Effects of Vasopressin on Femoral Arterial Blood Flow and Pressure in the Anesthetized Dog. (26386)

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The action of extracts of the posterior pituitary on renal reabsorption of water and electrolytes, milk let-down, and uterine activity has been stressed in studies of the physiological role of this endocrine gland. Little evidence is available regarding the action of exogenous vasopressin on the cardiovascular system, with the exception of studies in which the dose employed greatly exceeds the maximal antidiuretic dose(1,2,3); recently, Kitchin(4) has studied the effects of small doses of vasopressin on hand and forearm blood flow. The present study considers the dose-response relationship between vasopressin and femoral arterial blood flow and pressure.

Materials and methods. Five mongrel dogs weighing 9.5 to 14.6 kg were used. Sodium pentobarbital, 30 mg/kg, was used to induce anesthesia; supplementary doses were administered during the experiment to maintain a moderately deep surgical plane. Mepesulfate* or heparin was administered after completion of all dissections and before cannulation to prevent coagulation. The right jugular vein was cannulated percutaneously by means of a plastic needle described by Lundy (5); supplementary anesthesia, anticoagulant, and intravenous vasopressin were administered through it. Rate of flow in the left femoral artery was measured with a cannulating-type square wave electromagnetic flowmeter after the design of Denison and Spencer(6). The artery was cannulated proximally and distally through a single slit with polyethylene tubing (PE 280). A shunt around the flowmeter pickup allowed the zero flow to be established without producing occlusion of the arterial inflow to the bed under study. This shunt was occluded during the experiment. A short length of rubber tubing, inserted into the distal cannula, was used for intra-arterial injections. Lateral pressure was recorded distal to the flowmeter pickup with a Statham pressure transducer. The output of the flowmeter and pressure transducer was fed into a 2-channel Grass polygraph equipped with low-level D.C. preamplifiers. The flowmeter was calibrated at the end of each experiment by bleeding the animal through the pickup into a graduated cylinder at different rates.

Vasopressin† was injected intra-arterially (IA) in graded doses of 0.1 to 5.0 milliunits (mU) of pressor activity; intravenous (IV) doses of 5 to 100 mU were also studied. Dilutions were prepared for each experiment in 0.9% saline; IA injections were limited to 0.2 ml and I.V. to 3 ml so that they could be administered rapidly, *i.e.*, <2 seconds. Con-

TABLE I. Mean Response ± Standard Error Following IA Injection of Vasopressin Expressed as Per Cent of Control Flow, Pressure, and PRU.

Dose, mU	No. of animals*	Time, sec.	Flow, %†	Pressure, %	PRU, %†
.1	4 (5)	50 ± 5	93 ± .9	101 ± .3	108 ± 1
.2	4 (7)	49 ± 7	89 ± 1.4	101 ± .6	113 ± 2
.5	4 (6)	64 ± 4	81 ± 2.8	101 ± 4.8	126 ± 5
1.0	5 (6)	47 ± 7	68 ± 1.8	101 ± 2.0	149 ± 5
2.0	5 (6)	52 ± 9	60 ± 4.9	102 ± 1.7	176 ± 18
5.0	4 (4)	49 ± 11	36 ± 5.3	104 ± 1.0‡	306 ± 41

* No. of injections in parentheses.
† Flow and PR changes significantly different from control ($p < .01$).
‡ Significantly different from control ($p < .05$).

* Hoffmann LaRoche, Inc., Nutley, N. J.
† Pitressin,(R) obtained from Parke, Davis & Co.

trol saline injections were made by both routes in each experiment. A minimum of 4 minutes elapsed between subsequent injections.

Changes in mean pressure and flow were calculated at the point of greatest response, whether it represented a decrease or increase, and are expressed as percentage of control value. Resistance to flow was calculated in PRU(7) and expressed as percentage of control value.

Results. Control data. IA and IV saline did not produce a significant change in flow or pressure. The 2-minute period before each injection was used to establish the control flow and pressure for that injection.

Intra-arterial injections (Table I). The flow was observed to decrease following each of the 34 injections by this route; mean decrease at time of maximum response was found to be significantly different from the control ($p<0.01$) at all doses. Mean arterial pressure remained essentially constant during the entire flow response.

Intravenous injections (Table II). A biphasic flow response was observed after administration by this route; an initial increase in flow which had a duration of 40-180 seconds followed by a decrease in flow below the control level. In general, mean pressure change at either the maximum increase or maximum decrease in flow could not be interpreted as significant. Maximum mean increase in pressure observed during the entire response was significantly different from the control ($p< 0.05$), although only 5 mU fforteatohmrcmx 50 mU vrs 100 mU show significant differences from each other.

