Effect of lignocaine on conducting system of human heart

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The effects of lignocaine on atrioventricular conduction, particularly in relation to pre-existing disease of the specialized conducting tissues, were studied. Ten patients, 7 of whom had symptomatic coronary heart disease, were selected, and 4 had first-degree His-Purkinje system (HPS) block (HV interval > 55 msec). His bundle electrograms were recorded in each patient: (1) under basic resting conditions (basic tracings), (2) during stressing of the conducting system by atrial pacing at rates from 80 to 150 beats per minute (control tracings), (3) as in (2), but after the administration of 100 mg lignocaine intravenously (lignocaine tracings). The PA interval, representing intra-atrial conduction time, AH interval, representing AV nodal conduction time, HV interval, representing conduction time in the His-Purkinje system, and HS interval, representing total intra-ventricular conduction time, were measured for analysis of the basic tracings, and for comparison of the effects of lignocaine on the series of paced heart rates.

Lignocaine had a variable effect on AV conduction when the conducting tissues were stressed by atrial pacing. The changes due to lignocaine were confined almost exclusively to the AV node with no effect on intra-atrial or His-Purkinje system conduction and only minimal effect on intraventricular conduction. It was found that the AH interval after the administration of lignocaine was shortened at certain paced rates, and in other patients it was lengthened, compared with the control tracings at the same paced rates. The differences were not significant either for the group as a whole or for the AH values at each paced rate. A possible explanation of the variable effect of lignocaine on AV nodal conduction is discussed.

It is concluded that therapeutic doses of lignocaine have no significant effect on the specialized conducting tissues even in the presence of disease of the His-Purkinje system.

Lignocaine is an effective drug in the suppression of abnormal ventricular beats (Grossman *et al.*, 1967; Spracklen *et al.*, 1968). It is now the universally accepted agent of choice for management of ventricular ectopic activity in the early phase of acute myocardial infarction (Lown and Vassaux, 1968; Jewitt, Kishon, and Thomas, 1968). It has been shown that lignocaine in therapeutic doses has insignificant haemodynamic effects (Binnion *et al.*, 1969). However, Lieberman *et al.* (1968) found that it depressed cardiac conduction when given to dogs in high dosage, but few studies of the effect of lignocaine on conduction in the human heart have been reported (Rosen *et al.*, 1970). The purpose of this paper is to provide information about the effects of lignocaine on the specialized conducting fibres and, in particular, since atrioventricular conduction may

be impaired or blocked in myocardial infarction, to ascertain if the drug contributes to heart block, especially when the conducting tissues are diseased.

Methods

Ten patients were studied, 7 men aged between 45 and 70 years, and 3 women aged 50 to 52 years. The procedures to be adopted and the purpose of the study was explained to each patient and consent obtained. A His bundle electrogram was recorded by the method described by Scherlag *et al.* (1969) in which the rapid deflection of depolarization of the bundle of His is picked up by an electrode catheter placed alongside the main bundle as it lies in the right ventricle adjacent to the tricuspid valve. The technique employed has been described in detail by us previously (Bekheit *et al.*, 1971), and it will be summarized only briefly here. A bipolar electrode catheter was introduced into the femoral vein percutaneously and its tip advanced under fluoroscopic control to the inflow tract of the right ventricle. The catheter was attached to an AC input

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TABLE 1 Clinical data and basic His bundle electrogram measurements

No. of patients	Age (yr)	Sex	Weight (kg)	Disease	Basic His bundle electrogram (msec)			
					PA	AH	HV	HS
1	62	Male	70	Coronary heart disease	30	80	50	120
2	50	Female	83	Normal heart	10	90	40	120
3	61	Male	67	Coronary heart disease	15	105	50	120
4	52	Female	65	Coronary heart disease	20	85	65	120
5	65	Male	58	Coronary heart disease	30	65	55	125
6	68	Male	69	Calcific aortic stenosis	25	95	60	130
7	45	Male	78	Recent myocardial infarction	30	110	60	100
8	70	Male	73	Recent myocardial infarction	15	115	80	170
9	52	Male	73	Starr Edwards aortic valve	35	80	40	200
10	50	Female	58	Coronary heart disease	25	120	45	110

