Adverse reaction to disopyramide

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

N. R. WEBSTER
M.B., B.Sc.

St James's University Hospital, Leeds LS9 7TF

Summary

A case is reported where the use of i.v. disopyramide for a supraventricular tachycardia resulted in a more serious ventricular dysrhythmia giving hypotension and this probably contributed to the development of a myocardial infarction. Attention is drawn to the possible risk.

Introduction

The use of disopyramide (γ -di-isopropyl-amino- α -phenyl- α -(2-pyridyl) butyramide phosphate) as an anti-dysrhythmic agent is well described (Mokler and Van Arman, 1962; Katz *et al.*, 1963). Given intravenously it is active against both atrial and ventricular dysrhythmias. The drug reduces the rate of membrane depolarization and increases the atrio-ventricular conduction time. It has a negative inotropic effect which is accompanied by a dose-dependent decrease in intracellular calcium (Naylor, 1976).

A case is now reported where the administration of disopyramide resulted in the appearance of a serious ventricular dysrhythmia and possibly precipitated myocardial infarction.

Case report

A 48-year-old woman who had undergone a left adrenalectomy for Cushing's syndrome due to an adenoma of the left adrenal gland, and who was on cortisone acetate replacement therapy, was admitted with a supraventricular tachycardia with a 2 : 1 AV conduction (Fig. 1). She had been noted as having the Lown-Gannong-Levine variant of the Wolff-Parkinson-White syndrome (short PR interval with no delta waves) one year previously (Fig. 2).

Previous attacks of supraventricular tachycardia had terminated spontaneously in the past. Oral disopyramide 100 mg 3 times daily had been prescribed and there had been no recurrence over one year. This therapy had been discontinued one month before admission.

On admission she had no symptoms. Heart rate was 160/min, and BP was 130/95 mmHg. The patient was given 10 mg i.v. of practolol without response. Five hours later 75 mg of disopyramide was given i.v. over 5 min with ECG monitoring. Approximately 5 min from the start of injection the rhythm changed to a multidirectional ventricular

FIG. 1. Supraventricular tachycardia with 2 : 1 atrio-ventricular conduction.

tachycardia (Fig. 3). This was followed by an anoxic tonic convulsion. Blood pressure during this time remained normal. After a further 3-4 min the dysrhythmia reverted to a supraventricular tachycardia, although somewhat slower than previously, but this again changed to ventricular tachycardia. Lignocaine was given intravenously with little effect, followed by mexiletine by i.v. infusion. This had some effect but the rhythm continued to swing between ventricular and supraventricular tachycardia. After some 8 hr the patient reverted to stable sinus rhythm. However, during this period the patient was in cardiogenic shock and remained so for a further 8 hr. She had poor peripheral perfusion and a systolic BP of 60 mmHg. Serum calcium and potassium were both normal throughout. Her BP rose after approximately 18 hr to normal and she progressed to a good recovery despite one further episode

FIG. 2. Lown-Gannong-Levine syndrome.

of supraventricular tachycardia which was terminated successfully by DC countershock. Serum CPK rose to 830 i.u./l 2 days after this episode and WBC count to 14 000. Later ECGs showed no change compared with the one before this episode, the conduction abnormality being only intermittently present.

Discussion

No previous report of a similar occurrence after i.v. disopyramide in the literature had been found until 2 short letters appeared during the preparation of this paper (Harkonen, 1978; Siklos, Chalmers and Evans, 1978). There seems little doubt that the severe rhythm disturbances were precipitated by the drug. Yet the indications for its administration were strong; it had already been effective prophylactically by the oral route, and an atrial tachycardia due to the presence of an accessory bundle may be the one most responsive to treatment (Spurrell, 1976). In this case, it appears paradoxically to have caused an increase in myocardial excitability resulting in a serious dysrhythmia. It seemed probable that

the patient had suffered a myocardial infarction as a consequence of the fall in coronary perfusion as a result of the rhythm change; the evidence being the rise in CPKs, a leucocytosis and pyrexia, although there were no ECG changes. As she was stable before the injection, and had in fact been in the supraventricular tachycardia for at least 4 days before admission (she had declined admission previously), it was felt most unlikely that she had infarcted earlier causing the rhythm disturbances.

It was also notable that the dysrhythmias produced, ventricular ectopic beats and ventricular tachycardia, were ones which are most amenable to suppression by disopyramide under normal circumstances (Mizeala and Huvelle, 1976; Jones, 1976). The former authors mention 2 patients who had severe hypotension transiently after injection. One was critically ill, the blood pressure fell and the patient had convulsions although the rhythm reverted immediately to normal. The second patient had atrial flutter and, although the drug decreased the atrial rate, 1 : 1 AV conduction supervened and

FIG. 3. ECG trace in standard lead II after injection, showing the onset of multidirectional ventricular tachycardia with fusion beats, terminating in a slower supraventricular tachycardia with 2 : 1 atrio-ventricular conduction.

the blood pressure fell as a consequence until other measures reduced the ventricular rate.

The hypotension in this patient occurred after the ventricular dysrhythmia began, and so could not have caused it.

In view of the problem experienced with this patient, the authors suggest that i.v. disopyramide should only be used with continuous ECG monitoring and they feel that its use by any route may not be without risk of inducing other serious dysrhythmias. This would preclude its use as a routine antidysrhythmic agent for non-coronary care unit use as has been suggested recently by Zainal *et al.* (1977).

Acknowledgment

We would like to thank Dr E. W. Jackson for permission to report this case.

References

- HARKONEN, M. (1978) Increase of ventricular extrasystoles after disopyramide. (Correspondence), *Lancet*, **i**, 720.
 JONES, M.B.S. (1976) The use of oral disopyramide in the

treatment of symptomatic arrhythmias in ambulatory patients. *Journal of International Medical Research*, **4** (Suppl. 1), 86.

KATZ, M.J., MEYER, C.E., EL-ETR, A. & SLODKI, S.J. (1963) Clinical evaluation of a new anti-arrhythmic agent SC-7031. *Current Therapeutic Research*, **5** (7), 343.

MIZEALA, H.F. & HUVELLE, P.R. (1976) Acute termination of cardiac arrhythmias with i.v. disopyramide. *Journal of International Medical Research*, **4** (Suppl. 1), 82.

MOKLER, C.M. & VAN ARMAN, C.C. (1962) Pharmacology of a new antiarrhythmic agent γ -di-isopropyl-amino- α -phenyl- α -(2-pyridyl)-butyramide phosphate (SC 7031). *Journal of Pharmacology and Experimental Therapeutics*, **136**, 114.

NAYLOR, W.G. (1976) The pharmacology of disopyramide. *Journal of International Medical Research*, **4** (suppl. 1), 8.

SIKLOS, P., CHALMERS, T.M. & EVANS, D.W. (1978) Ventricular tachycardia after disopyramide. (Correspondence), *Lancet*, **i**, 98.

SPURRELL, R.A.J. (1976) The effects of disopyramide on the heart: an electrophysiological study. *Journal of International Medical Research*, **4** (Suppl. 1), 31.

ZAINAL, N., CARMICHAEL, D.J.S., GRIFFITHS, J.W., BESTERMAN, E.M.M., KIDNER, P.H., GILLHAM, A.D. & SUMMERS, G.D. (1977) Oral disopyramide for the prevention of arrhythmias in patients with acute myocardial infarction admitted to open wards. *Lancet*, **ii**, 887.