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Persistence of the Renal Response to Atrial Tamponade after Cardiac Denervation[1] (39411)

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Previous studies in our laboratory demonstrated that decreases in renal sodium excretion and urine flow are elicited when atrial transmural pressure is reduced in the dog by the infusion of isotonic saline into a specially constructed pericardial pouch which encloses the atria only (1, 2). This procedure (atrial tamponade) produced no significant changes in left atrial pressure or aortic pressure (2). Consequently, we suggested that the changes in salt and water excretion are elicited reflexly by the changes in atrial transmural pressure (1, 2) although other possibilities were considered (1).

In later experiments we found that central venous pressure consistently is increased by approximately 2-3 mm Hg during atrial tamponade (3), thus indicating that this procedure does cause distinct, though subtle, changes in systemic hemodynamics. The changes in renal excretion that occur during atrial tamponade therefore conceivably could be initiated either by changes in atrial receptor activity or by extra-atrial changes in systemic hemodynamics. In an attempt to differentiate between these two possibilities, we performed a series of experiments designed to determine the effect of atrial tamponade on renal function after known afferent pathways from the heart had been interrupted. The interruption of cardiac afferent pathways would be expected to abolish or attenuate the renal response if it is dependent upon atrial receptors. The results obtained indicate that the renal response to atrial tamponade does not depend upon atrial receptors.

Materials and methods. All experiments were performed on female mongrel dogs averaging 15.6 ± 1 kg (SE) in weight. The chest was opened through a midline sternotomy under aseptic conditions and an atrial pericardial pouch was made by trimming away the pericardium which covered the ventricles and suturing the remaining edge of pericardium to the atrioventricular groove. Thus the atria, but not the ventricles, were enclosed within the pericardial pouch. A catheter was placed into the pouch for the infusion and withdrawal of saline and for recording intrapericardial pressure. Other catheters were implanted in the aorta and superior vena cava, and in one group of dogs a catheter also was placed in the left atrium. Details of the operative procedure and postoperative management have been published (2).

During the thoracotomy, a bilateral partial sympathectomy was performed on all dogs by identifying and cutting the rami communicantes and removing the sympathetic trunk (stellate ganglion through T-5). This level of denervation was chosen because the efferent sympathetic fibers to the heart appear to arise from T-1 through T-4 (4). The more extensive denervation therefore should have eliminated the afferent and efferent impulses that travel in the sympathetic distribution to the heart. For convenience, we will refer to this procedure simply as a "sympathectomy" throughout this paper. In eight animals a vascular occluder with an inflatable cuff was placed around the descending thoracic aorta in order to allow us to control renal arterial pressure. In three of these animals the recurrent laryngeal nerves were cut bilaterally above the origin of the cardiac branches. The dogs were allowed to recover from the operation for at least 1 week.

On the day of the experiment, each dog

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was anesthetized with sodium pentobarbital (30 mg/kg body weight) and both vagus nerves were cut in the midcervical region. In those dogs having an occluder around the aorta, a catheter was inserted into the femoral artery and its tip was advanced to the level of the renal arteries. In all experiments urine flow was elevated above basal levels by the intravenous infusion of saline, and a relatively stable urine flow was established. The total amount of saline infused during prehydration averaged 240 ± 60 ml. Each experiment included a 30-min control period, a 30-min period of atrial tamponade that was produced by infusing saline into the pericardial pouch, and a 30-min recovery period that followed the withdrawal of the saline from the pericardial pouch.

Urine was collected over 10-min intervals through a self-retaining catheter, and a volume of saline equal to the urine volume was infused intravenously at the end of each collection period. The clearance of creatinine was used as an index of glomerular filtration rate. A priming dose of 20 mg of creatinine/kg body weight and a maintenance dose of 0.60 mg/kg min^{-1} were used. The creatinine was dissolved in 5% dextrose in water and infused intravenously at an average rate of 0.32 ml/min. Blood samples for creatinine analysis were withdrawn at the midpoints of each urine collection period and replaced with an equal volume of 6% dextran in isotonic saline. Creatinine determinations were made with a Technicon autoAnalyzer. Sodium concentrations were determined in duplicate by an IL model 143 flame photometer. Venous and arterial blood pressures were measured with Statham P23Db transducers which were zeroed at the spinous processes of the vertebral column at T4-T5. Pressures were recorded on an Electronics for Medicine DR-8 recorder.

At the end of each experiment, the carotid arteries were occluded bilaterally below the level of the carotid sinuses for 15 sec. This procedure did not produce changes in heart rate in these dogs, thus confirming that the efferent innervation to the heart had been effectively eliminated.

Student's paired t analysis (two-tailed) was used to compare data obtained during each 10-min interval of the tamponade and recovery periods with the mean control values. The unpaired t test was used to make comparisons between groups of animals. A P value of less than 0.05 was considered to be statistically significant.

Results. Figure 1 presents a summary of the changes in renal function which occurred during atrial tamponade in six dogs with an acute vagotomy and a chronic sympathectomy. Sodium excretion and urine flow decreased from their respective control values throughout the period of tamponade and returned toward control levels during the recovery period. The relative decreases in sodium excretion and urine flow at the end of tamponade were not different statistically ($P > 0.10$, $P > 0.90$, respectively) from the decreases observed at the end of tamponade in earlier experiments on intact, unanesthetized dogs (1).

