VAGAL INHIBITION OF HEART IN HYPOXIC DOGS*

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Slowing of heart can be brought about reflexly by the excitation of almost any afferent nerve in the body. The nerve which produces slowing or even arrest of the heart most readily, is the vagus (1). Motor component of this reflex is in the vagus itself. Wylie (5) suggested that reflex inhibition of the heart could be the cause of cardiac arrest during anaesthesia. He emphasised the importance of hypoxia, Co_2 excess, and direct interference with the heart and great vessels as the often underlying cause for setting up this reflex. Since hypoxia is more likely to occur during anaesthesia stimulation of the vagus nerve while such a condition existed could result in a dangerous inhibition of the heart. An endeavour was therefore made to investigate how the efferent vagal fibres affect the heart under varying degrees of hypoxia and then to investigate the probable origin of this vagal effect.

MATERIALS AND METHODS

Experiments were performed on 24 healthy mongrel dogs of both sexes, weighing between 8 and 16 *kg*. They were anaesthetised with pentobarbital sodium, 30 *mg/kg* given intravenously. No premedication was given. They were intubated with cuffed Magill's endotracheal tube. Blood pressure was recorded from the femoral artery. The respiration was recorded by inserting and inflating a soft rubber ballon in between the liver and the diaphragm through a midline epigastric incision.

In 19 dogs heart rate was recorded from a common carotid artery by a Hurthle's membrane manometer. The right vagus nerve was divided in the neck and the peripheral end was secured for stimulation. Six of these 19 dogs breathed room air (series A). The peripheral end of the cut right vagus nerve was stimulated by square wave pulses (6V, 5 m sec, 100/sec.) delivered from a Sigma Electronic stimulator (group A). In 8 dogs after vagotomy progressive hypoxia was instituted by connecting the endotracheal tube with a Collins spirometer containing nine litres of room air and sodalime for absorption of expired carbon dioxide, The peripheral end of the cut right vagus nerve was periodically stimulated (group B). The remaining 5 dogs were atropinised with 0.3 *mg* atropine/*kg* body weight given intravenously in 20 *ml* of normal saline. Absence of any cardiac irregularity on peripheral vagal stimulation was indicative of complete atropinization. These dogs were subjected to hypoxia and vagus stimulation in the same way as above (group C).

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In another 5 dogs (group D), a bipolar electrocardiogram in lead I was also recorded. In these animals, vagi were left intact but the region of bifurcation of common carotid arteries was denervated by careful dissection of the adventitia for a distance of 1 cm on either side of the point of bifurcation and then its carbolisation with 70% carbolic acid in saline. Progressive hypoxia was started after denervation. Blood samples were collected periodically from the other femoral artery and were analysed for oxygen content by the method of Peters and Van Slyke (4). The haemoglobin content of each sample was determined by acid haematin method in Haldanes Haemoglobinometer. The oxygen percentage saturation of each sample was determined by assuming 1.34 *ml* as the oxygen capacity of each gram of haemoglobin.

RESULTS AND DISCUSSION

On right peripheral vagal stimulation the fall in blood pressure from a mean of 121.9±11.1 mm Hg to 58.2±10.9 mm Hg in non-hypoxic dogs and to a mean of 57.0±10.7 mm Hg in hypoxic dogs was significant ($P<0.05$) but the degree of fall was not related to oxygen saturation (Tables 1 and 2). In atropinised animals, no such fall was seen, but the usual response to hypoxia consisting of an initial rise in blood pressure followed by a gradual fall to zero was observed in both atropinised and carotid denervated dogs (Tables 3 and 4). This was preceded by respiratory failure.

TABLE I

Non-hyposic dogs effect of vagal stimulation.

