Use of propranolol in atrial flutter

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Seven consecutive patients with atrial flutter are described, in six of whom sinus rhythm was restored by a combination of digoxin and propranolol. It is suggested that propranolol, used in this way, is a valuable addition to the available measures for the control of this arrhythmia.

Atrial flutter is a notoriously difficult arrhythmia to control by pharmacological means. It is a rhythm in which alterations in degree of atrioventricular block may produce wild fluctuations in ventricular rate. At the same time, it may be regarded as unstable in nature, being intermediate between sinus rhythm and atrial fibrillation, and capable of being transformed, either by therapeutic measures or spontaneously, into one or other of these relatively stable rhythms.

It is generally accepted that atrial flutter, with these inherent potentially lethal properties, is less desirable than either controlled atrial fibrillation, or the ideal, sinus rhythm, and various measures have been proposed to convert it to one or other of these.

The traditional drugs for this purpose are digitalis and quinidine, either alone or together. Classically, digitalis converts the rhythm to atrial fibrillation, after which, quinidine restores sinus rhythm.

Most observers, while accepting that this course can occur, are disappointed by its rarity. In fact three possible outcomes are more commonly met. First, digoxin may, by itself, restore sinus rhythm. Secondly, it may produce atrial fibrillation which does not convert to sinus rhythm with sub-toxic doses of quinidine. Thirdly, atrial flutter may be persistent, and fail to respond to drug treatment except by ventricular slowing.

In contrast to this unpredictable and refractory behaviour when challenged by drugs, atrial flutter responds gratifyingly easily to direct current (DC) countershock, so that in centres where this facility is available, it is the treatment of choice. There are, however, still many situations in which DC countershock is not available. Even where it is available, however, it may happen that atrial flutter has been unrecognized and treated as atrial fibrillation, or recognized and a preliminary trial of digoxin given. In this situation, DC shock may be dangerous unless digoxin is discontinued for a period of days, a delay that may be undesirable.

It is in these contexts that an alternative pharmacological approach to atrial flutter would be desirable. The obvious drug for trial is the β-adrenergic blocking agent, propranolol.

Reports of its use, however, have been uniformly disappointing. The manufacturers (Imperial Chemical Industries Ltd.) in their 1965 manual, quote complete control (i.e. restoration of sinus rhythm) in only one of six cases. Their later manual (December 1967) does not mention this arrhythmia.

We have now treated seven successive patients with atrial flutter, in six of whom a combination of digoxin and propranolol has been followed by restoration and maintenance of sinus rhythm.

Case reports

Case I A man of 54 years had sustained a myocardial infarction three years previously, followed by persistent angina pectoris. Hospital admission followed a further antero-septal myocardial infarction. He was moderately hypotensive and in early congestive cardiac failure for which digoxin was administered. On the ninth day, while receiving digoxin 0·25 mg. twice daily, he was noted to have atrial flutter with an atrial rate of 300 per minute and 2:1 AV block. Carotid sinus massage produced no significant slowing. Propranolol, 3 mg., was given intravenously without apparent effect, but when carotid massage was repeated, sinus rhythm was restored. Oral propranolol, 10 mg. 8-hourly, along with digoxin, was continued until four days later, when it was withdrawn because of mild hypotension. Sinus rhythm remained unaltered over the next month, when he was discharged from hospital.

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Case 2  A 58-year-old window-cleaner gave a three-month history of angina pectoris, and a two-week history of what he termed 'bronchitis'. Before admission, he had had some kind of epileptiform seizure. He had been digitalized for 'tachycardia' before admission.

In hospital he was found to be in left ventricular failure with a pulse rate of 150 a minute. An electrocardiogram initially was thought to show sinus tachycardia, but on closer scrutiny it was found to portray atrial flutter, with 2:1 block and partial concealment of alternate 'f' waves.

Digoxin was continued without benefit for two more days, after which propranolol, 3 mg., was given intravenously, with slowing of the ventricular rate from 160 (irregular) to 130 (regular) a minute. Oral propranolol, 10 mg. 6-hourly, was given without further benefit over the next 24 hours, and then increased to 15 mg. 6-hourly, after which sinus rhythm appeared the next day. The dose of propranolol was gradually reduced over the next three weeks, and he was discharged in sinus rhythm. Review over six months later revealed no recurrence of the arrhythmia.

