

BETA BLOCKADE IN SUPRAVENTRICULAR ARRHYTHMIAS

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INTRODUCTION

A number of beta adrenergic receptor blocking agents have been introduced in clinical practice over the last ten years. A vast amount of medical literature reporting their efficacy in the treatment of a variety of arrhythmias has been published during this time. It is not possible to deal with all aspects of their antiarrhythmic actions here and this paper chiefly concerns the use of beta blockade in treatment of supraventricular tachyarrhythmias.

We have used propranolol (Sloman and Stannard, 1967), dextro alprenolol (Vohra *et al*, 1970) and prindolol (Vohra *et al*, 1970) in the management of cardiac arrhythmias. However, during the last three years we have tended to use mainly practolol as an anti-arrhythmic agent and most of the patients in the present series were treated with this drug.

Pharmacology of Practolol

Practolol (Eraldin, I.C.I.) is a cardioselective beta adrenergic receptor blocking agent and has 40% of the potency of propranolol (Inderal, I.C.I.) in this respect. It has also a much weaker action than propranolol on peripheral vascular and bronchial musculature. (Barret *et al* 1967, Dunlop and Shanks 1968, MacDonald and McNeil 1968). This drug is reported to possess some intrinsic sympathomimetic activity and has only one-fortieth to one-sixtieth of the "quinidine like" action of propranolol (Sowton *et al* 1968). Practolol has a half life of ten hours (Fitzgerald and Scales, 1968) and is mainly excreted unchanged in the urine.

General Results in Atrial and Nodal Tachycardia

Table No.1 shows results of beta blockade in fifty-six patients with atrial or nodal tachycardias. Eighty per cent of these patients were treated with practolol and the remainder with propranolol. Patients treated suffered from a variety of cardiac conditions and included lone arrhythmias, rheumatic, cardiomyopathic, ischaemic heart disease and post-operative arrhythmias. The arrhythmias due to acute myocardial infarction are considered separately.

Intravenous administration was employed in most instances. Sinus rhythm was restored in 28 patients and in a further 9 there was a reduction in the ventricular rate. These results with practolol are somewhat similar to those reported in excellent review articles by Thielen and Wilson (1968) and Gibson and Sowton (1969). Most of the patients collected by these authors were treated with propranolol. When paroxysmal atrial tachycardia (P.A.T.) is associated with atrioventricular (A-V) block, beta blockade increases the A-V block and reduces the ventricular rate but reversion to sinus rhythm is uncommon (Gibson and Sowton, 1969).

Beta Blockade in Paroxysmal Tachycardias

Patients presenting with sustained or frequently recurring paroxysmal tachycardias often pose a therapeutic problem and may be refractory to standard therapy including digoxin, procainamide or quinidine. While not always effective, beta adrenergic blockers have proved useful in a number of these patients. These patients form a heterogeneous group, approximately 40% suffer from supraventricular tachycardia, some 30% from paroxysmal atrial fibrillation or flutter, 5% from ventricular tachyarrhythmias and in the remainder the exact nature remains undetermined (Luria, 1971).

Precise assessment of antiarrhythmic therapy is often difficult in this group of patients as they suffer from different types of arrhythmias and have variable precipitating factors. Spontaneous remissions and the frequent use of

more than one antiarrhythmic agent further complicate the issue. However, from the various published works beta blockade appears particularly effective in the following instances.

(A) Re-entrant or Reciprocating Tachycardia

Patients with W.P.W. (Wolff-Parkinson-White Syndrome) and frequently recurring episodes of supraventricular tachycardia often suffer from re-entrant or reciprocal tachycardias. Studies by Bigger and Goldreyer (1970) and Gettes and Yoshonis (1970) have shown that frequent paroxysmal tachycardia, even in patients without pre-excitation, is usually due to a reciprocating atrial tachycardia. The latter group found propranolol effective in controlling the arrhythmia in 7 out of 10 such patients. It is suggested that these drugs act by causing an antegrade and/or retrograde block in the additional A-V pathway, thus preventing or terminating reciprocal tachycardias.

(B) Paroxysmal Tachycardias in W.P.W.

Beta blockade is effective in suppression of recurrent tachycardia in most but not all patients with W.P.W. Gibson and Sowton (1969) report successful use of beta blockade in 11 out of 13 patients. Simcha and Bonham-Carter (1971) found propranolol ineffective in six out of nine patients and Gent *et al* (1970) found practolol ineffective in four such patients and suggested that propranolol may be more effective because of its "quinidine like" effect.

