Propranolol in Paroxysmal Ventricular Tachycardia

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Pronethalol, an adrenergic beta-receptor antagonist, has been used successfully in the treatment of supraventricular and ventricular arrhythmias (Stock and Dale, 1963; Johnstone, 1964). The usefulness of pronethalol has been limited by its carcinogenic activity in mice and its unpleasant side-effects in man. It has been replaced by propranolol (inalder; 1-isopropylamine-3-(1 naphthylloxy)-2-propanol hydrochloride), which has the same beta-sympathetic blocking action but is free from carcinogenic activity in mice and has a much wider therapeutic ratio (Hamer *et al.*, 1964; Chamberlain and Howard, 1964).

I report my experience of the treatment of a patient with recurrent syncope due to paroxysmal ventricular tachycardia, using propranolol.

Case Report

The patient was a man aged 65. For the previous two years he had been subject to recurrent attacks of weakness and faintness associated with paræsthesiæ in the upper limbs. The attacks lasted a few seconds and occurred mainly on exertion but occasionally when sitting. He did not have any attacks when lying in bed. He felt normal immediately after the attacks. There was no history of loss of consciousness or convulsive movements. The attacks recurred frequently, varying between one and six daily. The longest remission between attacks was three days. He was not conscious of the heart's action during the attacks. He had no symptoms suggestive of hyperthyroidism.

On examination he was of average nutrition, not anæmic or cyanotic. There was no thyroid enlargement and no tremor of the hands. Blood pressure was 160/90 mm. Hg and pulse 68 a minute, regular and of normal volume. No cardiac murmurs or extra sounds were audible. Examination of the other systems was unremarkable.

Hb 107 per cent. WBC 5,800/c.mm. Protein bound iodine 7.8 µg./100 ml. Chest radiograph revealed no pulmonary lesion and a normal cardiac silhouette. The serum cholesterol was 225 mg./100 ml.

The electrocardiogram revealed a dominant sinus rhythm. During the recording of a routine 12-lead car-

diogram three episodes of ventricular tachycardia were recorded, lasting 2, 3, and 10 seconds, respectively. The ventricular rate during the paroxysms was 214 a minute. The sinus complexes showed isoelectric S-T segments and T waves of normal polarity. There was no evidence of ischæmic heart disease or ventricular hypertrophy. During the paroxysms the pulse was impalpable. The last episode, which lasted 10 seconds, was accompanied by numbness of the upper limbs.

It was concluded that the bouts of syncope and paræsthesiæ of the upper limbs were caused by paroxysms of ventricular tachycardia.

Treatment with propranolol (inalder) 40 mg. thrice daily was commenced. The patient was examined 2, 4, and 20 weeks after starting therapy. On these examinations the pulse varied between 48 and 56 a minute and the blood pressure between 150/85 and 140/80 mm. Hg. Further cardiograms showed sinus bradycardia and no further episodes of ventricular tachycardia and no ventricular premature beats. He had no further attacks of syncope. One may conclude that propranolol had prevented paroxysms of ventricular tachycardia.

Comment

The beta receptors have predominantly inhibitory functions but have an excitatory effect on the myocardium. Pronethalol, synthesized in 1962, is an adrenergic beta-receptor antagonist, free from intrinsic sympathomimetic activity. Pronethalol, given intravenously to produce complete beta-receptor blockade, has no effect on cholinergic response (Benfey and Grillo, 1963).

Administration of pronethalol to dogs anaesthetized with cyclopropane, trichloroethylene, or halothane was found to decrease conspicuously the sensitivity of the myocardium to epinephrine-induced arrhythmias. From 4-15 times the minimum dose of epinephrine, causing multiple ventricular ectopic beats during the control period, was required to produce this arrhythmia 15 minutes after intravenous pronethalol. Ventricular fibrillation was not observed with even large doses of epinephrine after pronethalol but did not occur during the control

period in 2 of 3 dogs receiving halothane (Murray, McKnight, and Davis, 1963).

Use of pronethalol was discontinued after it was found to be a carcinogen in mice. Propranolol (inderal), a close chemical analogue of pronethalol, has been introduced. Propranolol has no carcinogenic activity in mice and its therapeutic ratio is 10–20 times greater than pronethalol. In animal experiments propranolol has been found to produce bradycardia and a marked antagonism of isoprenaline tachycardia. Intravenous injection produces no change in myocardial tension, but blocks the inotropic effects of stellate ganglion stimulation and isoprenaline.

Stock and Dale (1963) have shown that pronethalol abolishes the arrhythmias due to digitalis intoxication, including paroxysmal atrial tachycardia with block. They also reported good results in the treatment of multifocal ventricular ectopic beats. Suppression of digitalis-induced arrhythmias has also been achieved by propranolol.

In atrial flutter or tachycardia propranolol induces a reduction in the ventricular rate when used alone, and reduces the ventricular rate in the fully digitalized patient.

In atrial fibrillation propranolol causes slowing of the ventricular rate and further slowing in the already digitalized patient (Rowlands, Howitt, and Markham, 1965). The drug is of value with an uncontrolled ventricular rate and obstruction at the mitral valve.

The action of propranolol in repetitive paroxysmal ventricular tachycardia is similar to that of pronethalol (Stock and Dale, 1963). It causes a reduction in the percentage of ectopic beats and in the over-all heart rate, without completely suppressing the ectopic beats.

Propranolol has been used to abolish a large variety of the arrhythmias occurring during anaesthesia (Johnstone, 1964). Prophylactic use of propranolol has been suggested in premedication of patients who have frequent ectopic beats to reduce the risk of ventricular arrhythmias during the subsequent anaesthesia.

Propranolol has been used successfully in persistent ventricular fibrillation. Sloman, Robinson, and

McLean (1965) reported three cases of recurrent episodes of ventricular fibrillation controlled by propranolol given intravenously. In one with acute myocardial infarction this treatment was lifesaving.

Propranolol should not be used in patients with bronchial asthma, as it increases the degree of bronchospasm. In heart failure sympathetic drive is necessary to maintain cardiac function. For this reason propranolol should not be administered to patients with incipient cardiac failure unless they have been digitalized.

Summary

Propranolol, an adrenergic beta-receptor antagonist, has been used successfully to treat a patient with recurrent syncope due to paroxysmal ventricular tachycardia.

Propranolol is of value in the management of cardiac arrhythmias both in the treatment of the acute case and in the prevention of attacks.

I wish to thank the Medical Staff, Pharmaceutical Division, Imperial Chemical Industries Limited, for supplies of propranolol.

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