Case 3  This man of 58 gave no rheumatic history, but was known to suffer from aortic stenosis and regurgitation and mitral regurgitation, and was known to be in sinus rhythm one month before admission. He was admitted to hospital with an acute transmural anterior myocardial infarction. The electrocardiogram showed a supraventricular tachycardia, probably atrial flutter with variable AV block, for which he was digitalized. Atrial flutter persisted for five days, before propranolol, 2 mg., was given intravenously, after which the ventricular rate slowed from 150 a minute to about 90 a minute, with variably increased AV block. Oral propranolol, 5 mg., was then given, with a further fall in rate to 75 a minute, with a stable block. After this the oral dose was increased to 10 mg. 8-hourly, with restoration of sinus rhythm 36 hours later (Fig. 1).

Digoxin and propranolol were withdrawn 8 days later, and after a further week of sinus rhythm, atrial flutter recurred, only to be abolished by a single oral dose of 10 mg. propranolol. Quinidine prophylaxis thereafter maintained sinus rhythm, and on review 6 months later there had been no recurrence of arrhythmia.

Case 4  A 52-year-old warehouseman gave a three-week history of breathlessness on trivial exertion. He was seen in his home, and found to have a supraventricular tachycardia which responded to carotid sinus massage by slowing abruptly. He was digitalized at home without satisfactory result, and then admitted to hospital where treatment with digoxin was continued. On admission the electrocardiogram showed anterior myocardial infarction and atrial flutter. Two days later, it was atrial fibrillation, and three days afterwards, it changed to sinus. After 12 days of sinus rhythm, atrial flutter reappeared. Propranolol, 1 mg. intravenously, produced slowing of the ventricular rate to 80 a minute. Thereafter an oral dose of 5 mg., followed by 10 mg. eight-hourly, resulted in restoration of sinus rhythm the following day (Fig. 2). Apart from a transient episode of atrial flutter two days later, which settled without change in treatment, sinus rhythm was maintained, and was still present at review four months later, propranolol and digoxin having been continued throughout.

Case 5  This man of 43 had suffered from Friedreich's ataxia for many years. For at least three years he had been known to have what was variously reported as atrial flutter or coarse atrial fibrillation. At various times he had received digoxin, potassium chloride, and propranolol, and some months before admission he had had an episode of congestive cardiac failure which had responded well to treatment.

He was seen as an outpatient where he was found to have atrial flutter with impure ventricular response, the atrial rate being 330 a minute, the ventricle beating at 160 a minute. After admission he was digitalized with little immediate effect on the heart rate, but with conspicuous increase in sensitivity to carotid massage. A 5 mg. dose of propranolol was given orally without significant effect. This was followed by 10 mg. eight-hourly. The following day regular 4:1 block had developed with a ventricular rate of 80 a minute. The next day saw the appearance of sinus rhythm (Fig. 3). This remained unaltered on a regimen of digoxin and propranolol. Three months later, propranolol was withdrawn. After a further two months he was found to have developed atrial flutter once more. This again responded to combined digoxin and propranolol, and has not recurred.

Case 6  This man of 69 gave a three-month history of palpitation and chest pain, and was
admitted to hospital in mild congestive cardiac failure. Six years previously he had experienced pain in the arm, relieved by glyceryl trinitrate, and attributed to myocardial ischaemia. After admission he was digitalized before a regular cardiac rhythm was identified as atrial flutter with 3:1 block. After one week of digoxin, oral propranolol (10 mg. thrice daily) was added to the regimen, and after 48 hours he was found to have returned to sinus rhythm. Propranolol was then stopped, and sinus rhythm persisted. At review one month later, there had been no recurrence of atrial flutter.

Case 7 A man of 56 years was admitted to a surgical ward because of swelling of ankles and abdomen, with hepatomegaly. He was found to have congestive cardiac failure with tachycardia, and was digitalized. The electrocardiogram showed atrial flutter. Two days later, atrial flutter persisted with stable 4:1 block. Intravenous propranolol (3 mg.) produced no change, after which oral propranolol, 5 mg., then 10 mg. eight-hourly, had no effect over the next two days. The dose of propranolol was raised to 20 mg. eight-hourly for the next two days, by which time the cardiac rhythm was atrial fibrillation with a ventricular rate of 64 a minute. Both propranolol and digoxin were withdrawn, but six hours later, nodal bradycardia supervened which did not respond to a total of 3 mg. atropine, and which persisted for six hours before giving way to sinus rhythm.

