Influence of Angiotensin II on the Systemic and Pulmonary Circulations of Intact Anesthetized Dogs[1] (34320)

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Initial hemodynamic studies of angiotensin II were primarily concerned with the influence on arterial blood pressure (1–5). Our interest in the venous system and recognition of its importance in regulation of the circulation prompted these studies to define more clearly the effects of angiotensin II on the veins (6, 7). It was found that in proper doses angiotensin II can constrict systemic precapillary (resistance) vessels without affecting equally postcapillary (capacitance) vessels. Although some studies of the effects of angiotensin II on the pulmonary circulation have been reported (8, 9), the effect on small pulmonary veins of intact dogs has not been previously studied. In these experiments simultaneous pressures and volume flow measurements in many sites of the pulmonary and systemic circulations were obtained in intact dogs during an intravenous infusion of angiotensin II to learn whether or not the hemodynamic effects of angiotensin II on the pulmonary and systemic venous circulations differ.

Material and Methods. Fifteen mongrel dogs weighing 15.0–18.2 kg were lightly anesthetized with urethane (1.5 g/kg) and loosely taped supine to a fluoroscopic table. After the trachea was intubated, 100% oxygen was administered into the endotracheal tube via a plastic catheter at a rate of 2–2.5 liters/min in order to assure that the animals were not hypoxic.

Catheters were placed in the left atrium and a small pulmonary vein of the lower lobe of the left lung by the transseptal technique (10). The pulmonary vein catheter had an internal diameter of 0.5 mm and an external diameter of 0.91 mm. Previous studies showed that this catheter did not significantly alter the pressure in the pulmonary vein (11). Catheters were also placed in the main pulmonary artery, right femoral artery, right atrium, and a small vein of the left leg. Statham strain gauge transducers (P23Db) were used to monitor pressures which were recorded with an Electronics for Medicine research recorder. A catheter for infusion of angiotensin II was placed in the right femoral vein.

After control pressure tracings were recorded, cardiac output and pulmonary blood volume were determined by the indicator dilution technique using indocyanine green (Cardio-Green) (12). The stroke volume and pulmonary and systemic vascular resistances were calculated by methods previously described (13). The pulmonary venous resistance was calculated by the formula: Pulmonary venous resistance = PVS — PLA/CO, where PVS is pressure in small pulmonary vein, PLA is left atrial pressure and CO is cardiac output. Lead II of the electrocardiogram, heart rate and respiratory rate were also monitored.

After a "steady state" was reached for 10–15 min, as indicated by relatively constant cardiac output and pressures, angiotensin II (5 μg/min) was infused into the right femoral vein for 6 min. Pressure and dye-dilution curves were recorded at 3-min intervals during the infusion. These recordings were repeated 5 and 15 min after the infusion was stopped.

Results. The results are summarized in Table I and Fig. 1–2.

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Pulmonary veins and pulmonary circulation. Pressure in the small pulmonary vein (PVS) increased very little in 10 dogs and decreased slightly in 5 following infusion of angiotension II into a systemic vein. The slight increase in PVS was always associated with an increase in pressure in the left atrium (PLA). Mean pulmonary arterial pressure (PPA) increased in 12 dogs and slightly decreased in 3. The rise in PPA was always associated with either an increase in PLA and PVS or an increase in pulmonary blood volume (PBV) but not both. The *calculated* pulmonary vascular resistance increased very little in 13 dogs and decreased in 2, while the *calculated* pulmonary venous resistance decreased slightly in 13 dogs and increased in 2 dogs. A slight increase in pulmonary blood volume occurred in 8 dogs and a slight decrease occurred in 7.

Systemic circulation. Following intravenous administration of angiotensin II, systemic circulatory changes consisted of a decrease in cardiac output, an increase in arterial blood pressure, a decrease in heart rate and an increase in calculated systemic vascular resistance in all dogs. A relatively slight, probably not significant increase in pressure in the leg vein was noted in 12 of 14 dogs. The left atrial mean pressure increased in 13 dogs and was unchanged in 2 dogs. Right atrial pressures were recorded in 9 dogs and showed an increase in 5, decrease in 3 and no change in 1.

Discussion. Intavenous infusion of angiotensin II increases slightly the pressure in intact systemic venous segments of man. This response can be prevented by blocking the nerve supply to the vein (6, 7). Injection of angiotensin II into the isolated peripheral venous segment produced no change in its pressure and tone (6). These studies and studies with the digital rheoplethysmograph showed that angiotensin II in proper doses can constrict systemic precapillary (resistance) vessels with little associated constriction of postcapillary (capacitance) vessels of man (6, 7).

Like the systemic capacitance vessels noted in the above studies, the pressure in the small pulmonary vein remained essentially

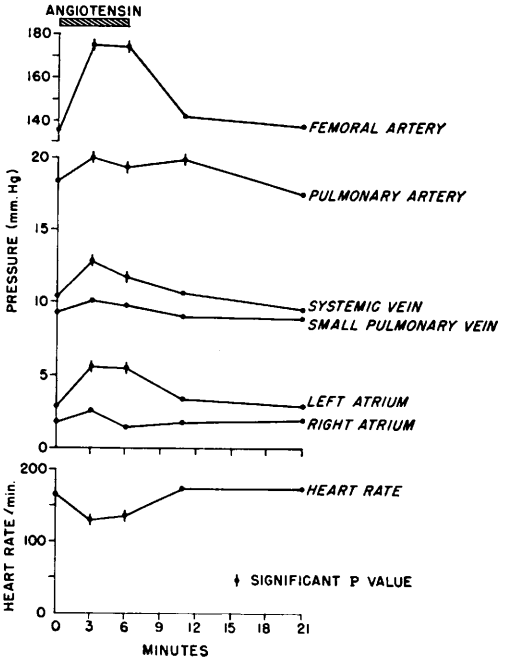

FIG. 1. Effect of angiotensin II injected intravenously (5 μg/min) on mean pressures in pulmonary vascular bed, right and left atria, systemic vein, femoral artery and heart rate of 15 intact normal dogs. The physiologic phenomena illustrated in Fig. 1 and 2 were all recorded simultaneously.

