Sinoatrial block

Autonomic influences and clinical assessment

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Seventeen patients with sinoatrial block and 16 healthy volunteers were investigated with recently developed autonomic tests of atrial pacemaker function.

Only one patient was found to be entirely normal in comparison with normal subjects, while another patient had supernormal responses. Fifteen patients had reduced responses relative to the controls implying impaired atrial pacemaker function or sinoatrial disease.

It is suggested that while in some cases sinoatrial block may be of physiological origin, it is more often due to sinoatrial disease. The latter group are liable to Adams-Stokes syncope and may have additional atrio-ventricular conduction abnormalities. The possible mechanisms and treatment of sinoatrial block are discussed relative to the autonomic and pacemaker function abnormalities described.

Sinoatrial block is an uncommon dysrhythmia of unknown mechanism, characterized by the omission of P waves in the setting of a basic regular rhythm (Greenwood and Finkelstein, 1964). It is found incidentally in normal asymptomatic subjects and in some having dizzy spells or syncope. It may occur as an isolated dysrhythmia or in association with sinus bradycardia (Easley and Goldstein, 1971), tachycardia (Short, 1954) or, sometimes, with atrioventricular conduction disorders.

A group of patients with sinoatrial block has been investigated using autonomic reflex and pharmacological tests of atrial pacemaker function. The aim of the study has been to define the mechanism of the dysrhythmia and to assess its clinical significance in individual subjects.

Subjects and methods

Sixteen healthy adults volunteered as control subjects after full explanation of the nature of the investigation. The age range of the controls was 21 to 68 years (mean: 44 years).

From 987 symptomatic patients referred to the Pacing Unit of this hospital, 47 were found to have recorded evidence of sinoatrial block using the criteria of Greenwood and Finkelstein (1964). Of these 47, 17 gave their fully informed consent to the investigation. The age range of the patients was 18 to 82 years (mean 60 years).

Patients with fixed-rate pacemakers were excluded.

Received 18 September 1974.

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Those with demand pacemakers were included since their units could be 'switched off' by external means, thus making the underlying rhythm apparent and available for study. For this purpose an external pulse generator was attached to the skin overlying the implanted pacemaker and set to stimulate the skin at a rate greater than the pacemaker takeover rate.

No patient was admitted to the investigation if the sinoatrial block could be related to drug therapy, untreated hypothyroidism, raised intracranial pressure, recent cardiac infarction, or cerebrovascular accident.

A history was obtained from each subject with particular attention to the occurrence and character of syncope. The differentiation of 'vasomotor syncope' from 'Adams-Stokes attacks' can be established from a detailed history or observation and is of great clinical importance. In the vasomotor attack consciousness is lost gradually with dimming of vision, nausea, and subjective feelings of temperature change. The onset of an Adams-Stokes attack is more abrupt though there may be time for the subject to subside into a chair or onto the floor before losing consciousness. The essential feature of the attack is the absence of the pulse, and flushing on recovery is often remembered by the patient as well as observed by witnesses.

All subjects were examined and weighed before investigation. Those with demand pacemakers had their units inhibited by the external pulse generator attached for at least 15 minutes before investigation.

(a) Reflex tests

With a continuous electrocardiographic recording (lead chosen to show largest P waves), all subjects performed

simple reflex manoeuvres designed to stimulate the dominant atrial pacemaker through the autonomic nerve supply. Recording started 10 to 15 seconds before the reflex test and was continued throughout and for 10 seconds after each manoeuvre. Recordings were made with quiet respiration, forced inspiration (with breath held in inspiration for a minimum of 15 seconds), a Valsalva manoeuvre, using a sphygmomanometer blown up to 40 mmHg (5.3 kPa), for a minimum of 15 seconds and continued for as long as possible, right and left carotid sinus pressure continued until maximum response obtained (up to 10 seconds usually), and straight leg raising for 30 seconds. All the tests were performed in the sitting position on a couch or bed. The electrocardiograms obtained were analysed for atrial rate using a standard rate calculating ruler averaging two consecutive PP intervals. The control rate was taken as the average of three estimates. The maximum or minimum rates during and after the manoeuvres were noted and expressed as the rate difference above or below the control rate. Any changes in P wave morphology or changes in rhythm were noted. As far as possible recordings were made only during regular sinus rhythm. Recordings with junctional rhythm or some totally irregular rhythm during either the control or test period were rejected and the manoeuvre repeated.

(b) Drug tests

Following the reflex tests, with the patient supine and at rest, intravenous bolus injections of the following drugs were made through a normal saline infusion into an antecubital vein.

