Preliminary Communications

Increased Pulmonary Arterial Pressures after Pentazocine in Myocardial Infarction

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Summary: In 15 patients with acute myocardial infarction intravenous pentazocine in a dose of either 30 or 60 mg. was followed by a significant increase in mean pulmonary arterial pressure. In the group receiving the 60-mg. dose this change was associated with a significant increase in systemic arterial pressure, total peripheral resistance, and left ventricular minute work. Because of these circulatory effects intravenous pentazocine in a dose of 60 mg. would seem to be unsuitable for the relief of pain in myocardial infarction.

INTRODUCTION

Pentazocine (Fortral) is a narcotic antagonist which possesses comparable analgesic potency to heroin, methadone, and morphine when given to patients with myocardial infarction (Scott and Orr, 1969). This paper presents preliminary observations on the cardiovascular effects of intravenous pentazocine in patients with myocardial infarction.

PATIENTS AND MATERIALS

Thirteen men and two women with acute myocardial infarction were studied (W.H.O., 1959 criteria). Their ages ranged from 47 to 69 years, with a mean of 60. The infarct site was anterior in all, with additional inferior damage in three. Five patients had cardiac pain and seven had radiological pulmonary oedema when the drug was given. All patients were in sinus rhythm and none had received other drugs for at least six hours.

The techniques used in this study have been described in detail elsewhere (Fluck *et al.*, 1967; Jewitt *et al.*, 1970a). Control observations of heart rate, pulmonary arterial pressure, aortic pressure, cardiac output, stroke volume, peripheral resistance, tension time index, and left ventricular external work were made at five-minute intervals over a period of 30 minutes. In nine patients 60 mg. of pentazocine was then injected in two minutes into a peripheral vein. The remaining

six patients received a 30-mg. dose intravenously given over five minutes. The observations were then repeated at intervals of 5, 10, 20, and 30 minutes after giving pentazocine. The differences between the individual mean control values and those recorded at intervals of 5, 10, 20, and 30 minutes after the drug were compared, Student's *t* test on a two-tail basis being used.

RESULTS

Patients with Myocardial Infarction.—The means of the six haemodynamic values during the control period and those 5 and 10 minutes after the administration of pentazocine at both dose levels are presented in the Table. The individual control and 10-minute values for mean pulmonary artery pressures at both dose levels are shown in Fig. 1.

Mean Pulmonary Artery Pressure.—This rose in all patients after pentazocine in a dose of 30 or 60 mg. at some time during the 30-minute period of observation. The mean values in the two dosage groups were significantly raised 5 and 10 minutes after the drug, and were still significantly raised 30

FIG. 1.—Changes in mean pulmonary arterial pressure in 15 patients with myocardial infarction given intravenous pentazocine in a dose of 30 or 60 mg.

Mean Haemodynamic Values after Pentazocine in 15 Patients with Acute Myocardial Infarction

				30 mg. Pentazocine		P	60 mg. Pentazocine		P
				Mean (±S.E.)	Mean Difference From control		Mean (±S.E.)	Mean Difference From control	
Mean pulmonary artery pressure (mm. Hg)	..	..	C	20.3 (3.1)			20.2 (3.1)		
			I	26.5 (3.0)	+ 6.2	<0.01	30.9 (3.7)	+10.7	<0.02
			II	33.2 (2.9)	+12.9	<0.02	31.4 (3.2)	+11.2	<0.01
Mean aortic pressure (mm. Hg)	..	..	C	107.7 (7.1)			98.0 (6.2)		
			I	112.8 (8.3)	+ 5.1	<0.05	113.9 (10.2)	+15.9	<0.02
			II	120.3 (8.3)	+12.6	n.s.	117.1 (10.2)	+19.1	<0.01
Heart rate (beats/min.)	..	..	C	80.2 (4.3)			90.1 (6.2)		
			I	83.5 (5.9)	+ 3.3	n.s.	93.2 (6.3)	+ 3.1	n.s.
			II	85.7 (4.2)	+ 5.5	n.s.	94.6 (6.7)	+ 4.5	n.s.
Cardiac output (l./min.)	..	..	C	5.43 (0.49)			4.87 (0.41)		
			I	5.60 (0.55)	+ 0.17	n.s.	4.43 (0.41)	— 0.43	<0.01
			II	5.52 (0.56)	+ 0.09	n.s.	4.92 (0.46)	+ 0.05	n.s.
Stroke volume (ml.)	..	..	C	64.9 (8.7)			55.9 (5.3)		
			I	63.5 (8.5)	— 1.4	n.s.	49.4 (5.6)	— 6.5	<0.05
			II	60.4 (5.9)	— 4.5	n.s.	54.3 (6.6)	— 1.6	n.s.
Total peripheral resistance (units)	..	..	C	22.0 (2.4)			20.9 (1.8)		
			I	22.6 (3.0)	+ 0.60	n.s.	26.8 (2.8)	+ 5.9	<0.01
			II	23.8 (1.2)	+ 1.80	n.s.	26.2 (3.0)	+ 5.3	<0.02
Left ventricular minute work (kp.m./min.)	..	..	C	7.70 (4.1)			6.51 (0.7)		
			I	8.30 (1.2)	+ 0.60	n.s.	6.97 (0.9)	+ 0.46	n.s.
			II	8.88 (1.6)	+ 1.18	n.s.	7.89 (1.1)	+ 1.38	n.s.
Tension time index (mm. Hg sec./min.)	..	..	C	2329 (229)			2048 (154)		
			I	2564 (331)	+235	n.s.	2401 (283)	+353	n.s.
			II	2864 (273)	+535	n.s.	2472 (284)	+424	<0.05

C=Control. I=5 minutes after Pentazocine. II=10 minutes after Pentazocine.

minutes after the 60-mg. dose. A typical example of the changes seen in pulmonary artery pressure is shown in Fig. 2. Most patients studied had control mean pulmonary artery pressures within the normal range, but in five the levels were raised and associated with radiological pulmonary oedema.