There is some controversy regarding the use of digitalis in W.P.W. It has been suggested that digitalis impedes conduction along the normal pathway in W.P.W. but has no action, or may actually facilitate conduction along the aberrant pathway (Schiebler *et al* 1959) and may allow rapid atrial fibrillation.

To elucidate the effect of beta blockade on aberrant pathway in W.P.W. we measured the atrial stimulus (P') to delta wave interval during atrial pacing in six patients. (Table II) There was no prolongation of conduction along the aberrant pathway after either 30 mg. of practolol or 10 mg. of propranolol. The practical implication of this study is that beta blockade, at least, leaves the aberrant pathway unaffected. These drugs may, therefore, be effective in the treatment of reciprocating tachycardias which utilise both the pathways, but unless they act by abolishing the ectopic focus through their "quinidine like" effect, ectopic tachycardias can still occur.

(C) Exercise induced Tachycardia

Another group where beta blockade has been shown to be very effective is the exercise induced paroxysmal tachycardias (Gibson and Sowton, 1969). We found beta blockade effective in 12 out of 13 such patients (Table III).

Supraventricular tachycardias, atrial fibrillation or flutter and even ventricular tachycardias induced on exercise respond well to beta blockade. The effectiveness of beta receptor blockade emphasises the role of sympathetic involvement in this type of arrhythmias.

An exercise test before and after the drug provides a useful simple method of assessing the efficacy of the proposed therapy (Sloman and Stannard, 1967).

(D) Bradycardia-Tachycardia Syndrome

We have employed beta blockade, in conjunction with electrical pacing, in the so-called bradycardia-tachycardia syndrome. Patients with this condition suffer from sinus bradycardia, sino-atrial block and frequent episodes of atrial tachy-arrhythmias. (Easley and Goldstein, 1971).

Fig. 1 shows an electrocardiogram of one such patient. The basic rhythm was sinus bradycardia and sino-atrial block. The patient suffered from frequent episodes of atrial flutter with a variable block and complained of syncope which usually followed spontaneous termination of this arrhythmia.

TABLE I
BETA BLOCKADE IN SUPRAVENTRICULAR ARRHYTHMIAS

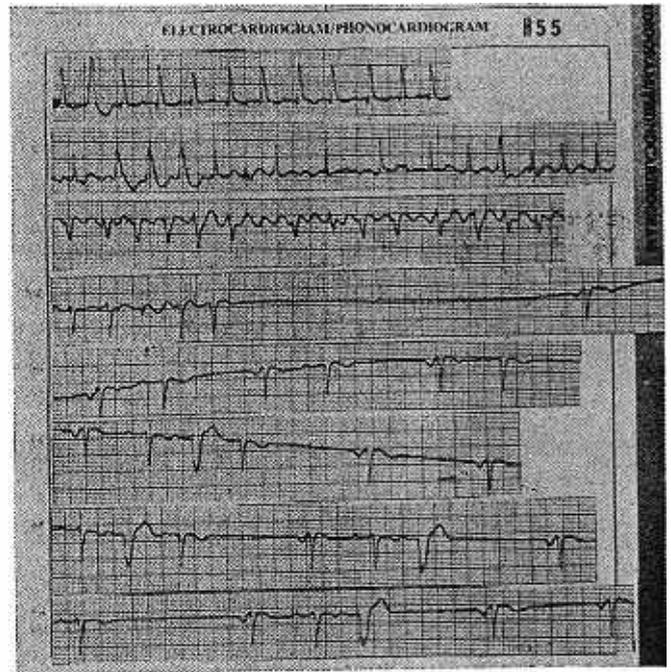
| | Patients | Drug | Sinus Rhythm | Results Slowed | No Effect |
|-------------------------|----------|-------------------|--------------|----------------|-----------|
| Present Series | 56 | Practolol (80%) | 28 (50%) | 9 | 19 |
| Theilen & Wilson (1968) | 56 | Propranolol (80%) | 34 (60%) | 3 | 19 |
| Gibson & Sowton (1969) | 73 | „ | 41 (56%) | 18 | 14 |

TABLE II
BETA BLOCKADE IN WOLFF-PARKINSON-WHITE

| Drug | Patients | P'-Delta Interval |
|--------------------------------|----------|-------------------|
| PRACTOLOL 30 mg. intravenous | 4 | unchanged |
| PROPRANOLOL 10 mg. intravenous | 2 | unchanged |

TABLE III
BETA BLOCKADE IN EXERCISE INDUCED TACHYARRHYTHMIAS

| Arrhythmias | Patients | Results | |
|-------------------------|----------|------------|--------|
| | | Controlled | Failed |
| ATRIAL TACHYCARDIA | 5 | 5 | — |
| ATRIAL FIBRILLATION | 3 | 3 | — |
| VENTRICULAR TACHYCARDIA | 5 | 4 | 1 |
| | 13 | 12 | 1 |



"BRADYCARDIA - TACHYCARDIA SYNDROME"
Fig. 1. Lead AVR shows an asystolic period of four seconds after spontaneous termination of an episode of atrial flutter.

