Effects of Carotid Occlusion on the Renal and Iliac Vascular Resistance During Constant Flow and Constant Pressure Perfusion[1] (37229)

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Occlusion of the common carotid arteries is commonly employed as a means of investigating the effects of altering baroreceptor reflex activity on the cardiovascular system. It is generally agreed that the major vascular response to this procedure is vasoconstriction resulting from a withdrawal of inhibition on the sympathetic vasoconstrictor centers. This change in vascular resistance appears to involve at least two major factors: An increase in sympathetic vasomotor nerve activity and a local myogenic response (autoregulation) to the resultant increase in perfusion pressure. The relative contribution of these factors in individual vascular beds will differ, depending upon their sensitivity to changes in sympathetic vasomotor nerve activity and their intrinsic ability to autoregulate. The neurogenic component of the baroreceptor reflexes exerts a greater effect upon the vascular bed of skeletal muscle than it does upon the renal vessels (1–3). Conversely the local autoregulatory response has been reported by Rein (4) and Hartmann, Orskov and Rein (5) to be the major cause of renal vasoconstriction during bilateral carotid occlusion (BCO). Contradictory reports (6–9) have indicated that a major portion of the renal response to BCO is mediated by the renal sympathetic nerves. The objective of the present study was to evaluate the relative contribution of the neurogenic and autoregulatory components of the response to BCO in the renal vascular bed. Our experimental approach was to compare the change in renal vascular resistance to BCO during perfusion of the kidneys at a constant rate of flow and at a constant pressure. We have also made a similar study on the vascular bed of the hindlimb to provide comparative data from a vascular bed which serves an organ anatomically and functionally different from the kidney. The response to norepinephrine was also studied in both vascular beds.

Methods. A total of 14 experiments on dogs (16 to 20 kg) were conducted in this study. All dogs were anesthetized with chloralose (100 mg/kg iv) following premedication with morphine (3 mg/kg sc). Supplemental chloralose (20–25 mg/kg hr) was given by iv drip. The trachea was cannulated and artificial ventilation with 100% O_2 was provided and adjusted to maintain arterial blood PCO_2 and pH in the normal range. Both vagus nerves were cut in the neck. Heparin (3–5 mg/kg) was given and supplemented hourly (1 mg/kg). The animals were prepared for perfusion of either the renal or iliac vascular bed.

Perfusion of the kidneys (8 dogs). Both kidneys were perfused by a finger type pump (Harvard Md. 500) with an adjustable output. The method of renal perfusion has been previously described (10). In brief this method involves vascular isolation and perfusion of the aortic segment from which the renal arteries arise. A cannula consisting of concentric glass tubes was introduced into the aorta below the renal arteries and advanced until the longer inner tube extended above the origin of the renal arteries. Ties were placed around the aorta above and below the renal arteries. Input to the pump was provided from the aorta through the inner tube of the cannula and the pump output was returned into the renal arteries through the outer shell of the cannula. Tygon tubing was used to complete the circuit, with the

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exception of a small segment of rubber tubing in the pump head. An electromagnetic flow sensor was incorporated in the circuit. The extracorporeal circuit was initially filled with a 6% dextran–saline solution (75 ml). Renal perfusion pressure was measured from a side tube in the circuit.

Perfusion of the iliac vascular bed (6 dogs). One hind limb was perfused through the common iliac artery in these experiments. Arterial inflow to the pump was provided from a cannula in the sacral artery. A flow probe and pressure tap were incorporated in the circuit.

Systemic arterial pressure was measured from a branch of the femoral artery of the normally perfused leg. All pressures were measured with Statham pressure transducers. Flows were measured with a Statham M-4000 electromagnetic flowmeter. Pressures and flows were recorded on an Offner oscillograph. Regional vascular resistance was calculated as the pressure (mm Hg)/flow (ml/min) ratio. Paired responses to each procedure were obtained during constant flow (CF) perfusion and during constant pressure (CP) perfusion. During CF perfusion the change in regional vascular resistance was reflected by the change in perfusion pressure. During CP perfusion the pump output was adjusted to maintain a constant pressure during the response. In this case the change in flow reflected the change in resistance. If the control resistance differed by more than 10% in the paired CF, CP perfusion responses, the responses were rejected. The paired responses were analyzed for significant differences by Student's *t*-test for paired data. The 2% probability level was the criterion for significance. Norepinephrine was given intra-arterially (ia) in most experiments and the resistance changes during CF and CP perfusion were compared. Fresh solutions of norepinephrine (Levophed bitartrate, Winthrop, doses in terms of the base) were made for each experiment.

Results. The average resistance changes in response to the different vasoconstrictor interventions are shown in Table I. In all cases the change in renal vascular resistance to BCO and intra-arterial norepinephrine was greater during CF perfusion than during CP perfusion.

During CP perfusion, the myogenic response to the increased perfusion pressure is eliminated. The resistance change therefore reflects the direct neurogenic effects of BCO or the direct effects of norepinephrine on the vascular smooth muscle. In the renal vascular bed the resistance change to BCO during CP perfusion was approximately 50% of that seen during CF perfusion. Thus it would appear that about 50% of the response during CF perfusion was due to a local vascular response associated with the rise in pressure. Based on this same assumption about 30% of the response to norepinephrine, in the dose used, was due to the autoregulatory response. However, in the latter case, renal pressure rose an average of 41 mm Hg to the 0.5 μg dose of norepinephrine while BCO caused an average response of 64 mm Hg in the kidneys perfused at a constant rate of flow. This greater pressure rise probably accounts for the larger autoregulatory response in the case of BCO.