The hemodynamic changes produced by atrial tamponade during these experiments are shown in Fig. 2. An increase of approximately 6 mm Hg in intrapericardial pressure increased central venous pressure significantly, a finding that was noted previously (3). Mean arterial pressure was decreased throughout the period of tamponade, a finding in contrast to previous results which demonstrated that mean arterial pressure does not change during atrial tamponade in intact dogs (1, 2). Apparently the extensive autonomic denervation procedures used in the present experiments prevented baroreceptor reflexes from maintaining a constant arterial blood pressure during atrial tamponade. Pulse pressure was not changed significantly from control levels. Heart rate changes were small, but a decrease of two beats/min at the onset of tamponade was significant statistically. This change probably was of no biologic significance, but it may have been elicited by a slight decrease in stretch of sinoatrial pacemaker tissue (5) as a result of the tamponade.

The decrease in arterial pressure which occurred during tamponade in these experiments raised the possibility that a small decrease in renal perfusion pressure could have been directly responsible for the observed decreases in sodium excretion and urine flow. This possibility was examined in experiments conducted on another group of eight dogs that had an inflatable occluder

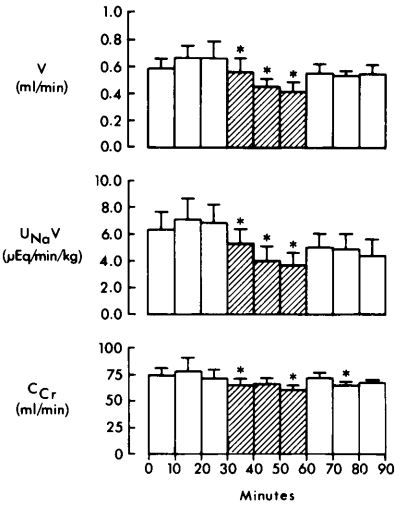

FIG. 1. Renal response to atrial tamponade in six sympathectomized, vagotomized dogs. Values are means ± SE. V, $U_{Na}V$, C_{Cr} denote urine flow, sodium excretion, and creatinine clearance, respectively. Control and recovery periods are depicted by clear bars and the period of atrial tamponade by cross-hatched bars. Asterisks indicate means which differ significantly from control values ($P < 0.05$ or higher levels of significance).

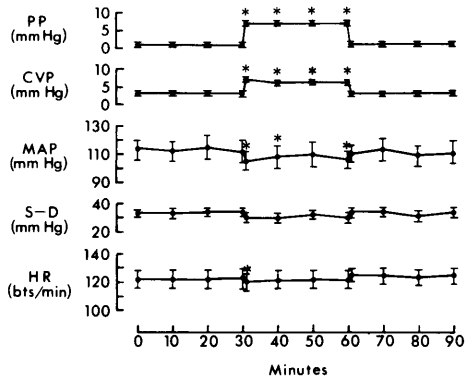

FIG. 2. Hemodynamics recorded in six sympathectomized, vagotomized dogs. PP, CVP, MAP, S-D, and HR denote intrapericardial pressure, central venous pressure, mean aortic pressure, pulse pressure, and heart rate, respectively. Other notations as in Fig. 1.

placed around the descending aorta at the time of their thoracotomy. Prior to the collection of the control urine samples, the aorta was partially occluded to create a pressure gradient of 15–20 mm Hg between the aortic arch and renal arteries. Subsequently, as pressure within the aortic arch decreased slightly during atrial tamponade the degree of aortic occlusion was reduced in order to maintain the renal artery pressure at control levels or to allow it to rise slightly. The aortic occluder was adjusted in the opposite direction at the end of the tamponade period.

As mentioned previously, the recurrent laryngeal nerves were cut bilaterally in three dogs of this group. The data obtained from these three dogs were combined for analysis with the data from the five other dogs because the decreases in sodium excretion and urine flow during atrial tamponade did not differ ($P > 0.30$ and $P > 0.40$, respectively) between the two groups. The effect of atrial tamponade on renal function in these experiments is summarized in Fig. 3. The magnitude of the decreases in sodium excretion and urine flow in these experiments did not differ significantly ($P > 0.70$ and $P > 0.30$, respectively) from the decreases observed previously in intact, unanesthetized dogs (1).

During tamponade there was an increase in central venous pressure and a decrease in mean aortic arch pressure (Fig. 4). Left atrial pressure and pulse pressure were not statistically different from control levels. Heart rate was not altered significantly dur-

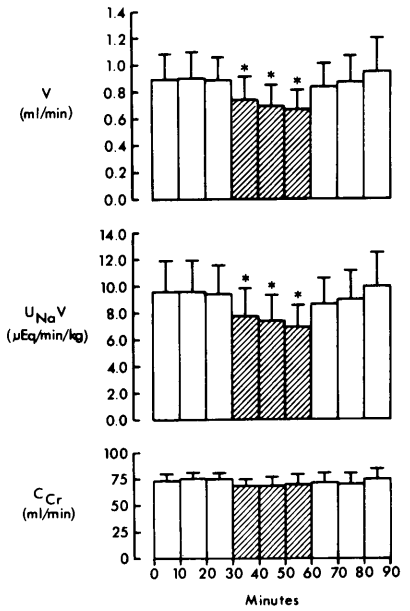

FIG. 3. Renal response in eight sympathectomized, vagotomized dogs in which mean pressure in the renal arteries was maintained constant during atrial tamponade. Notations as in Fig. 1.

