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Haemodynamic effects of dextro-propranolol in acute myocardial infarction

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Intravenous injections of 20–25 mg. D-propranolol did not change the heart rate or systemic pressure in 13 patients with cardiac infarction. Cardiac output was depressed in 10, but there was no clinical deterioration. D-Propranolol was better tolerated than DL-propranolol under these conditions and justifies further investigation as an anti-dysrhythmic agent. The major depressant effects of DL-propranolol following cardiac infarction appear to be due to beta-adrenergic blockade and not to a direct depressant action on cardiac muscle.

Racemic propranolol has been shown to be an effective antidysrhythmic agent in many circumstances (Frieden, 1967; Gettes and Surawicz, 1967; Gibson and Sowton, 1969), including the management of ventricular fibrillation following infarction (Sloman, Robinson, and McLean, 1965). Its depressant effects on myocardial function (Bay, Lund-Larsen, Lorentsen, and Sivertssen, 1967) limit its use in seriously ill patients, although Stannard, Sloman, and Sangster (1968) reported that the reduction in cardiac output could be largely prevented by the addition of atropine. The dextro-isomer of propranolol (I.C.I. 47,319) is almost devoid of blocking activity during an isoprenaline challenge in animal investigations (Howe and Shanks, 1966) and in normal volunteers (Shanks, 1968, personal communication). D-Propranolol possesses considerable antidysrhythmic activity and will rapidly revert ouabain-induced tachycardia in dogs and cats to sinus rhythm (Howe and Shanks, 1966). Howitt was able to control various dysrhythmias in 59 patients (Howitt, Husaini, Rowlands, Logan, Shanks, and Evans, 1968) and reported that 5–20 mg. of dextro-propranolol given intravenously was as effective as the racemic drug in treating ventricular and supraventricular ectopic beats. In six of his patients the dextro-isomer terminated digitalis-induced dysrhythmias. It seems possible that dextro-propranolol might be indicated in preference to the racemic drug in patients following cardiac infarction. This report concerns the haemodynamic effects of D-propranolol in 13 patients with recent cardiac infarction.

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MATERIAL AND METHODS

All patients were admitted to the coronary care unit of the National Heart Hospital and were being monitored both electrocardiographically and haemodynamically. There were 10 men and three women, with ages ranging from 35 to 65 years. Cardiac infarction was diagnosed with a typical history of pain supported by elevation of serum enzymes (SGOT and/or LDH) and characteristic ST–T changes in the cardiogram. All patients were studied within 24 hours of the onset of pain.

Aortic and pulmonary artery pressures were recorded via fine catheters introduced percutaneously, and cardiac output was measured by a dye dilution technique using cardiogreen dye and a Gilford cuvette, as in previous reports from this department (Balcon, Hoy, and Sowton, 1968). The zero level for pressures was the mid chest with the patient supine.

Following control readings 20–25 mg. D-propranolol was injected via the pulmonary artery catheter, and measurements were repeated at intervals of 15 and 30 minutes. Statistical analysis was by Student's 't' test.

RESULTS

There was no significant change in heart rate, systemic pressure, pulmonary artery pressure, peripheral resistance, stroke volume, stroke work, left ventricular work or Tension Time Index (TTI) during the 30 minutes after administration of the drug.

The cardiac output fell in seven patients, the maximal effect occurring at 15 minutes. The mean change for the whole group was 0·8 l./min., and this was not statistically significant ($0{\cdot}10>P>0{\cdot}05$). An overall reduction was still present at 30 minutes. In association with the changes in cardiac output, stroke volume and left ventricular work were also reduced, but the changes were not signi-

