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Influence of Carotid Occlusion on Pulmonary Vascular Resistance in Anesthetized Dogs[1] (40174)

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Studies concerned with analysis of the pulmonary sympathetic adrenergic innervation have shown that electrical stimulation of upper thoracic sympathetic outflows results in both an elevation of pulmonary vascular resistance together with a decrease in distensibility of the large pulmonary arteries (1–4). The increase in resistance arises from activation of alpha adrenergic mechanisms within the pulmonary vasculature (2). These studies indicate that the pulmonary circulation receives a functional adrenergic innervation. However, little is known concerning the functional significance of this innervation as regards its participation in reflex cardiovascular adjustments known to increase efferent sympathetic nerve activity. In this connection, excitation of the carotid sinus baroreceptor reflex results in enhancement of sympathetic adrenergic activity to various systemic vascular beds reflected in a rise in calculated vascular resistance (5, 6). Based on these studies, it may be postulated that a significant increase in sympathetic activity to the pulmonary vascular bed during carotid occlusion would be expected to produce a consistent rise in total pulmonary vascular resistance. On the other hand, if the adrenergic effects are weak or nonexistant then the pulmonary hemodynamic response during occlusion may be controlled primarily by mechanical extravascular effects arising from fluctuations in pulmonary venous pressure and pulmonary flow which may develop as a consequence of the systemic pressor response (7–9). Therefore, the purpose of this study was to analyze the pulmonary hemodynamic response during bilateral carotid occlusion in the anesthetized closed chest dog, in order to study the reflex with normal pulmonary function.

Materials and methods. Animal preparation. Thirteen mongrel dogs of either sex (average wt 20 kg) were anesthetized with sodium pentobarbital (30 mg/kg iv). Following tracheal intubation, the animals were ventilated with a Bird Mark IV respirator. Under sterile technique, a thoracotomy was performed through the third intercostal space. The pericardium was opened and a large bore, soft polyvinyl catheter was advanced into the left atrial chamber via the appendage. An identical cathether was placed in the right atrium. Next, the pulmonary artery was dissected free of connective tissue for a length of 1.5 cm in order to receive an electromagnetic flow probe (CME No. EP400RC). Care was taken to avoid transection of autonomic nerves passing along the medial aspect of the main pulmonary artery. A probe size was selected which produced less than a 10% constriction in vessel diameter. A catheter (0.047 in i.d.) was inserted into the lumen of the main pulmonary artery using a modified Seldinger technique. The catheter was placed 0.5–1.0 cm proximal to the flow probe. The chest was then closed and the catheters tunneled under the skin and secured in a subcutaneous pocket. During the first three postoperative days the animals received prophylactic antibiotics with procaine penicillin (500,000 μm im) and streptomycin (250 mg im). Animals were studied between the 7th and 10th postoperative day.

Experimental design. At the time of study the animals were anesthetized with chloralose (80 mg/kg iv). A femoral artery was entered with a polyvinyl catheter advanced into thoracic aorta in order to measure systemic pressure. A midline incision was made in the neck and both carotids and vagi isolated and loosely ligated with umbilical tape. The chest catheters were exteriorized and attached to pressure gauges (Statham P23Gb) positioned at heart level. Pulmonary blood flow was measured with an electromagnetic flowmeter (CME #501). Probes were precalibrated by the manufacturer. Pressure and flow pulses were recorded on an Offner type R Dynograph.

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The carotid sinus reflex was activated by clamping the carotid arteries. Measurements of pressure and flow were obtained in the steady state approximately 1–2 min after the onset of occlusion. After control occlusion responses were obtained the vagi were transected and the occlusion was repeated. Bilateral cervical vagotomy was performed in order to eliminate aortic arch baroreceptor buffering of the sympathetic response to carotid occlusion, thereby allowing sympathetic effects to reach their maximum potential. Next, carotid occlusion was repeated after beta blockade with either propranolol (1 mg/kg) or pindinol (0.1 mg/kg). Finally, the response to occlusion was then repeated following alpha blockade with phenoxybenzamine (2–3 mg/kg) or phentolamine (1–2 mg/kg). Records were taken in the supine position with the animal lying on his right side.

Data analysis. Ten parameters of pressure and flow together with heart rate were derived for analysis (see Table I). Zero flow reference was taken as the flow level in late diastole. For a given condition, measurements of pressure and flow were determined by averaging three to six pulses during respiratory diastole. The respiratory period could be easily determined from the cyclic variations in pulmonary arterial and left atrial pressures associated with respiratory movements. This method of pulse averaging provides an average value of pressures and flow during respiratory diastole. Thus, this approach takes into account normal fluctuations in pressures and flow as well as heart rate changes associated with respiratory variations in the spontaneously breathing animal. With the exception of stroke volume, which was determined by dividing mean flow by heart rate, all pressure and flow parameters represent average values of individual pulses during the expiratory period.