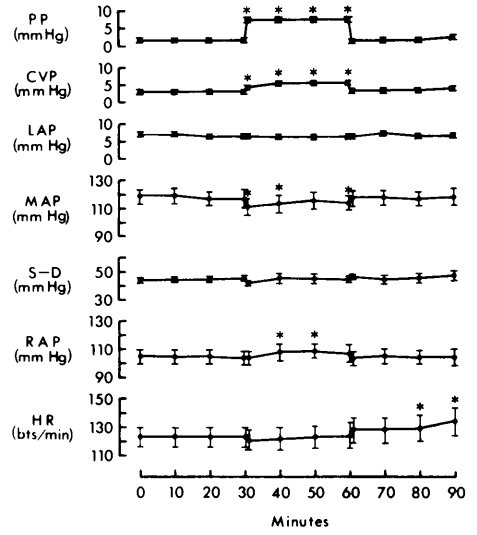

FIG. 4. Hemodynamics recorded in eight sympathectomized, vagotomized dogs in which mean pressure in the renal arteries was maintained constant during atrial tamponade. LAP denotes left atrial pressure, and RAP denotes renal artery pressure. Other notations as in Fig. 2.

ing tamponade but did increase during the latter portion of the recovery period. Pressure at the level of the renal arteries increased slightly, thus the decreases in sodium excretion and urine flow that occurred during tamponade are not attributable to a decrease in the perfusion pressure of the renal arteries in these experiments.

Discussion. These experiments demonstrate that atrial tamponade continues to cause decreases in sodium excretion and urine flow after the known afferent pathways from the heart are severed. Although it is possible that some vestiges of afferent cardiac innervation remained in these dogs, it is highly probable that the majority of fibers were destroyed. The vagus is considered to be the main afferent pathway for impulses from cardiac receptors, and the vagi were divided bilaterally in the midcervical region. In addition, there is considerable evidence indicating that some afferent impulses from the heart reach the central nervous system via the sympathetic rami communicantes (6–8). Therefore all dogs in this study also were sympathectomized from the stellate ganglion through T-5. Although there was no effective way to test for complete afferent denervation of the heart in our studies, we did demonstrate that the efferent pathways were effectively eliminated because bilateral carotid occlusion below the carotid sinuses caused no change in heart rate in these animals. The effectiveness of efferent denervation suggests that afferent cardiac pathways were effectively eliminated also. Finally, since it recently was reported that some afferent impulses from the atria may travel via the laryngeal communicans of the rat (9, 10), we cut the recurrent laryngeal nerves bilaterally in three dogs in order to eliminate this potential pathway for afferent cardiac impulses. Although efferent as well as afferent fibers were eliminated by these procedures, our specific purpose in this study was to eliminate afferent neural pathways from the heart and hence to abolish any reflex effects on renal function which might be initiated by cardiac receptors.

In the experiments in which renal artery pressure was controlled, a direct effect of changes in renal perfusion pressure was ruled out, but it is possible that the reduction in arterial pressure above the occluder may have elicited reflex changes in kidney function which were initiated by carotid sinus baroreceptors. Thus one could argue that the changes in renal function observed during our earlier experiments with intact, conscious animals were mediated at least partly by cardiac reflexes, and that other factors were responsible for the renal response during tamponade in the denervated heart. However, since the magnitude of the antidiuresis and antinatriuresis during atrial tamponade is not altered after cardiac denervation, we favor the conclusion that atrial receptors did not contribute significantly to the renal response elicited by atrial tamponade in our earlier experiments with conscious dogs. We have discussed in detail elsewhere (11) the more general question of whether atrial receptors participate in the physiologic regulation of extracellular fluid volume.

The present experiments did not elucidate the specific mechanisms by which atrial tamponade causes alterations in renal function. The results of this study, however, do imply that the renal excretion of salt and water is quite sensitive to subtle changes in systemic

hemodynamics and that this sensitivity is not noticeably altered following rather extensive denervation of the heart.

Summary. Atrial tamponade was used as a method to reduce atrial transmural pressure in dogs whose afferent pathways from cardiac receptors were interrupted by sympathectomy and vagotomy. Under these conditions, atrial tamponade caused decreases in renal sodium excretion and urine flow which were comparable to those previously observed in intact dogs. These observations lead us to conclude that the changes in renal function which occur during atrial tamponade are not caused by a reflex initiated by atrial receptors. Rather, the alterations in renal function appear to be attributable to unidentified changes in systemic hemodynamics that are elicited by atrial tamponade.

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