	Initial			*After right vagotomy*			*During right efferent vagal stimulation*					
Dog No.	*Blood Pressure mm Hg*	*Heart rate per min.*	*Rhythm of heart*	*Blood pressure mm Hg*	*Heart rate per min.*	*Rhythm of heart*	*Lowest blood pressure mm Hg*	*Heart rate per min.*	*Duration of asystole in sec.*	*Rhythm of heart*	*Arterial O_2 staturation*	*Percent fall in blood pressure*
1	—	—	—	80	132	Reg	16	64	8.3	Reg	—	80.0
2	120	132	Reg	130	144	Reg	66	80	7.0	Reg	88.0	49.2
3	100	144	Reg	90	125	Reg	64	75	0.0	Reg	—	28.8
4	80	104	Reg	72	102	Reg	72	102	0.0	Reg	68.4	0.0
5	180	216	Reg	182	216	Reg	60	80	5.0	Reg	94.6	67.0
6	110	168	Reg	110	186	Reg	30	80	5.2	Reg	88.2	72.7

Reg - Regular

TABLE II

Hypoxic dogs

	Before hypoxia						*During hypoxia*								
	Initial			*After right vagotomy*			*Just before vagal stimulation*			*During right efferent vagal stimulation*					
Dog No.	*Blood pressure mm Hg*	*Heart rate*	*Rhythm of heart*	*Blood pressure mm Hg*	*Heart rate*	*Rhythm of heart*	*Blood pressure mm Hg*	*Heart rate*	*Rhythm of heart*	*Lowest blood pressure mm Hg*	*Duration of asystole in sec.*	*Heart rate*	*Article O_2 saturation*	*Rhythm of heart*	*Percent fall in blood pressure*
7	150	156	Reg	150	174	Reg	154	186	Reg	94	0.0	60	83.4	Irr	39.0
8	90	192	Reg	114	174	Reg	120	138	Reg	40	0.0	60	42.5	Irr	66.7
9	170	168	Reg	170	168	Reg	80	78	Reg	30	5.0	30	—	Irr	62.5
10	160	192	Reg	130	192	Reg	170	192	Reg	60	1.6	84	7.7	Reg	64.7
11	140	114	Reg	130	164	Reg	148	162	Reg	100	0.0	66	—	Reg	32.4
12	160	162	Reg	150	156	Reg	148	138	Reg	22	6.4	48	67.5	Irr	85.1
13	170	192	Reg	136	168	Reg	140	156	Reg	76	1.4	56	92.3	Reg	45.7
14	120	156	Reg	130	156	Reg	100	144	Reg	35	3.6	45	82.3	Irr	66.0

Reg=Regular ; Irr=Irrigular.

Such a vagal stimulation produced a temporary asystole of the heart lasting for 4.1 ± 1.3 sec. in nonhypoxic dogs and for 2.2 ± 0.9 sec. in hypoxic dogs. In nonhypoxic dogs, there was no irregularity in the rhythm of the heart either during or after the period of vagal stimulation, but in hypoxic dogs the irregularity in the rhythm was present during the period of vagal stimulation but not afterwards at a mean arterial oxygen saturation of 63.8%. No irregularity in the rhythm of the heart was observed till the arterial oxygen saturation fell to zero in atropinised hypoxic dogs, or to near zero in carotid denervated dogs exposed to hypoxia. The difference in the period of asystole in nonhypoxic and hypoxic dogs was found to be statistically insignificant ($P > 0.05$). Young *et al.* (6) had also observed a decrease in the period of asystole in hypoxic dogs. After this period of asystole in hypoxic dogs the heart always escaped the effect of vagal stimulation by a progressively decreasing bradycardia.

In two of the hypoxic dogs irregularities in the rhythm of the heart appeared during the period of vagal stimulation when arterial oxygen saturation was more than 82%. Kuma

and Srivastava (2) did not observe cardiac irregularities in hypoxic dogs at such high arterial oxygen saturations. It thus appeared that vagal stimulation if superimposed over a hypoxic state invariably led to the development of cardiac irregularities. Maier *et al.* (3) observed in human beings an increasing susceptibility of the heart to arrhythmias when it was being directly or reflexly stimulated under hypoxia. Although they had not attempted any vagal stimulation but direct stimulation of the heart could possibly involve stimulation of the vagal efferents within the heart, because in completely atropinised dogs of this study no cardiac irregularities could be obtained till the arterial oxygen saturation was almost zero. That the origin of this vagal effect could be from the region of carotid bifurcation, became obvious when carotid denervated dogs were exposed to hypoxia and no irregularity in cardiac rhythm was observed when the arterial oxygen saturation fell below 20 percent, or even to zero in one of the dogs.