TABLE

MEAN RESULTS FOR THE 13 PATIENTS

Time (min.)	Heart Rate (beats/min.)	Pulmonary Artery Pressure (mm. Hg)	Aortic Blood Pressure (mm. Hg)	Systolic Ejection Time (sec.)	Tension Time Index (mm. Hg sec./min.)	Cardiac Output (l./min.)	Cardiac Work (kg.m/min.)	Stroke Work (g.m.)	Total Peripheral Resistance (units)	Stroke Volume (ml.)	Systolic Ejection Pressure (mm. Hg)
Control	81	11·8	92	0·26	2,267	4·6	5·8	60·0	21·6	58·3	109
15	76 0·4>P>0·3	11·8 P>0·9	93 P>0·9	0·26 P>0·9	2,190 P>0·9	3·8 0·10>P>0·05	3·8 0·3>P>0·2	52·0 0·4>P>0·3	26·3 0·3>P>0·2	50·9 0·3>P>0·2	109 P>0·9
30	76	14	91	0·26	2,185	4·0	5·5	54·0	25·4	54·9	108

ficant. Peripheral resistance increased, reaching a maximum at 15 minutes after the administration of D-propranolol, but this change was also not significant. Systolic ejection time increased slightly immediately following the injection but returned to control levels after 15 minutes. The mean results for the whole group are shown in the Table. In two patients measurements were continued until all readings had returned to control values. This occurred in both cases by 60 minutes (Figure).

There were no side-effects noted during this investigation.

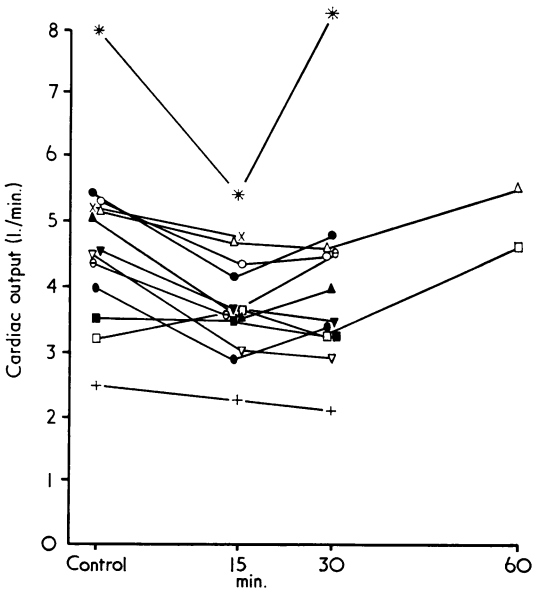

FIGURE. *Individual cardiac output measurements in* 13 *patients before (control) and at* 15–30 *min. following intravenous injection of* 20–25 *mg. dextro-propranolol. In two patients the values after one hour are also shown. The mean levels for the whole group* 15–30 *min. after the drug are not statistically significantly different from the control, but individual patients show considerable falls.*

DISCUSSION

The doses of D-propranolol administered were far larger than would have been safe had the racemic mixture been used. Yet the depression of cardiac function was not great and cardiac output was the only variable to show an appreciable change. A similar reduction in cardiac output following dextro-propranolol has been observed in other centres (Julian, 1969). The other criteria of cardiac function showed no significant change either in our own or in other investigations. These results suggest that most of the depression of function produced by the racemic mixture is due to the beta-blockade produced by the laevo isomer. Although both isomers of propranolol have direct depressant action on the myocardium in animals, these are not prominent at dose levels equivalent to those used clinically (Barrett, 1969).

Dextro-propranolol produces a transient reduction in coronary vascular resistance followed by an increase to above control levels when injected into the coronary arteries of dogs (Whitsitt and Lucchesi, 1967), and this effect has been attributed to a non-specific action of the drug, unrelated to adrenergic receptor blockade. This effect is shared by DL-propranolol and does not influence a clinical choice between the drugs.

It still remains to be shown that D-propranolol is a useful antidysrhythmic drug following cardiac infarction in man. In view of its effects in controlling dysrhythmias in animals and patients undergoing anaesthesia (Howitt *et al.*, 1968), it seems possible that this isomer will prove as effective as the DL mixture and certainly justifies further clinical trial. We gave it in larger doses and with less myocardial depression than racemic propranolol to 13 patients with recent myocardial infarction.

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