Further studies of larger numbers of patients should look at the trends that were found for those who suppressed normally to have more adverse childhood experiences and more obsessional personality features, and for the non-suppressors to have a greater number of past episodes of affective illnesses in themselves and their families. In addition, in our own clinical practice more of the non-suppressors are given E.C.T.

We are grateful to Dr. R. M. Mowbray, reader in medical psychology, for his advice on the statistical methods used.

REFERENCES

- Bunney, W. E., Fawcett, J. A., Davis, J. M., and Gifford, S. (1969). *Archives of General Psychiatry*, **21**, 138.
 Butler, P. W. P., and Besser, G. M. (1968). *Lancet*, **1**, 1234.
 Carroll, B. J. (1969). *British Medical Journal*, **3**, 27.
 Carroll, B. J., Martin, F. I. R., and Davies, B. (1968). *British Medical Journal*, **3**, 285.
 Davies, B. M. (1969). *Medical Journal of Australia*, **1**, 487, 557.
 Hamilton, M. (1960). *Journal of Neurology, Neurosurgery and Psychiatry*, **23**, 56.
 McLeod, W. R., Carroll, B. J., and Davies, B. (1969). Unpublished observations.
 Mattingly, D. (1962). *Journal of Clinical Pathology*, **15**, 373.
 Taylor, J. A. (1953). *Journal of Abnormal and Social Psychology*, **48**, 285.

Clinical Experience with Dextro-Alprenolol

J. K. VOHRA,* M.D., M.R.C.P. ; P. L. THOMPSON,† M.R.A.C.P. ; J. G. SLOMAN,‡ F.R.C.P.ED., F.R.A.C.P.

British Medical Journal, 1970, **1**, 791-792

Summary: Experience with dextro-alprenolol in nine patients has shown that it is relatively ineffective in treating arrhythmias associated with acute myocardial infarction. Marginal effectiveness in the control of ventricular ectopic beats after myocardial infarction is outweighed by an appreciable hypotensive effect with risk of infarction. The drug was ineffective in the management of supraventricular arrhythmias.

Introduction

Beta-adrenergic receptor blocking drugs have been used successfully in the control of supraventricular and ventricular arrhythmias after myocardial infarction, in digitalis intoxication, and during anaesthesia (Sloman and Stannard, 1967; Epstein and Braunwald, 1966; Vohra *et al.*, 1970). This group of drugs, in addition to beta-adrenergic receptor blockade, have a direct effect on the myocardial cell membrane, termed "quinidine-like" activity (Sekiya and Vaughan Williams, 1964). This concept is supported by the demonstration that the two properties may reside in different stereo isomers of pronethalol, propranolol, and alprenolol (Johnsson *et al.*, 1966).

The dextro isomer of alprenolol (Dextro H 56/28, D-alprenolol, D-Aptin, Astra Pharmaceuticals (Aust.) Pty. Ltd.) was reported to be as effective as the racemate in control of ouabain-induced ventricular arrhythmias (Duce *et al.*, 1967; Lord *et al.*, 1968) but has only minor beta-blocking activity. Linko *et al.*, (1968) used dextro-alprenolol in 14 patients with a variety of acute arrhythmias and found that, in a dose of 5 to 20 mg. intravenously, it had no effect on the arrhythmias and no side-effects were observed. In order to evaluate this drug we have used it to treat arrhythmias arising in patients while in the coronary care unit.

Patients and Methods

Details of nine patients aged 37 to 71 years admitted to the coronary care unit for treatment are given in Table I. Eight

TABLE I.—Details of Cases

Case No.	Age	Dose	Arrhythmia	Systolic Blood Pressure change (mm.)	Effect on Arrhythmia
1	71	10 mg. I.V. bolus	Atrial flutter with variable block, ventricular rate 105/min.	140 to 118	Nil
2	37	10 mg. I.V. bolus	Atrial flutter with 2:1 block	85 to 75	Increased carotid sinus sensitivity
3	71	20 mg. I.V. bolus	Supraventricular tachycardia	100 to 70	Nil
4	38	20 mg. I.V. bolus	Supraventricular tachycardia	80 to 70	No immediate effect on arrhythmia. Collapsed after propanidol. Slow nodal rhythm
5	57	25 mg. I.V. bolus	Ventricular ectopics bigeminy	140 to 110	Nil. Arrhythmia controlled with lignocaine
6	42	25 mg. I.V. bolus and 200 mg. infusion over 12 hours	Ventricular ectopics bigeminy	140 to 100	Ventricular ectopics abolished. S-T segment raised with pain
7	50	300 mg. I.V. infusion over 12 hours	Ventricular ectopics bigeminy	100 to 70	Ectopics abolished. S-T segment raised
8	47	25 mg. I.V. bolus, then 10 mg. I.V. 2-hourly	Ventricular ectopics 1 in 8 beats	125 to 100 immediately after 25 I.V. bolus	Ventricular ectopics persisted
9	42	300 mg. I.V. infusion over 12 hours	Slow ventricular tachycardia	105 to 70	Ventricular tachycardia persisted. S-T segment raised

were subsequently shown to have suffered an acute myocardial infarction in the 48 hours before admission and one had viral myocarditis. All these patients were admitted with or developed serious cardiac arrhythmias requiring treatment. Dextro-alprenolol was used as the initial form of therapy and also as an infusion in a dose up to 0.45 mg./minute. The patients were monitored and carefully observed during its administration. In the event of an adverse effect, or when the arrhythmia failed to respond, the patient was treated with other drugs or direct current counter shock.

* Ethnor Research Fellow

† Registrar.

‡ Director, Cardiac Laboratory.
The Royal Melbourne Hospital, Victoria 2050, Australia.