Pulmonary vascular resistance was calculated as the difference between mean pulmonary arterial pressure and left atrial mean pressure divided by mean pulmonary flow. Systemic vascular resistance was calculated as the ratio of mean systemic arterial pressure to mean pulmonary flow. Flow was expressed per kg body weight. This method does not provide a true measure of SVR, since mean right atrial pressure was not included in the calculation. However, this exclusion should not result in a large error, since the magnitude of mean right atrial pressure is less than 5% of mean systemic pressure.

Results. The combined data from thirteen animals showing heart rate with ten parameters of pressure and flow are presented in Table I. In the control, bilateral carotid occlusion resulted in an increase in systemic arterial pressure and total systemic vascular resistance. On the other hand, pulmonary vascular resistance was unaffected, while pulmonary arterial mean pressure, left atrial mean pressure and mean flow were all slightly increased during occlusion. Following vagotomy, occlusion resulted in a greater rise in systemic pressure associated with a greater increase in systemic vascular resistance. However, in contrast to the control, pulmonary vascular resistance was significantly decreased during occlusion. After beta blockade, heart rate no longer increased during occlusion. As was the case prior to beta blockade, systemic pressure and systemic resistance increased during occlusion. Similarly, pulmonary resistance again decreased as both pulmonary arterial mean and left atrial mean pressures increased, while mean flow remained essentially constant. After the administration of alpha blocking agents the rise in systemic pressure was attenuated, but not obliterated during occlusion. After alpha block systemic resistance still increased but the change was attenuated. Pulmonary resistance again decreased and, as was the case with systemic resistance, the absolute change was diminished after alpha blockade.

Discussion. The results indicate that in the spontaneously breathing, closed chest, chloralose anesthetized dog, bilateral carotid occlusion is not associated with a rise in pulmonary vascular resistance, and therefore suggests that reflex sympathetic activity is of questionable significance in the control of *total* pulmonary vascular resistance in this reflex. Rather, the data indicate that pulmonary vascular resistance is primarily under the control of extravascular effects controlling the level of LAMP (7, 8). Carotid occlusion produced marked elevations in systemic arterial pressure and the ensuing increased afterload on the left ventricle resulted in consistent elevations in left atrial pressure. It is interesting to note that in the control prior to

TABLE I. PULMONARY AND SYSTEMIC VASCULAR RESPONSES TO CAROTID OCCLUSION CONTROL.[a]

HR (beats/min)	PASP (mmHg)	PADP (mmHg)	PAMP (mmHg)	Q mean (ml/min/Kg)	SV (ml)	SAMP (mmHg)	LAMP (mmHg)	RAMP (mmHg)	PVR (mmHg·Kg/ml/min)	SVR (mmHg·Kg/ml/min)
110 ± 21	21.9 ± 4.7	7.3 ± 2.6	12.6 ± 2.9	158 ± 32	28 ± 7	110 ± 16	3.3 ± 1.4	4.2 ± 1.9	61.2 ± 17	69.4 ± 14
					BCO					
140 ± 44 ($P < 0.01$)	24.2 ± 4.8 ($P = 0.02$)	8.8 ± 2.9 ($P < 0.05$)	14.1 ± 2.3 ($P < 0.01$)	162 ± 38 (N.S.)	23 ± 6 ($P = 0.02$)	149 ± 34 ($P < 0.01$)	4.2 ± 1.4 ($P < 0.01$)	4.4 ± 2.1 (N.S.)	64.0 ± 21 (N.S.)	96.7 ± 21.1 ($P < 0.01$)
					After bilateral vagotomy					
					Control					
154 ± 27	19.5 ± 5.1	8.3 ± 2.5	13.1 ± 3.2	136 ± 32	17.5 ± 5	127 ± 14	2.6 ± 1.9	3.9 ± 2.4	78.8 ± 18	94.8 ± 21.0
					BCO					
176 ± 33 ($P < 0.01$)	23.7 ± 7.1 ($P < 0.05$)	11.2 + 5.7 (N.S.)	16.5 ± 5.7 (N.S.)	146 ± 56 (N.S.)	16 ± 8 (N.S.)	188 ± 14 ($P < 0.01$)	7.1 ± 6.2 (N.S.)	4.1 ± 2.7 (N.S.)	67.9 ± 18.8 ($P < 0.05$)	137.9 ± 45.7 ($P < 0.01$)
					After beta blockade					
					Control					
125 ± 30	21.4 ± 6.1	7.6 ± 3.3	13.9 ± 2.4	140 ± 40	21 ± 7	114 ± 17	3.3 ± 1.4	4.5 ± 1.9	76.4 ± 18.2	85.6 ± 19.8
					BCO					
131 ± 28 (N.S.)	23.6 ± 4.8 (N.S.)	11.5 ± 3.2 ($P < 0.05$)	16.6 ± 3.4 ($P < 0.05$)	143 ± 47 (N.S.)	21 ± 8 (N.S.)	170 ± 20 ($P < 0.01$)	7.8 ± 4.7 ($P < 0.01$)	5.0 ± 3.7 (N.S.)	64.9 ± 25.0 ($P < 0.02$)	130.5 ± 38.5 ($P < 0.01$)
					After alpha blockade					
					Control					
130 ± 26	20.6 ± 5.6	8.0 ± 2.4	12.8 ± 4.4	135 ± 43	21 ± 8	122 ± 32	3.32 ± 2.4	4.6 ± 2.1	80.7 ± 24.0	100.8 ± 38.3
					BCO					
143 ± 31 ($P < 0.01$)	20.7 ± 6.2 (N.S.)	9.1 ± 3.5 (N.S.)	13.0 ± 4.5 (N.S.)	132 ± 48 (N.S.)	18.7 ($P < 0.02$)	158 ± 49 ($P < 0.01$)	5.4 ± 4.3 ($P < 0.01$)	4.6 ± 1.8 (N.S.)	74.1 ± 29.7 ($P < 0.05$)	143.2 ± 47.0 ($P < 0.01$)