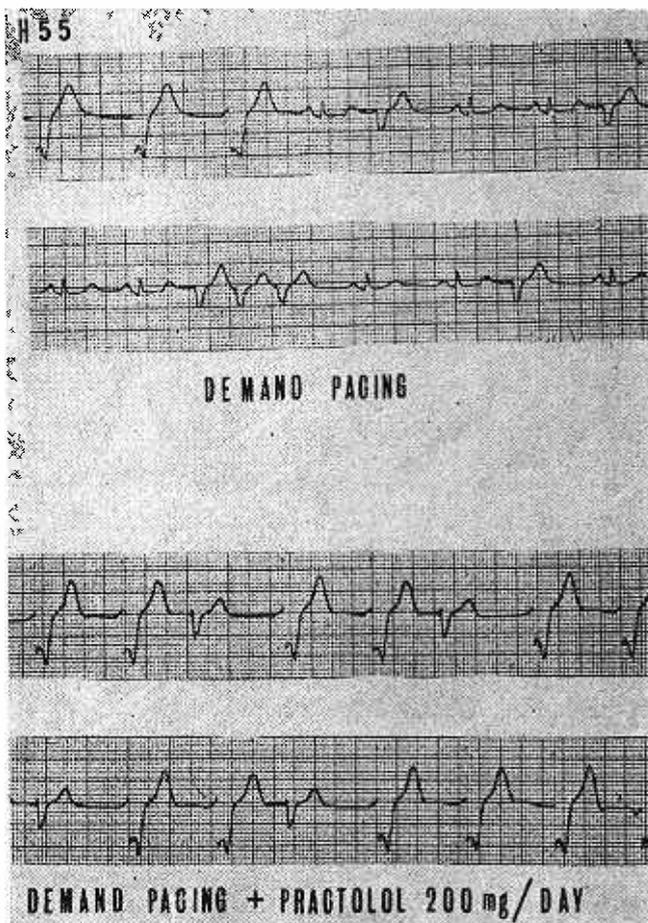
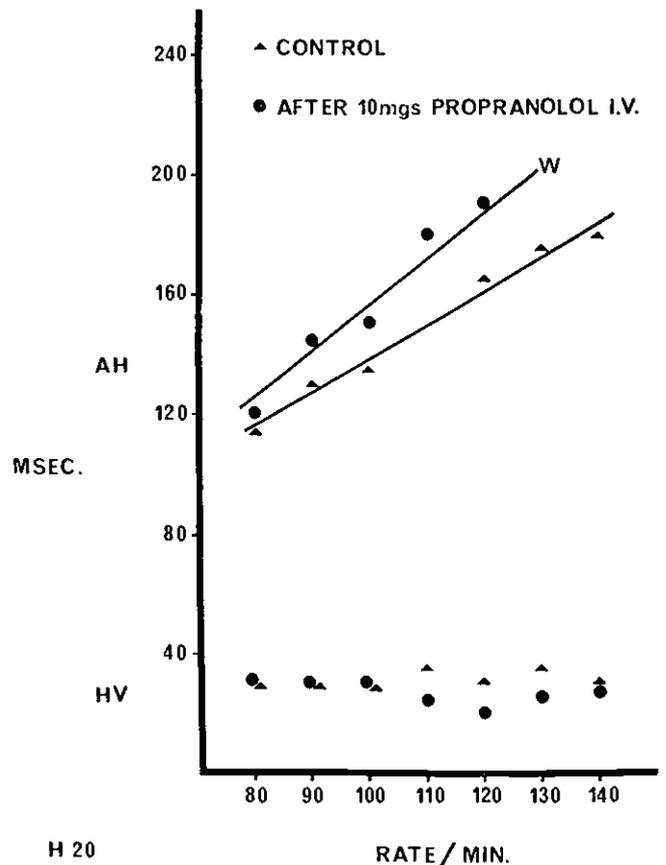


Fig. 2. Ventricular demand pacing abolished the sino-atrial block but the tachyarrhythmia required addition of oral practolol.