PA, internodal atrial conduction time; AH, AV nodal conduction time; HV, His-Purkinje system conduction time; HS, total intraventricular conduction time.

preamplifier (Sanborn No. 350-2700) with a frequency response 15-1500 cycles a second, and manipulated until a rapid deflection (H wave) appeared in each beat on the oscilloscope. The His bundle electrogram was then photographed with a standard limb lead at a paper speed of 100 mm per second. The tracing obtained in this way is referred to as the 'basic tracing' in the

analysis of results. A second electrode catheter was then introduced through a right arm vein and attached to an external pacemaker (Medtronic 5880A). The tip of the catheter was advanced to a pacing position against the wall of the right atrium. The atrium was paced to override the sinus node at rates from 80 to 150 beats a minute. If Wenckebach block occurred no further in-

TABLE 2 His bundle electrogram measurements before and after lignocaine

Case No.		Pacing rate per minute															
		80				90				100				110			
		P ₁ A	AH	HV	HS	P ₁ A	AH	HV	HS	P ₁ A	AH	HV	HS	P ₁ A	AH	HV	HS
		(msec)				(msec)				(msec)				(msec)			
1	C													50	95	50	120
	L													50	95	50	120
2	C									80	90	40	120				
	L									80	100	40	120				
3	C									60	140	40	115	60	160	40	115
	L									60	140	40	115	60	160	40	115
4	C									45	90	65	120	45	120	65	120
	L									45	90	65	120	45	120	65	120
5	C					55	75	50	125	55	80	50	125	55	80	50	125
	L					55	75	50	125	55	80	50	125	55	90	50	125
6	C	45	120	60	155	45	130	60	160	45	150	60	160	45	170	60	160
	L	40	140	60	160	45	150	60	160	45	155	60	160	45	160	60	160
7	C									50	120	60	100	50	140	60	100
	L									50	120	60	100	50	140	60	100
8	C									30	290	80	150				
	L									30	165	80	150				
9	C													70	90	40	200
	L													70	100	40	200
10	C					40	145	45	110	40	155	45	110	40	175	45	110
	L					40	145	45	110	40	165	45	110	40	180	45	110
t test for pooled A-H values		—				0.20 > P > 0.25				0.20 > P > 0.25				0.40 > P > 0.45			

P₁A, inter-atrial conduction time; AH, AV nodal conduction time; HV, His-Purkinje system conduction time; HS, total intraventricular conduction time; C, control measurements; L, measurements after lignocaine.

crease in the paced rate was employed. The His bundle electrogram together with a standard surface lead was recorded at each paced rate. The procedure was then repeated to confirm the constancy of the increments of conduction for each selected paced rate. The His bundle electrograms obtained by this method represent the 'control tracings'. Lignocaine in a dose of 100 mg was then administered intravenously over a period of one minute and the pacing procedure repeated in duplicate at identical rates as in the controls, within a 10-minute interval from the administration of lignocaine. These tracings are referred to in the analysis of results as 'lignocaine tracings'. As in the controls, the measurements of the two sets of lignocaine tracings were identical, thus confirming the stability of the system. The dose of lignocaine used in this study (100 mg i.v.) can be assumed to maintain therapeutic plasma concentrations (1-4 µg/l.) for the weight range of the patients (57-83.4 kg) (Binnion *et al.*, 1969). The lignocaine paced recordings were completed well within the half-life of the drug in the body (Sung and Truant, 1954; Hayes *et al.*, 1967). The following increments of conduction were measured for analysis of the basic tracings and for comparison of the effects of lignocaine on the series of paced heart rates. (1) PA interval, representing intra-atrial conduction time, from the sinus P wave in the basic tracings or the spike of the artificial impulse (P₁) in the

control and lignocaine tracings to the A wave recorded by the His bundle electrode atrial fibres immediately adjacent to the AV node. (2) AH interval, representing atrio-ventricular (AV) nodal conduction time. (3) HV interval representing conduction time in the His-Purkinje system (HPS). (4) HS interval representing total intraventricular conduction time. The normal values of these intervals are shown in Table 1 (Bekheit *et al.*, 1971).