Discussion. Our results indicate that vasopressin administered IA induces vasoconstriction without significant elevation of arterial pressure; a consistent dose-response relationship was found. Kitchin(4) observed a similar reduction in forearm flow during IA infusion of vasopressin. The transient increase in flow preceding vasoconstriction reported by Woodbury and Ahlquist(2) was not observed in any of our experiments. They attributed this increase to a dilation

TABLE II. Mean Response ± Standard Error (S.E.) Following I.V. Injections of Vasopressin Expressed as Per Cent of Control Flow and Pressure.

Dose, mU	No. of animals*	Maximum flow increase			T_c, sec.†	Maximum flow decrease			Maximum pressure	
		Time, sec.	Flow, %	Pressure, %		Time, sec.	Flow, %	Pressure, %	Time, sec.	Pressure, %
5	4 (6)	53 ± 11	114 ± 3.9	100 ± .4	116 ± 27	214 ± 39	90.8 ± 2.1	101 ± 1.1	57 ± 16	103 ± .5‡
10	5 (6)	42 ± 7	128 ± 5.6	103 ± 2.3	93 ± 16	183 ± 20	86.2 ± 2.0	105 ± 2.0‡	73 ± 22	106 ± 1.9‡
25	4 (4)	41 ± 8	134 ± 9.4	107 ± .5‡	106 ± 22	234 ± 25	80.8 ± 2.0	103 ± 1.6	82 ± 35	104 ± 1.4‡
50	5 (5)	35 ± 4	144 ± 8.2	102 ± 1.3	97 ± 21	186 ± 29	65.7 ± 4.6	105 ± 1.5‡	103 ± 29	108 ± 1.0‡
100	3 (3)	38 ± 5	163 ±21	103 ± 0 ‡	64 ± 11	143 ± 35	66.7 ± 2.8	108 ± 5.7	83 ± 6	112 ± 3.2‡

* No. of injections in parentheses.
† Time to return to control flow following initial increase.
‡ Pressure changes significantly different from control ($p < .05$).

of the cutaneous beds supplied by the femoral artery. Experiments are in progress to study the comparative effects of vasopressin on cutaneous and muscular flow.

A consistent dose-response relationship for flow was noted following IV administration both at the time of maximum flow increase and decrease; in the latter case, saturation seems to occur at higher doses. This biphasic response was also observed by Woodbury and Ahlquist(2), who used considerably larger doses than we employed. The initial increase in flow probably results from the slight elevation of arterial pressure; the inconsistent dose-response relationship for pressure suggests that other factors may also be important. It was therefore postulated that reflex adjustment of the peripheral resistance was necessary to explain fully the initial increase in flow.

The secondary decrease in flow results primarily from the direct action of vasopressin on the peripheral bed. This interpretation considers the time fatcor as well as an estimate of the effective concentration of the drug in the periphery. It appears unlikely that this vasoconstriction occurs reflexly since a moderate elevation of pressure was observed to prevail before and during the secondary flow response.

It has been repeatedly demonstrated that small amounts (0.25 mU/kg) of exogenous vasopressin produce a pronounced antidiuretic response in the dog(8). It has been argued that vasopressin is not important physiologically in control of cardiovascular function in that relatively large quantities (200 mU) are required to elevate the arterial pressure of the dog(8), and that significant reduction in arterial pressure has not been reported following hypophysectomy. The results of the present study indicate that elevation of arterial pressure is not an adequate criterion for assessing vascular activity of vasopressin whereas the elevation of peripheral resistance reveals the sensitivity of the peripheral bed. It is tentatively postulated that submaximal antidiuretic amounts of the exogenous material are really vasoactive amounts. This hypothesis is currently under investigation.

Conclusions. The dose-response relationships which describe the effects of small amounts of vasopressin on femoral arterial pressure and flow have been presented. The IA and IV routes of administration were examined in 5 experiments on anesthetized dogs. The decrease in flow following IA administration and the secondary decrease in flow following IV administration have been attributed to vasoconstriction in the vascular bed supplied by the femoral artery. The primary increase in flow following IV administration has been discussed in terms of elevation of central arterial pressure and reflex vasomotor activity. It is postulated that submaximal antidiuretic amounts of exogenous vasopressin are vasoactive.

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