THE EFFECT OF PROPRANOLOL ON THE INTRA - CARDIAC CONDUCTION

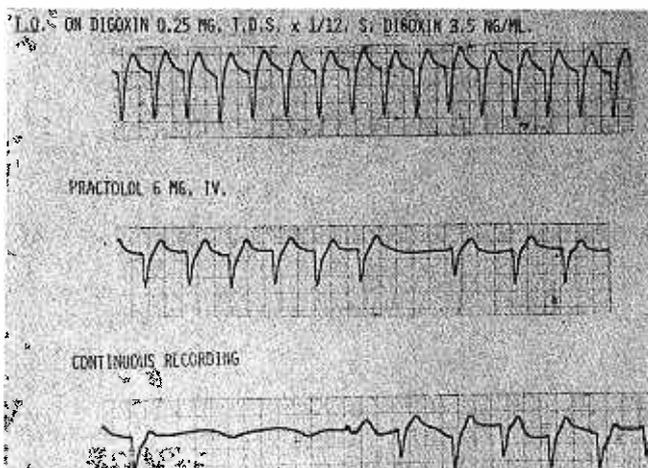
Fig. 3. Effect of propranolol on the atrioventricular conduction assessed by His bundle electrogram. The atrium to His bundle spike interval (A-H interval) shows a linear increase with the increase in heart rate by atrial pacing. After the administration of 10 mg. of propranolol there is a further increase in the A-H interval and a Wenckebach block is produced at a heart rate of 130/min.

TABLE IV
BETA BLOCKADE IN DIGITALIS
UNRESPONSIVE SUPRAVENTRICULAR
TACHYARRHYTHMIAS

| Arrhythmias | Patients | Sinus Rhythm | Results Slowed | No Effect |
|-------------------------------|----------|--------------|----------------|-----------|
| ATRIAL FIBRILLATION | 10 | 1 | 5 | 4 |
| ATRIAL FLUTTER | 13 | 5 | 4 | 4 |
| SUPRAVENTRICULAR TACHYCARDIAS | 13 | 10 | 1 | 2 |
| | 36 | 16 | 10 | 10 |

TABLE V
BETA BLOCKADE IN ACUTE MYOCARDIAL
INFARCTION

| Arrhythmia | Patients | Sinus Rhythm | Results Slowed | No Effect |
|-------------------------------|----------|--------------|----------------|-----------|
| SUPRAVENTRICULAR TACHYCARDIAS | 13 | 8 | — | 5 |
| ATRIAL FIBRILLATION | 9 | 4 | 2 | 3 |
| ATRIAL FLUTTER | 5 | 2 | 2 | 1 |
| TOTAL | 27 | 14 | 4 | 9 |



JUNCTIONAL TACHYCARDIA DUE TO DIGITALIS TOXICITY
Fig. 4. The patient was on 0.75 mg. of digoxin daily for a month. Serum digoxin level was 3.5 Ng./ml. Six mg. of intravenous practolol resulted in a short period of asystole and a temporary reduction in the ventricular rate.

Electrical pacing abolished syncope (Fig. 2) but he continued to complain of palpitations due to atrial flutter which was suppressed by oral practolol. We have treated six such patients successfully with a combination of electrical pacing and practolol.

BETA BLOCKADE IN DIGITALIS UNRESPONSIVE SUPRAVENTRICULAR TACHYARRHYTHMIAS

Inability to control ventricular rate in atrial fibrillation despite the usual therapeutic doses of digitalis is not uncommon. The ventricular rate in atrial fibrillation and atrial flutter is determined by the extent of the A-V block and His bundle recordings have shown that this block is proximal to the His spike (Lau *et al* 1969). Digitalis prolongs the atrioventricular conduction proximal to His bundle (Damato and Lau, 1969) and this probably explains the effectiveness of digitalis in reducing the ventricular rate. In patients where the arrhythmia is of acute onset this reduction in ventricular rate may lead to reversion to sinus rhythm.

Our results with practolol in digitalis unresponsive supraventricular arrhythmias are summarised in Table IV. Only one out of 10 patients with atrial fibrillation reverted to sinus rhythm and reduction in ventricular rate was achieved in five out of 13 patients with atrial flutter and 10 out of 13 patients with supraventricular tachycardias.

Fig. 3 shows effect of propranolol on atrioventricular conduction assessed by His bundle electrogram recording in a normal undigitalised control. The pacing spike to His bundle spike interval (P-H) increased with the increase in heart rate by atrial pacing while the His spike to the onset of QRS (H-V) interval remained unchanged. Following the administration of 10 mg. propranolol intravenously, the increase in the P-H interval following atrial pacing is more marked while the H-V interval remains unchanged.