On the following day he developed a left-sided hemiparesis which seemed likely to be due to cerebral embolism, and which improved spontaneously. Two further episodes of atrial flutter occurred during the next 10 days, both subsiding spontaneously. He developed bronchopneumonia and progressively deteriorated, dying on the 26th day after admission.

Discussion

These cases have been presented in detail because all but one follow an almost identical pattern of behaviour in the presence of propranolol. In each case the immediate effect was enhanced sensitivity to vagal stimulation and increase in atrioventricular block. In Case 1, carotid massage restored sinus rhythm at this stage. In all the others, however, the conversion to sinus rhythm occurred after an interval of 12 to 48 hours.

Had this sequence of events been noted on only one occasion, the association between propranolol administration and restoration of normal rhythm could well be disputed. Its occurrence in the identical fashion on five successive occasions appears reasonable evidence that there is a causal relation between treatment and outcome.

It is well recognized that the effects of propranolol are a mixture of β-adrenergic blockade and 'quinidine-like' action, much of the anti-arrhythmic potential being attributable to the latter effect. It is also clear that these effects are not equally related to the dosage of the drug, the anti-arrhythmic dose, for example, may be homeopathic in comparison with the anti-anginal dose. It appears from these reports that there is, in addition, a different time factor involved, in that the β-adrenergic blocking, or vagus-potentiating, effect appears immediately, manifesting itself as increased atrioventricular block, whereas the quinidine-like effect on ectopic atrial activity, to which we attribute the restoration of sinus rhythm, takes many hours to be manifest. Whether this is due to delay in action,
or to cumulative effect, is, of course, not apparent in this series, nor did we try the effect of using larger doses of propranolol to see if they might be more rapidly effective. We are wary of the use of large doses of propranolol in the presence of digoxin (Watt, 1968).

It is apparent that most authors have regarded conversion of atrial flutter to sinus rhythm with propranolol as an exceptional occurrence. It is also clear that in almost all of the successful occurrences, propranolol has been used in combination with other anti-arrhythmic agents, usually digitalis (Table).

Rowlands, Howitt, and Markman (1965) comment that in none of their cases did propranolol influence the atrial rate in atrial flutter though the ventricular rate was slowed. This, however, was a study of response to a single dose of propranolol. Harrison, Griffin, and Fiene (1965) restored sinus rhythm in one patient of 5 years with atrial flutter. This patient was already digitalized. Cherchi et al. (1966) showed increased AV block, but no correction of the arrhythmia in a group of patients treated both orally and intravenously. Nielsen and Jørgensen (1966) restored sinus rhythm in one patient after a week of combined digitalis and propranolol. Likewise, Luria, Adelson, and Miller (1966) report one patient with paroxysmal flutter in whom treatment with digitalis and propranolol restored sinus rhythm.

Gianelly, Griffin, and Harrison (1967) converted atrial flutter to sinus rhythm in one out of seven patients. Wolfson and his colleagues (1967) restored sinus rhythm in one patient with post-operative flutter by combined digitalis and propranolol.

McLean, Stoughton, and Kagey (1967) succeeded only in reducing the ventricular rate in two patients with atrial flutter. Irons, Ginn, and Orgain (1967) had no conversions to sinus rhythm among six patients with flutter treated with propranolol, though three showed ventricular slowing.

Reynolds and VanderArk (1967) describe successful treatment of two patients with paroxysmal atrial flutter with a combination of quinidine and propranolol.

Sloman and Stannard (1967) record one success with propranolol where digoxin failed to control atrial flutter.

We believe that, in combination with digoxin, propranolol is an effective drug in the management of atrial flutter, both chronic and paroxysmal.

It lacks the speed and effectiveness of direct current countershock which must remain the most satisfactory procedure in atrial flutter. Where, however, this facility is not available, or where circumstances render its use undesirable, we feel that pre-treatment with digitalis followed by propranolol conversion may well be the treatment of choice.

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References


### TABLE Effect of combined therapy with propranolol on response of atrial flutter

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