Results

Atrial Flutter (2 cases).—In these two patients (Cases 1 and 2) there was no change in the atrial rate and no increase in the degree of atrioventricular block. The arrhythmia was subsequently reverted to sinus rhythm with direct current counter shock.

Supraventricular Tachycardia (2 Cases).—In one patient (Case 3) with supraventricular tachycardia complicating myocardial infarction there was no significant effect on the arrhythmia, but a fall in blood pressure occurred after 20 mg. of dextro-alprenolol. The second patient (Case 4) had a supraventricular tachycardia complicating acute viral myocarditis. After 20 mg. of dextro-alprenolol by the intravenous route there was no change in the arrhythmia but a fall in blood pressure from 80 to 70 mm. Hg. Twenty minutes later, during injection of propanidid (Epontol), preparatory to direct current reversion, there was circulatory collapse. The monitoring electrocardiogram then showed a slow nodal rhythm, and D.C. counter shock was not given. Prolonged energetic cardiopulmonary resuscitation with external massage, controlled ventilation, and the drugs atropine sulphate, isoprenaline, and hydrocortisone were required to support the circulation. Bronchospasm occurred during the period of collapse, but with the administration of isoprenaline and hydrocortisone gradual recovery occurred and the patient was discharged after four weeks.

Ventricular Ectopic Beats (4 Cases).—Three patients (Cases 5, 6, and 7) had coupled ventricular ectopics, and in two (Cases 6 and 7) these were abolished by dextro-alprenolol. In the third (Case 5) bigeminy failed to respond to dextro-alprenolol, but was promptly controlled with lignocaine. In the fourth (Case 8) hypotension occurred without control of the ectopics. Two of these patients (Cases 6 and 8) had infusion of the drug over 24 hours, and both developed a fall in blood pressure. The hypotension persisted for several hours after the drug was stopped, and in both a recurrence of chest pain and further electrocardiographic changes suggested an extension of the area of infarction.

Ventricular Tachycardia (1 Case).—One patient (Case 9) with a paroxysm of "slow ventricular tachycardia" was treated with an infusion of dextro-alprenolol (0.45 mg./min.). The blood pressure dropped to 70 mm. Hg and the arrhythmia recurred. After 22 hours the infusion was stopped and the systolic pressure gradually returned to 100 mm. Hg. A raised S-T segment was noted on the electrocardiogram during the period of hypotension produced by dextro-alprenolol.

Discussion

Dextro-alprenolol was found to be ineffective in the treatment of supraventricular arrhythmias. This was also the experience of Linko *et al.* (1968). Though the reduction in the frequency of ventricular ectopic beats might be expected we found the drug only moderately effective, and concomitant

hypotension limited its usefulness. Though there was usually only a moderate fall in blood pressure (10-30 mm. Hg systolic), in four cases (Table II) worsening of the patients' condition could have been due to the hypotensive effect of the drug.

TABLE II

Arrhythmias	No. of Cases	Effect on Arrhythmia	Adverse Effects
Atrial flutter	2	Nil	Fall in blood pressure
Supraventricular tachycardia	2	Nil	Fall in blood pressure
Ventricular ectopics	4	Controlled in two patients	Fall in blood pressure
Slow ventricular tachycardia	1	Nil	Fall in blood pressure

In Case 4 cardiovascular collapse occurred during injection of propanidid 20 minutes after 20 mg. of dextro-alprenolol had been ineffective in controlling the supraventricular tachycardia. Though propanidid may cause a fall in blood pressure, collapse of this severity is at variance with our experience and the work of others (Cole, 1969), and we attribute the collapse to the dextro-alprenolol or to the combination of the two drugs.

The use of dextro-alprenolol by intravenous infusion for the treatment of arrhythmias in patients with acute infarction appears to be contraindicated. The drug caused hypotension when administered by infusion, and this is in accord with the findings of K. Saunamäki and A. Pedersen (personal communication, 1969), who reported hypotension during infusion and used noradrenaline to maintain adequate circulation. This mode of therapy seems inappropriate when treating arrhythmias after myocardial infarction and limits the drug's potential. On the other hand, G. Nyberg (personal communication, 1969) did not report any significant hypotension following a bolus injection of the drug (dosage 0.3 mg./kg.) given to patients with coronary artery disease and angina pectoris.

We wish to thank the physicians of the Royal Melbourne Hospital staff who permitted us to study patients under their care.

Drug supplies of Dextro H 56/28 were made available through the courtesy of Astra Pharmaceuticals (Aust.) Pty. Ltd.

REFERENCES

- Cole, W. H. J. (1969). *New Ethicals*, **10**, 9.
- Duce, B. R., Garberg, L., and Johansson, B. (1967). *Acta Pharmacologica et Toxicologica*, **25**, Suppl. No. 2, p.41.
- Epstein, S. E., and Braunwald, E. (1966). *New England Journal of Medicine*, **275**, 1106.
- Johansson, G., Norrby, A., Solvell, L., and Ablad, B. (1966). *Läkertidningen*, **63**, Suppl. No. 1, p.47.
- Linko, E., Ruosteenoja, R., and Siitonen, L. (1968). *American Heart Journal*, **75**, 139.
- Lord, C. O., Katz, R. L. and Eakins, K. E. (1968). *Anaesthesiology*, **29**, 288.
- Sekiya, A., and Williams, E. M. V. (1964). *British Journal of Pharmacology*, **21**, 473.
- Sloman, G., and Stannard, M. (1967). *British Medical Journal*, **4**, 508.
- Vohra, J. K., Dowling J. T. and Sloman, J. G. (1970). *New Ethicals*, **10**, 49.