Results

Table 1 summarizes the clinical details of the patients and shows the measurements of conduction in the basic tracings. Seven of the patients had coronary heart disease including 2 with recent myocardial infarction (Cases 1, 3, 4, 5, 7, 8, 10). Case 2 had a normal heart, Case 6 calcific aortic stenosis, and Case 9 a Starr-Edwards aortic valve prosthesis. Cases 6 and 7 were on maintenance digoxin 0.25 mg twice daily, at the time when the His bundle electrogram was recorded.

The measurements of the increments of conduction for the 'control' and 'lignocaine' tracings, at serial paced rates from 80 to 150 beats a minute are shown in Table 2. Each interval was constant at each paced rate over not less than 20 cycles.

120				130				140				150				Pooled AH
P ₁ A	AH	HV	HS	P ₁ A	AH	HV	HS	P ₁ A	AH	HV	HS	P ₁ A	AH	HV	HS	
(msec)				(msec)				(msec)				(msec)				(msec)
				50	100	50	120	50	130	50	125	50	135	50	120	460
				50	100	50	120	50	105	50	125	50	140	50	120	440
80	120	40	120					80	120	40	120					330
80	120	40	120					80	120	40	120					340
60	170	40	115	60	180	40	115					60	190	40	115	840
60	170	40	115	60	180	40	115					60	190	40	115	840
45	120	65	120	45	120	65	120					45	120	65	120	570
45	120	65	120	45	120	65	120					45	120	65	120	570
55	95	50	125	55	100	50	120	55	105	50	120	55	110	50	120	645
55	95	50	125	55	100	50	120	55	105	50	120	55	110	50	120	655
45	180	60	160	45	190	60	160					W				945
45	200	60	160	45	245	60	160									1040
50	160	60	100	50	180	60	100	50	190	60	100	50	195	60	100	985
50	160	60	100	50	160	60	100	50	190	60	100	50	195	60	100	965
W																295
																170
70	100	40	200	70	110	40	200	70	120	40	200	70	125	40	200	545
70	110	40	200	70	110	40	200	70	120	40	200	70	125	40	200	565
40	180	45	110	40	200	45	110	W								855
40	180	45	110	40	160	45	110									830
0.5 > P > 0.10				0.35 > P > 0.4				0.15 > P > 0.20				0.15 > P > 0.20				0.30 > P > 0.35

Intra-atrial conduction

In the 47 instances of paced rate in the 10 patients the P_1A interval in the lignocaine tracings was identical with the control tracings. Lignocaine therefore had no effect on the velocity of atrial conduction between the site of the artificial impulse and the AV node. Further, atrial conduction was not altered by change in the paced rate but the P_1A interval at the paced rates exceeded the PA intervals of the basic tracings (Table 1). The explanation appears to de-

pend on the nonhomogeneous conduction of atrial muscle. Sinus impulses reach the AV node rapidly through preferential pathways (James and Sherf, 1971). When the atrium is artificially paced, on the other hand, impulses may fail to travel preferentially at least by the shortest routes to the AV node, thereby resulting in prolongation of the P_1A interval. Prolonged intra-atrial conduction is therefore a function of pacing and it is not influenced by lignocaine.

FIG. 1 The effect of lignocaine on AV nodal conduction (AH) interval in Case 8. Note the shortening of the AH interval from 290 msec before lignocaine to 165 msec after lignocaine (cf. Fig. 2). (Distance between 2 light divisions equals 40 msec.)

AV nodal conduction

Wenckebach block occurred in Cases 6, 8, and 10, at paced rates 150, 110, and 140, respectively, both in the control and in the lignocaine tracings. There was no evidence therefore that lignocaine was responsible for complete block of impulses in the AV node. However, lignocaine had a variable effect on the AH interval, e.g. in Case 8, at a paced rate of 100 beats a minute the AH interval was shortened from 290 msec in the control to 165 msec after lignocaine, whereas in Case 6, at a paced rate of 130 beats a minute the AH interval was prolonged from 190 msec in the control to 245 msec after lignocaine. These paradoxical effects on the AH interval are illustrated in Fig. 1 and 2. In order to determine the significance of the variation in the AH intervals after lignocaine the serial AH values for each

patient were summated (pooled numbers Table 2). The difference in pooled numbers of the control and lignocaine tracings varied from (+95) to (-125) msec, but for the group as a whole the difference between them was not significant ($P=0.35$). The AH values at each paced rate in the group were then compared and in no instance was the difference significant ($P=0.20$ at rates 140, 150 a minute to $P=0.45$ at 110 beats a minute Table 2). Lignocaine had no significant effect on AV conduction for the group as a whole at the paced rates studied. Fig. 3 illustrates the slight range of variation of AH intervals expressed as a summation of AH values at various paced heart rates.