(i) 5 µg isoprenaline per 70 kg body weight (BW) (using a freshly prepared solution in 2 ml vials, 5 mg/ml containing sodium metabisulphate).

(ii) 0.02 mg atropine sulphate per kg BW.

(iii) 0.8 mg prostigmine per 70 kg BW, given 20 minutes following the dose of atropine.

The drugs were given in the order shown and flushed in with not more than 2 ml normal saline. A period of approximately 10 minutes elapsed between the doses of isoprenaline and atropine while the heart rate returned to previous control level. Only one dose of each drug was given.

The doses given were chosen to give an easily measurable response without resulting in undue side effects. The dose of prostigmine was suggested by the work of Fielder *et al.* (1969).

Electrocardiograms were recorded continuously, from 10 seconds before to 1 minute after the dose of isoprenaline. The same procedure was followed for the atropine dose but further electrocardiograms (5 to 10 second strips) were taken every 5 minutes until 20 minutes after the injection. Twenty minutes after the atropine injection the dose of prostigmine was given. After the dose of prostigmine, 10-second recordings were made every minute for 10 minutes.

The electrocardiograms were analysed for atrial rate with a standard rate calculating ruler. The control rates were taken as an average of five estimates during the control period before each dose, only regular sinus rhythm being acceptable during this period. In the case

of both atropine and isoprenaline the atrial rate was analysed with one estimate at every 3-second intervals during the first minute. Further estimates were made at 15-second intervals for a further 2 minutes. Thereafter, in the case of atropine, estimates of atrial rate were made at 5-minute intervals until prostigmine was given. During this analysis changes in rhythm or P wave morphology were noted. During the prostigmine response an average of 5 estimations was made at each minute.

The results were plotted as atrial rate against time in each case. From these graphs two parameters of atrial response were noted. (i) The maximum or minimum rate obtained above or below the mean control rate; and (ii) the maximum rate of rise or fall in atrial rate during the response.

This was estimated from a gradient drawn through the steepest four points on the response curve.

Results

The *clinical features* of the patients are presented in Table 1.

The *electrocardiographic features* are presented in Table 2.

TABLE 1 *Clinical features of 17 patients with sinoatrial block*

Symptoms	No.	Past history	No.
Dizzy spells	8	Cardiac infarction	4
Vasomotor syncope	5	Hypertension	3
Adams-Stokes syncope	7	Diabetes	1
Palpitation	6	Myxoedema	1
Cardiac pain	4	Rheumatic fever	1
		Diphtheria	0

TABLE 2 *Electrocardiographic features in 17 patients with sinoatrial block*

	No.	
Atrial rate < 50/min	3	All with AV nodal rhythm at times
Abnormal P waves	4	
PR > 0.20s	5	(1 with Wenckebach periodicity)
Right bundle-branch block	3	
Left bundle-branch block	0	
T wave: flat/inverted (no bundle-branch block)	4	
ST segments: flat/depressed	4	(2 with angina: 1 previous infarct)
Second degree sinoatrial block	10	
Sinus arrest	10	
Transient nodal rhythm	7	
Nodal escape	8	
Atrial fibrillation	4	(including 2 with ischaemic heart disease)

TABLE 3 Results of reflex and pharmacological tests in sinoatrial block

Investigation	Change in atrial rate relative to control (beats/min)				P t-test
	Controls (N=16) Mean	Range	Sinoatrial block (N=17) Mean	Range	
(A) Reflex tests					
Respiratory arrhythmia	9.2	3, 18	9.1	4, 20	0.2
Forced inspiration	-4.6	-2, +7	-1.9	-1, +15	0.2
Valsalva: (during)	+23.6	+10, +47	+15, 19	+2, +38	<0.05
(after)	-38.9	-19, -78	-20.4	0, -48	<0.02
Right carotid sinus pressure	-22.4	-2, -47	-13.7	0, Sinus arrest	0.1
Left carotid sinus pressure:	-14.7	0, -32	-8.6	0, Sinus arrest	0.1
Straight leg raising	+16.6	+2, +30	+17.7	+2, +45	<0.10
(B) Pharmacological tests					
Isoprenaline (a)	+30.6	+22, +39	+19.4	+5, +53	<0.01
(5 µg/70 kg BW)					
(b)	+1.9	+0.9, +3.0	+0.05	+0.01, 2.0	<0.01
		junctional			
Atropine (a)	+34.8	+14, +53	+28.6	+12, +50	0.10
(0.02 mg/kg BW)					
(b)	+1.97	+0.85, +2.6	+1.4	+0.6, +3.5	0.10
Prostigmine (a)	-25.6	-15, -46	-19.5	-5, -49	0.2
(0.8 mg/70 kg BW)					
(b)	-3.9/min	-3, -5.7	-2.9/min	-0.85, -11.0	0.2
	/min		/min		

(a) Increase in atrial rate (beats/min).

