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Intrarenal Blood Flow Distribution: Effect of Carotid Occlusion[1] (39029)

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The influence of carotid occlusion on intrarenal blood flow distribution was first described by Pomeranz, Birtch, and Barger (1). Using an inert gas washout method to determine intrarenal blood flow distribution, they found that activation of renal nerves, either by carotid occlusion or by mild stimulation of the splanchnic nerve, decreased perfusion of outer cortical peritubular capillaries and increased perfusion of the outer medulla. In contrast, Aukland, using implanted hydrogen electrodes, found a decrease in outer medullary flow during direct renal nerve stimulation (2). As Pomeranz *et al.* pointed out (1), part of the discrepancy may be related to the strength of nerve stimulation employed. In view of these conflicting reports and the criticisms which have been advanced against inert gas methods in general (3), we have evaluated the influence of carotid occlusion on intrarenal hemodynamics using labeled microspheres as indicators of inner and outer cortical blood flow changes. Studies were performed before and during carotid occlusion in dogs that were volume expanded with either mannitol or saline.

Methods. Ten mongrel dogs of either sex (10–15 kg) were anesthesized with pentobarbitol (30 mg/kg iv). The animals were tracheotomized and ventilated with a Harvard Apparatus positive pressure respirator. Six animals were saline expanded with 10 ml saline/kg body wt., administered during a 20-min time interval via a PE60 catheter in the external jugular. Urinary fluid loss was then balanced by saline administration at appropriate rates. Four dogs were expanded with 5% mannitol in saline, infused at a rate of 0.5 ml/min/kg/body wt. An intravenous solution containing paraaminohippurate (PAH) and creatinine was also infused via the external jugular at 0.2 ml/min. A PE-100 catheter was inserted into the left femoral artery and served for blood pressure monitoring (physiograph recorder & transducer). Another PE-100 catheter was inserted into the right femoral artery and advanced so that the catheter tip was in the thoracic aorta. This catheter served for collection of arterial samples and injection of microspheres (see below for details). Ureters were cannulated with PE-100 tubing and Kifa catheters (U.S. Catheter Corp.) were positioned in the renal veins via the femoral veins.

When urine flow had stabilized (1–2 hr), two consecutive clearance periods were performed with midpoint arterial and renal venous samples. The ^{169}Yb-labeled microspheres (15 μm $\pm$ 5 μm, 3M Corp.) were rapidly injected into the thoracic aorta and flushed with 3 ml of saline. Both internal carotid arteries were then ligated below the level of the carotid sinus. At least 30 min were then allowed to assure a new steady state had obtained. Two additional clearance periods were then performed, as described above, except that ^{85}Sr-labeled microspheres (15 μm $\pm$ 5 μm, 3M Corp.) were injected. At the termination of each experiment the kidneys were removed, weighed, and placed in 10% formaldehyde overnight. Two cortical zones were easily discernible with this procedure. With the exception of the inferior and superior renal poles, the entire outer cortex was removed, weighed, and counted. Any outer cortex remaining on the renal pieces was then removed and the entire inner cortex dissected free, weighed and counted. Radioactivity was determined on a Packard gamma scintillation counter (Model 3002).

Creatinine concentration was estimated by the picric acid method of Folin and Wu (4) and PAH by the diazotization procedure of Bratton and Marshal (5). Na and K

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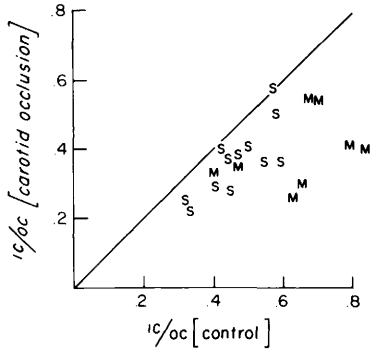

FIG. 1. This figure shows the ratio of inner to outer cortical blood flow (IC/OC) before and during bilateral carotid occlusion. The letters S and M refer to saline and mannitol expanded animals, respectively. The line of identity is shown.

concentrations were measured with flame photometry (Advanced Instruments Corp.).