unchanged in the dog. Since pulmonary blood volume remained constant, pulmonary venous tone was also probably unchanged (Figs. 1, 2). However, a slight increase in pressure in the small pulmonary vein was noted in some dogs. This was always associ-

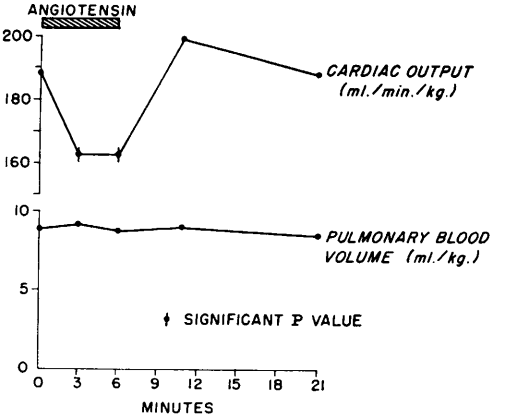

FIG. 2. Effect of angiotensin II injected intravenously (5 μg/min) on mean cardiac output and pulmonary blood volume of 15 intact normal dogs.

TABLE I. Hemodynamic Responses to Angiotensin II in Intact Dog (av for 15 dogs).

	Control	Angiotensin II (5 μg/min iv; 6 min)	Recovery after infusion 5 min	Recovery after infusion 15 min	p value[a]
Cardiac output (ml/kg/min)	188	163	200	189	.01
Heart rate (beat/min)	165	139	173	173	.001
Stroke volume (ml)	19.1	19.9	19.2	18.4	.5
Femoral artery (mean) pressure (mm Hg)	135	174	142	136	.001
Systemic resistance (units)	46.4	71.1	46.8	45.9	.001
Leg vein (mean) pressure (mm Hg)	10.4	11.8	10.5	9.6	.30
Pulmonary artery (mean) pressure (mm Hg)	18.4	20.8	19.8	17.6	.05
Left atrial (mean) pressure (mm Hg)	2.9	5.4	3.3	2.7	.01
Right atrial (mean) pressure (mm Hg)	1.8	2.3	1.7	2.1	.4
Small pulmonary vein (mean) pressure (mm Hg)	9.4	9.7	8.9	8.9	.6
Pulmonary vascular resistance (units)	5.10	6.08	5.20	4.96	.1
Pulmonary venous resistance (units)	2.18	1.67	2.06	2.12	.05
Pulmonary blood volume (ml/kg)	8.92	8.77	9.00	8.57	.7
Respiratory rate (per min)	30.7	29.9	35.1	36.6	.9

[a] p values were obtained by the t test as described in Fisher and Yates, "Statistical Tables for Biological, Medical and Agricultural Research," Oliver and Boyd, Edinburg and London (1938).

ated with a slight increase in left atrial pressure. Because most dogs had an increase in left atrial pressure without an increase in pulmonary vein pressure, calculated pulmonary venous resistance was low in spite of an associated low cardiac output (pulmonary blood flow). Such differences in pressure between that in the left atrium and small pulmonary vein have been described by us previously (14). The decrease in calculated pulmonary venous resistance in association with a low cardiac output (pulmonary blood flow) (Table I) is compatible with low venous tone following the administration of angiotensin II.

The increase in pulmonary arterial pressure observed in some dogs was not striking, and in 3 dogs the pressure actually decreased. This was consistent with studies on animals in which pulmonary blood flow and left atrial pressure were controlled (8, 9, 15). In these latter studies the rise in pulmonary arterial pressure was considered to be due to an increase in left atrial pressure (8) or to systemic effects resulting in an increase in PBV (15).

In view of the finding of little to no increase in pulmonary vein pressure and in pulmonary blood volume, the slight increase in pulmonary arterial pressure most likely was due to action of the angiotensin II, in the doses used, on the pulmonary arterial vessels. It is interesting that angiotensin II has strong vasoconstrictive action on the systemic arterial system in relatively small doses and little effect upon the pulmonary arterial system, pulmonary veins, and systemic veins. Since the dogs were intact except for the anesthesia, these findings are particularly significant and not influenced by major operative procedures.

Systemic precapillary constriction is evident from the increase in femoral arterial pressure and calculated systemic vascular resistance (Table I). It has been suggested that some of the decrease in cardiac output is a secondary to decreased myocardial blood flow (16, 17). However, the bradycardia produced by the rise in systemic arterial pressure most probably accounts for a major proportion of the decrease in cardiac output. The systemic venous pressure changed very little.

Summary. Responses of the small pulmonary veins to systemic intravenous infusion of angiotensin II were measured directly in 15

intact anesthetized dogs. Systemic and pulmonary venous pressures were essentially unchanged. Change in pulmonary arterial pressure was not marked and probably due to action of angiotensin on the pulmonary arterial system. Systemic arterial pressure increased markedly while cardiac output decreased. Thus, angiotensin II in the doses used constricts precapillary systemic vessels but at the same time has little effect on the pulmonary and systemic veins and on the pulmonary arterial system.

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