His-Purkinje system conduction

The HV interval remained fixed at all paced rates

FIG. 2 The effect of lignocaine on AV nodal conduction (AH) interval in Case 6. Note the lengthening of the (AH) interval from 190 msec before lignocaine to 240 msec after lignocaine (cf. Fig. 1). (Distance between 2 light divisions equals 40 msec.)

FIG. 3 The histogram shows the slight range of variation of the pooled values for AV nodal conduction (AH) intervals at paced heart rates ranging between 90 to 150 beats a minute. The number of cases studied at each paced rate is shown between brackets above the columns.

in each patient and its measurements in the control and lignocaine tracings were identical and these in turn were identical with the HV intervals of the basic tracings (Table 1). Lignocaine therefore did not affect the velocity of conduction from the time of initial depolarization of the main bundle of His to the arrival of the impulse at the Purkinje myocardial function either in patients with normal His-Purkinje system conduction in whom the HV interval was initially prolonged (HV > 55 msec in Cases 4, 6, 7, and 8).

Intraventricular conduction

The HS interval was constant at all paced rates in the control and lignocaine tracings. In some cycles, however, it was either slightly longer or shorter after lignocaine (Fig. 1 and 2). It was concluded nevertheless that lignocaine had no significant effect on intraventricular conduction.

Discussion

Of the 10 patients in this study, 9 had organic heart disease; 7 had symptomatic coronary heart disease; 2 of whom were studied within two weeks from the onset of acute myocardial infarction; 2 patients had advanced aortic valve disease. It should be noted that first-degree His-Purkinje system block was associated with coronary heart disease in 4 patients. The results of our observations confirm that lignocaine has a variable effect on atrioventricular conduction when the specialized conducting tissues are

stressed by atrial pacing. Moreover, changes due to lignocaine are confined almost exclusively to the AV node, with minimal effect on intraventricular conduction, and no effect on intra-atrial or HPS conduction, even in the presence of disease of the His-Purkinje system. In no instance was the sinus conduction completely blocked at any site. The effect on the AV node requires particular comment. The reciprocal innervation of the sinus and AV nodes by autonomic nerve endings ensures that the increased rate of discharge of the former is accompanied by increased velocity of conduction in the latter, e.g. the release of vagal tone in the normal heart after exercise. The autonomic response of both nodes may therefore be said to be 'in phase'. Artificial atrial impulses, on the other hand, are independent of autonomic nerve impulses and increasing paced rates reveal decremental conduction as an intrinsic property of AV nodal tissue. Nevertheless, reciprocal innervation of the AV node remains intact during atrial pacing and the slight variation in AV nodal conduction obtained with lignocaine may reflect changes in vagal tone rather than a direct action of the drug on the fibres of the AV node.

The clinical implications of the effects of lignocaine on AV conduction are important. Our results are similar to those of Rosen *et al.* (1970) who showed that therapeutic doses of the drug had no significant effect on AV conduction. Atrioventricular block may occur in the acute phase of myocardial infarction, and it is not clear in the two cases of Gianelly *et al.* (1967) whether the heart block occurred in the natural history of infarction or whether it was related to the administration of lignocaine. In contradistinction to the findings of Nagle and Pilcher (1968) ectopic ventricular rhythms did not occur in any of the 47 paced rates in our series. We suggest, therefore, that lignocaine can be administered with confidence in acute myocardial infarction to suppress ventricular ectopic activity without producing any significant effect on myocardial conduction, and if heart block occurs it is likely to be part of the natural history of infarction and not related to lignocaine in therapeutic doses. Further, when a temporary pacemaker is inserted for the management of heart block, lignocaine can continue to be used to suppress undesirable ventricular arrhythmias without likelihood that the drug will maintain heart block or delay the spontaneous restoration of normal conduction.

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