Propranolol, therefore, prolongs the atrioventricular conduction time proximal to His bundle. Smithen *et al* (1971) reported a 17% increase in the P-H interval following propranolol in doses of 0.02 to 0.05 mg./Kg. but found that practolol did not prolong the P-H interval. We have found similar prolongation of P-H interval with practolol employing higher doses (10 to 40 mg. intravenously). (unpublished)

The effectiveness of beta blockade in digitalis unresponsive supraventricular tachyarrhythmias would, therefore, appear to be a result of further increase in the atrioventricular conduction time proximal to the His bundle.

These results suggest that combination of digoxin and beta adrenergic blockers is often effective in supraventricular tachycardias where either of the drugs are ineffective individually.

BETA BLOCKADE IN DIGITALIS TOXICITY

Digitalis induced ventricular ectopics respond well to beta blockade (Stock, 1966, Szekely *et al*, 1966).

The situation regarding the use of beta blockade in other arrhythmias due to digitalis toxicity is not so clear.

Junctional tachycardia induced by digitalis toxicity is often associated with an A-V dissociation which may not be apparent without an intra-atrial E.C.G. Beta receptor antagonists may depress the junctional pacemaker and in one such patient (Fig. 4) a transient asystole was produced following the administration of 6 mg. practolol intravenously. In a second similar patient 10 mg. of intravenous practolol was ineffective.

Dextro isomers probably deserve a wider trial but diphenylhydantoin would appear to be the drug of choice. Beta blockers, however, may be useful where the dilemma exists between digitalis overdosage and underdosage.

BETA BLOCKADE IN ACUTE MYOCARDIAL INFARCTION

Supraventricular (S.V.) arrhythmias following myocardial infarction are often recurrent and require drug therapy for adequate control.

In 27 patients with supraventricular arrhythmias (Table V) treated with practolol in doses up to 20 mg. intravenously, reversion to sinus rhythm was achieved in 14 and reduction in the ventricular rate in another 4 patients. Although slight fall in systolic pressure (up to 20 mm.Hg.) occurred in two patients in whom the drug was ineffective in reverting the arrhythmia, no significant adverse reaction occurred in any of these 27 patients.

Alone, or in combination with digoxin, practolol is successful in the majority of patients with S.V. tachyarrhythmias following myocardial infarction and we believe that its introduction has provided a useful drug for use in the Coronary Care Unit.

Haemodynamic investigations by Jewitt *et al* (1971) have shown that at lower dose level (5 mg.) practolol administered intravenously to patients with acute myocardial infarction causes no fall in the cardiac output and even with 25 mg. the reduction in cardiac output is modest compared to 5 mg. of propranolol.

BETA BLOCKADE IN POST-OPERATIVE PATIENTS

Supraventricular arrhythmias in post-operative patients deserve a special mention. Digitalis requirements are difficult to assess in this situation as the renal function, electro-

lyte and acid base balance are often impaired. We have been impressed by the fact that often 2.5 to 5 mg. of practolol are effective in the treatment of these arrhythmias.

BETA BLOCKADE IN SINUS TACHYCARDIA

In certain clinical situations the ability of beta blockers to reduce the sinus rate may be utilised with advantage. Hyperkinetic heart syndrome is a recognised clinical entity under various names for many years. Gorlin's (1962) work has defined the haemodynamic alterations which can best be summarised as a hyperbeta-adrenergic state.

We have treated seven such patients and in five oral practolol (200 to 300 mg./day) was effective in abolishing palpitations and improving the effort tolerance.

Rate reduction either at rest or on exercise may also be useful in other conditions, such as muscular subaortic stenosis, thyrotoxicosis and phaeochromocytoma (Warkentin and Cunningham, 1968).

SIDE EFFECTS

Various side effects both major and minor are well known and need no reiteration. Practolol has fewer side effects than propranolol but we have had occasional instances of side effects with small intravenous doses and once even with an oral dosage. Same care and caution is necessary with the use of practolol as with other drugs. Bronchial asthma, however, is not necessarily a contraindication of treatment with practolol, particularly when bronchodilator therapy is administered concurrently.

SUMMARY

Beta receptor blockade has provided a valuable means of treating a variety of tachyarrhythmias. These drugs are particularly successful in exercise induced tachycardia and reciprocal or re-entrant arrhythmias. They are successful when combined with electrical pacing in the treatment of bradycardia-tachycardia syndrome. Practolol has proved to be safe and effective in arrhythmias due to acute myocardial infarction and in the post-operative stage.

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