(b) Rate of change of atrial rate in beats min⁻¹ s⁻¹ (unless otherwise stated).

The 16 control subjects were fit and free from cardiovascular abnormalities.

(a) Reflex results

The results are shown in Table 3. The responses by the sinoatrial block patients and the control subjects to forced inspiration and straight leg raising were not distinguishable. However, there was a significant difference in the two groups to the Valsalva manoeuvre, the rate changes being less in the group with sinoatrial block. The responses to carotid pressure were varied and there was a change in rhythm in some of the group with sinoatrial block group but not in the controls.

Right carotid pressure produced diminished responses in 3; 4 had increased responses to right carotid pressure, i.e. 2 developed second degree sinoatrial block and 2 sinus arrest. With left carotid sinus pressure 1 patient developed transient complete heart block: this patient had developed second degree sinoatrial block with right carotid pressure. One patient developed second degree sinoatrial block with left carotid sinus pressure, while one other developed sinus arrest.

(b) Pharmacological tests

The results are shown in Table 3.

(i) Isoprenaline responses In the control subjects the increase above control resting rate was at least 22 beats a minute, but in 9 of the patients with sinoatrial block this increase in rate was not achieved. Similarly the acceleration of rate was less than in controls in 6 of the patients.

Both the increase in rate and the acceleration of rate in response to isoprenaline were reduced in the patients with sinoatrial block compared with the controls ($P < 0.01$).

During the isoprenaline responses junctional rhythm occurred in one patient with change of P wave shape occurring in another. No similar changes were seen in the control subjects though T wave flattening was seen in 2 controls.

(ii) Atropine responses One patient had a diminished rate response while 7 others had a reduced rate of change response. The difference between the controls and those with sinoatrial block, however, was not found to reach a level of statistical significance. Junctional rhythm was seen during the response of 2 patients, and during the response of 1 control subject. Sinoatrial block occurring regularly before atropine was seen to disappear soon after the drug was given to 2 patients.

(iii) Prostigmine responses Compared to the controls 6 patients had a diminished drop in atrial

rate with this drug and 9 patients had a reduced rate of change response. All the patients with a reduced rate response also had reduced rate of change responses. No significant difference could be shown between the group with sinoatrial block and the controls. One patient had a response to prostigmine that was greater than that of any control subject.

Results and clinical features

Only one patient was entirely normal to all tests, with one other responding supernormally. Of the reflex responses only the Valsalva manoeuvre was significantly different from those of the controls. Ten patients had reduced Valsalva responses, with 8 of the 10 having reduced responses to isoprenaline, 5 to prostigmine, and 3 to atropine.

Five patients had either sinoatrial block (2 cases) or sinus arrest (3 cases), in response to carotid sinus pressure. Only one of these patients had a reduced Valsalva response while 2 had reduced responses to prostigmine and one to isoprenaline.

Nine patients had reduced responses to isoprenaline: 5 of them had reduced Valsalva responses, 5 had reduced prostigmine responses, and 4 had reduced atropine responses. Of the 7 patients with Adams-Stokes attacks, 4 had reduced isoprenaline responses.

Of the 7 patients with Adams-Stokes syncope, 2 had very reduced responses to both reflex and drug tests, i.e. the Valsalva manoeuvre, isoprenaline, and prostigmine tests. Three others had reduced responses to one or two of these responses while the remaining 2 had abnormal but borderline responses to the three tests. No patient with Adams-Stokes attacks was found to be entirely normal to testing.

Of the 3 patients with vasomotor syncope only one could be regarded as responding normally to both reflex and pharmacological challenge. Of the 2 patients with pronounced dizzy spells or near syncope, 1 responded supernormally to prostigmine while the other had reduced reflex and isoprenaline responses.

All 5 patients with a prolonged PR interval had reduced reflex and drug responses, as did the 3 patients with right bundle-branch block. Both patients with paroxysmal atrial fibrillation had abnormal responses, while the one patient with low voltage P waves had reduced reflex and drug responses.