Renal blood flow was calculated using PAH clearance and renal extraction data. Blood flow per gram outer and inner cortex was calculated according to the method of Katz *et al.* (3).

Results. The effect of bilateral carotid occlusion on blood flow distribution is illustrated in Fig. 1. In this figure we have plotted the ratio of cpm/gm inner cortex to cpm/gm outer cortex (IC/OC ratio) before and during carotid occlusion. As may be seen in Fig. 1, there was a significant reduction ($P < .01$) in the IC/OC ratio during the period of carotid occlusion. The redistribution of intrarenal blood flow following carotid occlusion was further analyzed in terms of regional flows per gram of tissue. These data are shown in Fig. 2 which is a plot of blood flow per gram inner and outer cortex before and during carotid ligation. Significant increases in outer cortical blood flow were observed with carotid occlusion ($P < .01$) whereas significant decreases were found in inner cortical flow ($P < .01$).

To determine whether the intrarenal events associated with carotid occlusion represented active or passive vascular changes, regional vascular resistance, calculated from mean arterial pressure and blood flow per gram inner and outer cortex, were compared before and after ligation. These data are shown in Fig. 3. As may be seen in this figure, there was a significant increase in

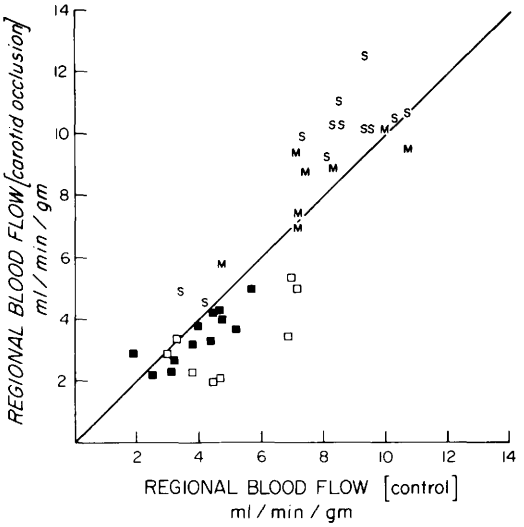

FIG. 2. Regional blood flows to inner and outer cortices in ml/min/g inner or outer cortex are compared before and during carotid occlusion. The letters S and M refer to outer cortical flow during saline or mannitol expansion, respectively; closed and open squares refer to inner cortical flow during saline or mannitol expansion, respectively. Line of identity is drawn.

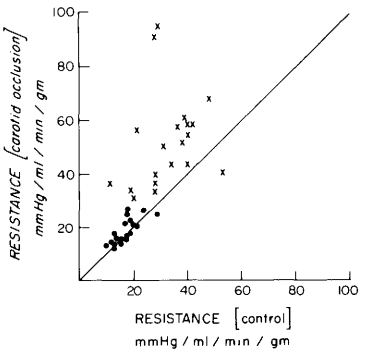

FIG. 3. Inner cortical resistance (X) and outer cortical resistance (·) in mmHg/ml/min/g are shown before and during carotid occlusion. As in Figures 1 and 2, the line of identity is shown.

inner cortical resistance to flow with carotid occlusion ($P < .01$) whereas no significant changes occurred in outer cortical resistance.

The average mean arterial pressure before carotid clamping was 130 ± 25 mmHg (SD $n = 10$) and 166 ± 28 mmHg (SD) during carotid occlusion. Paired t test analysis showed no significant changes in renal blood flow, creatinine clearance or fractional

Na excretion with carotid occlusion. Thus, ΔRBF (RBF control − RBF carotid occlusion) was −0.24 ml/min/gm k wt ($P > .1$), ΔGFR was +0.02 ml/min/gm k wt ($P > .4$) and ΔF_{ENA} was − 0.003 ($P > .3$). In contrast, fractional K excretion decreased significantly with carotid occlusion ($\Delta F_{EK} = -0.05$, $P < .005$).