In the perfused iliac vascular bed the responses to the vasoconstrictor influences during CF perfusion are a fraction of those seen during CP perfusion. Comparison of the responses in the limb and kidneys to BCO during CP perfusion indicates a greater neural influence in the limb than in the renal vascular bed. The autoregulatory component of the response to both BCO and norepinephrine in the vascular bed of the limb cannot be estimated; however, it is small and inadequate to offset the distending pressure forces.

In one vascularly isolated, perfused gastrocnemius muscle we obtained results essentially identical to those described for the whole limb. Our data from the limb therefore probably represents the behavior of the vascular bed of skeletal muscle.

Discussion. The evidence presented suggests that in the artificially perfused kidneys, both the local autoregulatory response and the increased renal nerve activity play nearly equal roles in determining the change in renal resistance to a general increase in sympathetic activity caused by BCO. Similarly the response to norepinephrine is increased by the local response to the rising pressure. This effect would be expected to play an

TABLE I. Average Resistance Changes (± SEM) to BCO and Intra-arterial Norepinephrine in the Renal and Iliac Vascular Beds Perfused with a Constant Flow (CF) or at a Constant Pressure (CP).

Procedure	Control perfusion pressure (mm Hg)	Control flow (ml/min)	Control regional resistance (P/F)	Change in resistance (%)	N	p
			Perfused kidneys			
BCO, CF	99 ± 9	328 ± 31	0.321 ± 0.05	64 ± 12	8	
BCO, CP	99 ± 9	328 ± 29	0.314 ± 0.04	29 ± 5	8	<.02
NorEp (0.5 μg), CF	101 ± 1	287 ± 35	0.376 ± 0.04	41 ± 7	6	
NorEp (0.5 μg), CP	98 ± 2	291 ± 26	0.352 ± 0.03	29 ± 8	6	<.02
			Perfused hind limb			
BCO, CF	119 ± 9	92 ± 8	1.38 ± 0.17	45 ± 7	6	
BCO, CP	118 ± 7	92 ± 7	1.36 ± 0.15	263 ± 79	6	<.02
NorEp (1.5 μg), CF	122 ± 10	93 ± 10	1.39 ± 0.20	32 ± 8	6	
NorEp (15. μg), CP	116 ± 8	90 ± 8	1.34 ± 0.14	75 ± 18	6	<.02

even greater role in the normally perfused than in the pump perfused kidneys. Rein (4) reported that the renal flow response to BCO was unaffected by renal denervation in dogs. Thus, his studies suggest that the renal response to BCO is entirely due to the autoregulatory response. Iriuchijima and Wilson (6) studied the changes in renal resistance and the activity in the renal nerves during BCO. They found renal nerve activity increased during BCO. They failed to estimate the relative contribution of the neurogenic and autoregulatory components of the renal vascular response to BCO. Study of their data suggests, however that the autoregulatory component was minimal. Gilmore (8) concluded from his studies on the perfused kidney of the dog that the primary renal response to carotid occlusion was vasoconstriction mediated by the renal sympathetic nerves.

Changes in sympathetic activity appear to be the predominant factor in increasing vascular resistance to BCO in the iliac vascular bed. During CF perfusion a large part of the neurogenically increased vascular resistance appears to be overcome by the vessel distention which results from the increased perfusion pressure. Thus the response to BCO and to the vasoactive agents is a fraction of that seen during CP perfusion. Davis and Hammond (11) also obtained much greater resistance changes to sympathetic nerve stimulation during CP perfusion than during CF perfusion in the limb of the dog. A likely explanation for this difference is that the physical conditions of the vascular smooth muscle are changing in opposite directions in the two cases. During CP perfusion smooth muscle shortening results in a decrease in vessel radius which is unopposed by a rising perfusion pressure. As the vessel radius decreases, further shortening becomes more effective due in part the fact that a given degree of shortening produces a relatively greater radius reduction at the smaller radius. In contrast to this, during CF perfusion the distending forces oppose the reduction in vessel radius thus reducing the effectiveness of vascular smooth muscle contraction.

In the renal vascular circuit the same physical forces act upon the vessel wall as in the limb. However, the kidney is a less distensible organ than the limb and the renal vessels also exhibit a more pronounced autoregulatory response. These factors balance or exceed the distending forces over a wide range of pressures. Kirchheim, Gross and Kentzel (12) postulated that at 140 mm Hg the distending pressure forces were balanced and the renal vessels behaved as indistensible tubes. This balance of the distending forces provides a situation in which the vascular smooth muscle may more effectively reduce the radius of the renal vessels. This mechanism may serve to sensitize the renal vascu-

lar bed to vasoconstrictor influences in hypertension as suggested by McNay and Kishimoto (13).

Summary. Bilateral carotid occlusion (BCO) caused an average pressure increase of 64% in kidneys perfused at a constant rate of flow and a 20% reduction in flow when the perfusion pressure was held constant. Calculated renal resistance changed 64 and 29%, respectively. The responses to norepinephrine ia were also greater during CF perfusion than during CP perfusion. The results suggest that about one-half of the renal response to BCO during CF perfusion is due to the local resistance changes in response to the rise in perfusion pressure and about one-half due to the action of the vasoconstrictor nerves. In the perfused hind limb the response to each of these procedures during CF perfusion was a fraction of that seen during CP perfusion.

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