FIG. 2.—Changes in pulmonary arterial pressure in a patient with acute myocardial infarction who received 60 mg. of pentazocine intravenously. Mean control pulmonary artery pressure 28 mm.Hg rising to 46 mm.Hg 15 minutes after pentazocine.

The largest individual change was seen in a patient receiving the 30-mg. dose whose mean pressure rose from a control level of 12 to 48 mm.Hg at 20 minutes.

Mean Aortic Pressure.—This increased in all patients at both dose levels. In those receiving 60 mg. of pentazocine the mean level was significantly raised at all times up to 30 minutes after the drug, while with a 30-mg. dose the mean level was significantly raised only at five minutes. An initial fall in pressure was not found.

Heart Rate.—Changes in heart rate were variable. The mean level was higher 10 minutes after both 30 and 60 mg. of pentazocine, but the differences from mean control values were not significant.

Cardiac Output.—Control cardiac outputs ranged from 4 to 6.6 l./min. in the patients receiving the 30-mg. dose and from 3.1 to 7.1 l./min. in those receiving 60 mg. The mean cardiac output fell transiently in those receiving 60 mg. of pentazocine from a mean control value of 4.9 l./min. to 4.4 l./min. five minutes after the drug. This difference was significant ($P < 0.01$). Thereafter the mean levels for the group did not differ significantly from control values though at 20 and 30 minutes after the drug they were raised. Mean cardiac output did not change significantly after 30 mg. of pentazocine.

Stroke Volume.—The mean stroke volume in the group receiving 60 mg. of pentazocine had fallen significantly five minutes after the drug but thereafter returned to the control level. No other significant mean change occurred with either 30 or 60 mg.

Total Peripheral Resistance.—The mean total peripheral resistance did not change significantly after the 30-mg. dose of pentazocine, but after the 60-mg. dose it was significantly higher at 5, 10, and 20 minutes.

Left Ventricular Minute Work.—External left ventricular work rose in all patients after pentazocine. The mean change, however, was significant only at 20 minutes after the 60-mg. dose (control 6.8 ± 0.7 kp.m./min.; 20-minute value 8.5 ± 1.0 kp.m./min.; $P < 0.05$).

Tension Time Index.—This rose after both doses, but the mean change was significant only after 60 mg. ($P < 0.05$ at 10 minutes).

Duration of Haemodynamic Changes.—In four patients the rise in the pulmonary and systemic arterial pressures was noted to persist for at least 60 minutes after a 60-mg. dose and for 40 minutes after a 30-mg. dose.

Clinical Effects.—After intravenous pentazocine seven patients were noted to be sweating profusely and two complained of dizziness and a sense of disorientation. These effects were more prominent after a 60-mg. dose. Cardiac pain was promptly relieved in four out of five patients in whom it

was present. One patient who received 60 mg. of pentazocine experienced severe cardiac pain 20 minutes later. This coincided with the peak of his increase in pulmonary arterial pressure. No definite evidence of general clinical deterioration was noted during the course of these studies with pentazocine at either dose level.

DISCUSSION

The ideal analgesic for use in acute myocardial infarction would relieve pain rapidly without causing nausea, vomiting, or significant haemodynamic side-effects. In the present study we have shown that 30 or 60 mg. of pentazocine intravenously results in a significant rise in mean pulmonary artery pressure. Central aortic pressure rose at the same time, and this change provides an after-load stress to the heart by increasing the resistance to left ventricular ejection. An increase in left ventricular work would therefore be anticipated, and was present 20 minutes after giving 60 mg. of pentazocine. The raised pulmonary artery pressure after pentazocine may be due either to altered left ventricular function or to a direct increase in pulmonary vascular resistance. Left ventricular pressures were not measured in these patients with acute myocardial infarction. In similar studies with intravenous pentazocine made in patients with severe angina pectoris, however, raised aortic and pulmonary arterial pressures were associated with an increase in left ventricular end-diastolic pressure (Jewitt *et al.*, 1970b).

These haemodynamic changes may be compared with those that occur after morphine, which is associated with potentially dangerous systemic hypotension in some patients (Thomas *et al.*, 1965), and pethidine, which causes an initial rise in arterial pressure followed by a fall to below control levels (Rees *et al.*, 1967). In contrast, heroin in an intravenous dose of 5 mg. has no important effects on the circulation of patients with myocardial infarction (MacDonald *et al.*, 1967).

No definite evidence of clinical deterioration was noted when pentazocine was given in the present study, but the haemodynamic observations made provide a more sensitive method of assessing the drug's cardiovascular effects. In contrast to earlier reports (Lal *et al.*, 1969; Scott and Orr, 1969), the results suggest that the use of intravenous pentazocine, particularly in a dose of 60 mg., may be unsuitable after acute myocardial infarction. Further evaluation of intramuscular pentazocine is required, since it is most commonly given by this route outside coronary care units.

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Requests for reprints to be sent to Dr. D. E. Jewitt.

D. E. JEWITT, M.R.C.P.

B. J. MAURER, M.R.C.P.I.

P. J. B. HUBNER, M.R.C.P.

Department of Medicine and M.R.C. Cardiovascular Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London W.12.

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