TABLE III

Dogs atropinised after right vagotomy and exposed to progressive hypoxia.

	Before hypoxia							*During progressive hypoxia under vagal stimulation*														
	Initial		*After right vagotomy*		*After atropine under vagal stimulation*			1			2			3			4					
Dog No.	*Blood pressure mm Hg*	*Rate/Rhythm of heart*	*Blood pressure mm Hg*	*Rate/Rhythm of heart*	*Blood pressure mm Hg*	*Arterial O_2 saturation*	*Rate/Rhythm of heart*	*Blood pressure mm Hg*	*Arterial O_2 saturation*	*Rate/Rhythm of heart*	*Blood pressure mm Hg*	*Arterial O_2 saturation*	*Rate/Rhythm of heart*	*Blood pressure mm Hg*	*Arterial O_2 saturation*	*Rate/Rhythm of heart*	*Blood pressure mm Hg*	*Arterial O_2 saturation*	*Rate/Rhythm of heart*
15	130	222 Reg	84	234 Reg	96	86.5	210 Reg	86	—	210 Reg	74	72.2	210 Reg	68	68.1	192 Reg	58	65.0	198 Reg
16	90	150 Reg	96	150 Reg	84	86.5	150 Reg	80	59.7	156 Reg	94	39.0	156 Reg	84	0.0	126 Irr	6	0.0	62 Irr
17	60	156 Reg	76	156 Reg	56	108.8	156 Reg	46	92.3	168 Reg	76	19.9	174 Reg	34	0.0	138 Irr	—	—	—
18	140	150 Reg	142	150 Reg	134	109.9	156 Reg	122	83.8	156 Reg	124	77.7	138 Reg	114	70.3	150 Reg	104	30.1	162 Reg
19	170	114 Reg	160	204 Reg	150	74.3	216 Reg	140	72.5	216 Reg	138	60.2	216 Reg	160	33.1	216 Reg	64	0.0	180 Reg

TABLE IV

Carotid denervated dogs exposed to hypoxia.

Dog. No.	Before hypoxia			During progressive hypoxia											
				1			2			3			4		
	Blood pressure in mm Hg	*Arterial O_2 saturation*	*Rate/Rhythm of heart*	*Blood pressure in mm Hg*	*Arterial O_2 saturation*	*Rate/Rhythm of heart*	*Blood pressure in mm Hg*	*Arterial O_2 saturation*	*Rate/Rhythm of heart*	*Blood pressure in mm Hg*	*Arterial O_2 saturation*	*Rate/Rhythm of heart*	*Blood pressure in mm Hg*	*Arterial O_2 saturation*	*Rate/Rhythm of heart*
20	120	87.3	140 Reg	142	9.6	147 Reg	94	7.6	88 Reg	30	0.1	30 Irr	90	0.0	24 Irr
21	140	80.9	134 Reg	150	28.0	117 Reg	128	19.2	117 Reg	60	11.0	20 Irr	94	0.0	60 Irr
22	130	85.8	200 Reg	140	39.3	180 Reg	128	4.4	140 Reg	46	0.0	17 Irr	—	—	—
23	120	97.0	180 Reg	134	88.1	180 Reg	120	9.0	180 Reg	6	0.0	3 Irr	—	—	—
24	140	66.7	210 Reg	156	41.4	240 Reg	120	14.2	180 Reg	82	0.0	120 Reg	—	—	
													—	—	

Reg=Regular ; Irr=Irregular

SUMMARY

The response of the dog's heart to efferent vagal stimulation under hypoxia has been studied. Irregularities in the rhythm of the heart appeared in mildly hypoxic dogs during vagal stimulation. No such irregularity appeared in completely atropinised, or carotid denervated dogs even under severe hypoxia. It is suggested that hypoxia sets up a reflex from the region of carotid bifurcation which is responsible for the development of cardiac irregularities.

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