Discussion. The data presented in this paper clearly show that bilateral carotid occlusion leads to a redistribution of blood flow within the renal cortex (Fig. 1). These intrarenal flow changes were characterized by an increase in outer cortical blood flow and a decrease in inner cortical blood flow (Fig. 2).

The changes in cortical perfusion with carotid occlusion noted above appear to be a reflection of both active and passive flow-resistance changes. This conclusion is based on the finding that outer cortical resistance showed essentially no change during carotid ligation whereas inner cortical resistance increased substantially (Fig. 3). Thus, since systemic pressure increased with carotid ligation, a passive increase in outer cortical flow was observed. In contrast, the increase in inner cortical resistance with carotid occlusion was greater than the increase in pressure; hence, flow to this region decreased.

Two possible explanations might be advanced to account for the above findings; (1) that the renal vascular adjustments were a consequence of renal sympathetic activation, localized primarily to the inner cortex or (2) that these changes were pressure related phenomena. There is, however, evidence against the latter possibility. Abe *et al.* (6) have examined the influence of arterial pressure, alone, on intrarenal blood flow distribution. They found no redistribution of intrarenal blood flow when renal arterial pressure was reduced from approximately 140 mmHg–100 mmHg by means of aortic clamping. While our pressure range (130 to 166, pre- versus postocclusion) slightly exceeded those of Abe *et al.* (6), it would appear that pressure changes, per se, did not contribute significantly to our results.

Pomeranz *et al.* (1), using inert gas to estimate intrarenal blood flow distribution, found a decrease in outer cortical perfusion and an increase in inner cortical perfusion during carotid occlusion. However, in contrast to our approach, they employed controlled femoral hemorrhage to maintain renal arterial pressure constant. Recently, Katz and Shear (7), using microspheres, reported that carotid occlusion with controlled hemorrhage decreased midcortical flow but had no effect on superficial or juxtamedullary flow. Undoubtedly, differences in inert gas and microsphere methods account for some of these discrepancies. Nonetheless, comparison of our results with those of Katz and Shear (7) also reveal differences. Our results show that carotid occlusion, without bleeding to control pressure, increases outer cortical blood flow and decreases inner cortical flow. As Katz and Shear pointed out (7), controlled femoral hemorrhage to maintain constant renal perfusion pressure is a stressful procedure and may well account for the differences in our results.

In contrast to the present findings of selective activation of inner cortical nerve fibers with carotid occlusion, Rector *et al.* (8), using microspheres, and Aukland (2), using the hydrogen electrode method, found no redistribution of intrarenal blood flow when norepinephrine was directly infused into the renal artery. These studies were characterized by substantial decreases in renal blood flow whereas the selective changes we have described were not accompanied by significant changes in total flow.

Finally, in spite of the fact that we were able to demonstrate flow changes between inner and outer cortices, no marked differences in sodium excretion were found. In contrast, fractional K excretion did change with changes in intrarenal blood flow distribution but other experiments will be required to establish a cause and effect relationship. Thus, the physiological implications of intrarenal blood flow distribution remain to be elucidated.

Summary. In this study we have examined the influence of bilateral carotid occlusion on intrarenal blood flow distribution. Using labeled microspheres to determine intrarenal

hemodynamics, bilateral carotid ligation in mannitol or saline expanded dogs resulted in an increase in outer cortical blood flow and a decrease in inner cortical flow. Total renal blood flow and glomerular filtration rate did not change significantly during carotid occlusion whereas the average mean arterial blood pressure rose from 130 to 166 mmHg. Inner cortical flow resistance increased substantially after carotid occlusion; outer cortical resistance was unchanged. These results suggest that bilateral carotid occlusion selectively activates inner cortical renal sympathetic fibers.

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