Discussion

In a survey from the literature of over 200 cases of sinoatrial block, Greenwood and Finkelstein (1964) found that two-thirds of the patients had some evidence of cardiac pathology or drug toxicity

associated with the arrhythmia. Cardiac ischaemia and previous rheumatic fever were found to be major causes. One-third of the patients were fit young adults thought to be clinically normal. The natural occurrence of sinoatrial block is suggested by the finding of only 5 asymptomatic cases in an electrocardiographic survey of 67 375 American servicemen aged 20 to 24 years (Hiss, Averill, and Lamb, 1960). In the series of 17 patients with sinoatrial block reported here, 6 had evidence of ischaemic heart disease, and 1 of rheumatic valve disease. There was no evidence of heart disease in the other patients though 1 gave a definite history of rheumatic fever and 1 had treated myxoedema.

The mechanism of sinoatrial block has been in question (Scherf, 1969) since it was described by Wenckebach (1907). There is no evidence that true 'block' occurs at the sinoatrial nodal level. On the basis of experimental work (Eyster and Meek, 1917; Scherf, 1946) it seems unlikely that a pathological process could reversibly block the transmission of impulses from the sinoatrial node to atrium. The term sinoatrial 'block' may, therefore, be unjustified, a view supported by the present work which suggests defective atrial pacemaker function in most of the patients. The sinoatrial node in sinoatrial block possibly produces impulses which are regular but at times subthreshold and unable to conduct to the atrium. This mechanism, previously suggested by Resnik (1925), would explain the omission of an exact number of cycles in otherwise regular rhythm – a criterion that has been used to define sinoatrial block (Greenwood and Finkelstein, 1964).

The majority of patients investigated were shown to have defective sinoatrial function suggesting that some pathological process in the atrium was responsible for the dysrhythmia in most cases. The pathological process in the atrium has presumably to be widespread to account for the lack of takeover by surrounding atrial pacemakers. Additional disease of the atrioventricular conducting tissue might account for the lack of atrioventricular nodal takeover and subsequent asystole in some cases. It is possible that diminished pacemaker function in the atrioventricular node and lower sites might be present before conduction defects are apparent with routine electrocardiography.

Although only 1 patient was entirely normal to testing there were 4 with borderline responses – just below normal range to one drug test. Sinoatrial block in some patients may be caused, therefore, by a transient physiological depression of sinoatrial function rather than by significant sinoatrial disease. Since carotid sinus pressure can produce the arrhythmia in some cases a vagal mechanism is possible. Rather than continuous vagal stimulation a

transient or phasic type (Dong and Reitz, 1970) is a possible cause. 'Vagal epilepsy' caused by an unstable cerebral focus is an unproven but possible cause of sinus arrest in some patients.

One case in this series had a response to vagally mediated reflexes and prostigmine in excess of the normal response. This patient may represent a group of patients with a hypersensitivity to normal phasic vagal stimulation.

Some patients in this series were paced up to 15 minutes before investigations. The influence of long-term ventricular pacing on atrial pacemaker function is unknown. Certainly in short-term atrial pacing it is characteristic for atrial rhythm to return within seconds after the cessation of pacing (Mandel *et al.*, 1971).

It is suggested that there are two groups of subjects with sinoatrial block, those that have symptoms due to sinoatrial disease who may also have other evidence of heart disease, and those that are fit and free from other cardiac pathology. Though the majority of patients were shown to have some defect of atrial pacemaker function there were 4 borderline normal patients, 1 entirely normal patient, and another who, in some respects, had greater than normal responses. The lack of evidence of significantly reduced pacemaker function in these patients suggests a transient physiological depression of the atrial pacemakers, possibly vagally mediated, as a cause of their dysrhythmia. Simultaneous vagal stimulation of the atrioventricular node could also explain the absence of atrioventricular nodal take-over.

A clinical value of these investigations is suggested by the fact that 5 of the 7 patients having Adams-Stokes syncope had definitely reduced drug responses, while 2 had borderline responses. Others with reduced responses had either dizzy spells or faint attacks resulting in near syncope. Palpitations occurred in patients who were both normal and abnormal to testing. Angina of effort occurred in 4 patients, all of whom had evidence of reduced atrial pacemaker function. Symptomatic patients with reduced atrial responses to the tests described will

probably require a pacemaker whereas asymptomatic patients with reduced responses alone should be observed closely. Those with normal or borderline responses may need no treatment if asymptomatic. Symptomatic patients with normal responses may respond to drug treatment, but pacing may be required if drug treatment fails. It is suggested that the investigation of atrial pacemaker function as presented is useful in the assessment and further management of patients with sinoatrial block. They have so far been in use in this department for the past 3 years.

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