[a] Table showing average data with plus-minus one standard deviation for ten parameters of pressure and flow before and during bilateral carotid occlusion (BCO). The level of significance of the change between control and BCO was determined using the Student's *t* test for paired data. P values are shown in parenthesis. N.S. = nonsignificant change from control. Significance was determined from thirteen experiments in thirteen animals for control and for alpha blockade and from nine experiments for vagotomy and for beta blockade. HR = heart rate; PASP = pulmonary arterial systolic pressure; PADP = pulmonary arterial diastolic pressure; PAMP = pulmonary arterial mean pressure; Q mean = mean pulmonary blood flow; SV = stroke volume; SAMP = systemic arterial mean pressure; LAMP = left atrial mean pressure; RAMP = right atrial mean pressure; PVR = total pulmonary vascular resistance; and SVR = systemic vascular resistance.

vagotomy carotid occlusion was without effect on pulmonary vascular resistance, whereas occlusion after vagotomy resulted in a significant decrease in resistance. Hence, vagal effects may be important for maintaining a constant pulmonary vascular resistance in the face of passive effects of increases in mean left atrial pressure. In those instances where pulmonary resistance was significantly decreased (vagotomy, alpha and beta block) the absolute increase in left atrial pressure exceeded the increase in pulmonary arterial pressure while mean flow remained essentially unchanged (10), thus resulting in a fall in calculated resistance.

Beta blockade was without effect on altering the direction or the magnitude of changes in systemic arterial pressure, systemic resistance and pulmonary resistance which developed during occlusion after vagotomy. The administration of alpha blocking agents, on the other hand, attenuated the rise in systemic pressure, left atrial pressure and systemic resistance. Attenuation of systemic changes was associated with a diminished fall in pulmonary resistance thus suggesting that the magnitude of the fall in pulmonary resistance was primarily dependent upon the magnitude of the rise of aortic pressure, which then affects left atrial pressure, and not upon neurogenic mechanisms. In addition, since pulmonary vascular resistance is dependent on the level of left atrial pressure, alterations in left ventricular function would also be expected to alter calculated pulmonary vascular resistance. Hence, the level of left atrial mean pressure will depend upon the rise in aortic pressure together with concomitant changes in left ventricular function (11). Therefore, in the carotid sinus reflex, changes in pulmonary vascular resistance will depend upon the magnitude of the pressor response as well as upon the degree of cardiac augmentation as may occur during the reflex response (12, 13).

Normally, carotid sinus hypotension results in widespread activation of the sympathetic nervous system with detectable changes in vasomotor tone in most systemic vascular beds. However, the magnitude of the vascular response varies considerably in different organ systems. In this respect, carotid sinus control of skin and muscle vascular beds is of greater physiological significance than control of the renal and splanchnic circulations (6). Hence, a certain degree of specificity is inherent in the response. The present study indicates that the pulmonary vascular adrenergic innervation probably does not have a physiologically significant participation in the carotid sinus reflex. Although experiments involving direct stimulation show that the neuroeffector system is capable of profound changes in pulmonary vasomotor tone, these mechanisms are not sufficiently activated during carotid occlusion. Therefore, this innervation is of questionable significance in the postural control of the pulmonary circulation.

Summary. Bilateral carotid occlusion in the spontaneously breathing, closed chest, chloralose anesthetized dog increased systemic arterial pressure and systemic vascular resistance, but was without effect on total pulmonary vascular resistance. Occlusion following bilateral vagotomy resulted in a significant decrease in pulmonary vascular resistance which was accompanied by an elevation in mean left atrial pressure. The fall in resistance was not changed after beta blockade; however, the administration of alpha blocking agents reduced the rise in mean left atrial pressure and systemic arterial pressure, and markedly attenuated the fall in pulmonary vascular resistance during occlusion. During carotid occlusion pulmonary vascular resistance was primarily controlled by passive effects arising from fluctuations in mean left atrial pressure and, therefore neurogenic effects appeared to be of little significance in the control of pulmonary vascular resistance in the carotid sinus reflex.

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