmonary vasculature^{17),19)} or a secondary effect caused by an elevation of left ventricular filling pressure. The latter was thought to occur as a result of an increased afterload on the left ventricle.^{1),10),14)}

Our data indicate that any elevation in pulmonary arterial pressure was inconsistent and, in considering the whole group of patients, was statistically insignificant.

Although we did not directly measure left ventricular pressure it was unlikely that left ventricular filling pressure was altered due to an afterload induced reduction in left ventricular function. There was no change in peripheral vascular resistance which had been observed by several authors.^{1),10),12),13),15),16)} In addition, pentazocine caused no alterations in the indirect measurements of left ventricular function, that is, LVSWI, MSER, or the DBAP/IVCP ratio.

In considering the potential constricting effects of pentazocine on the pulmonary resistance vessels, previous investigators have invoked the Euler-Liljestrand reflex and the respiratory depressant effect of pentazocine.^{4)-6),9),11)} Our data indicate little if any respiratory depression shown by the insignificant changes in arterial PO₂, pCO₂ and pH. Thus, in those patients who showed an increase in pulmonary arterial pressure it was likely a direct effect of pentazocine on the pulmonary resistance vessels.

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