ROLE OF CATECHOLAMINES IN ANGIOTENSIN INDUCED HYPERGLYCAEMIA

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Summary: The effects of angiotensin II were studied on blood sugar level in dogs. Intracerebroventricular administration of pressor dose of angiotensin caused a rise in blood sugar level. The hyperglycaemia and pressor response was not affected by bilateral vagotomy and was less marked in adrenalectomized dogs. The hyperglycaemic effect and pressor response was not observed in reserpinized and spinal vagotomized dogs.

It is suggested that centrally administered angiotensin stimulates the hypothalamic or medullary accelerator neurons (central sympathetic structures) to cause a marked release of catecholamines from peripheral stores specially adrenal medulla. This excessive release of catecholamines is responsible for hyperglycaemia and pressor response of angiotensin II in dogs.

Key words: angiotensin, cerebroventricular perfusion, catecholamines, hyperglycaemia, adrenalectomy, spinal vagotomy

INTRODUCTION

It has been long known that most of the pressor agents have significant metabolic effects. The catecholamines cause a rise in blood sugar level (19).

Angiotensin is a well known pressor agent when administered centrally or peripherally (3, 15,17). Angiotensin is also responsible for pheripheral release of endogenous hormones like aldosterone (4,13) and catecholamines (6,12).

It was the observation of increased excretion of aldosterone and its metabolites in urine of patients with hypertension that led Benetato *et al.* (4) to investigate the action of angiotensin on suprarenals and subsequently Laragh *et al.* (13), to show increased secretion rate of angiotensin in subjects with severe or malignant hypertension. This pressor effect was due to excessive secretion of catecholamines from its stores by the action of angiotensin on central or peripheral sympathetic structures (7,15,17).

Triner *et al.* (18) demonstrated an insignificant change in blood sugar level, when angiotensin was administered intravenously in dogs. Heindenreich *et al.* (10) observed a transient rise in blood glucose during intravenous infusion of angiotensin in dogs. But Healy *et al.* (9) and Iizuka *et al.* (11) did not find any significant change in blood glucose level in dogs on administration of angiotensin II. Nakano and Kusakari (14) reported a fall in blood glucose level when angiotensin was infused intravenously in dogs. Angiotensin has been reported to markedly interfere with the autonomic nervous system activity and has been claimed to affect release, uptake and synthesis of the adrenergic neurotransmitters (8). Besides, there is now evidence suggesting that angiotensin is endogenous to brain and like most tissues the brain also

cerebral ventricle following bilateral vagotomy in five dogs. The increase in blood sugar level was observed within 15 minutes reaching its maximum level within 60 minutes and then gradually decreased to basal level within 135 minutes (Table I, Fig. 1). There was increase in mean blood pressure level to 147.74±12.76 *mm* Hg from a control mean value of 106.35± 13.28 mm Hg (Table I, Fig. 2-B). The maximum blood pressure was observed within 5 minutes reaching its control level within 30 minutes.

TABLE I: Effect of intracerebroventricular administration of angiotensin II (4 μg) on blood sugar and blood pressure in dogs following different experimental procedures.

No. of Experiments	*Experimental procedure*	*Control blood sugar (mg/100 ml) Mean value±SD*	*Maximum rise in blood sugar (mg/100 ml) Mean value±SD*	*Control blood pressure (mm Hg) Mean value±SD*	*Maximum rise of blood pressure (mm Hg) Mean value±SD*
Ten	Normal	102.76±11.94	198.54±13.59	95.84±12.67	137.24±13.54
Five	Bilateral vagotomy	108.28±12.17	196.68±14.26	106.35±13.28	147.74±12.76
Five	Adrenalectomy	98.78±10.98	119.27±12.86	56.73± 6.14	87.94±8.36
Five	Reserpinized	87.94±12.36	No rise	62.68± 6.28	No rise
Five	Spinal section and vagotomy	91.28±12.68	No rise	61.82± 8.53	No rise

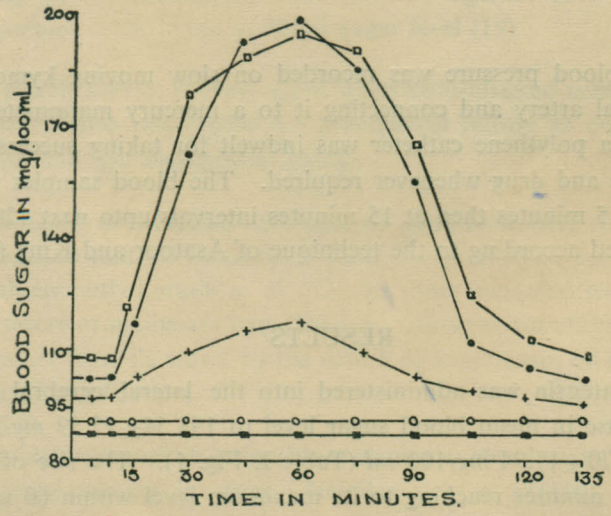

Fig. 1: Showing effects of intracereboventricular administration of angiotensin II (4.0 μg) on blood sugar level in dogs under different experimental procedures.

1. Normal dogs
2. Vagotomized dogs
3. Adrenalectomized dogs
4. Reserpinized dogs
5. Spinal section and vagotomized dogs.

When angiotensin was administered into lateral cerebral ventricle of five adrenalectomized dogs, there was increase in mean blood sugar level to 119.27±12.86 *mg*/100 *ml* from a control mean value of 98.78±10.98 *mg*/100 *ml*. The maximum rise in blood sugar level was observed

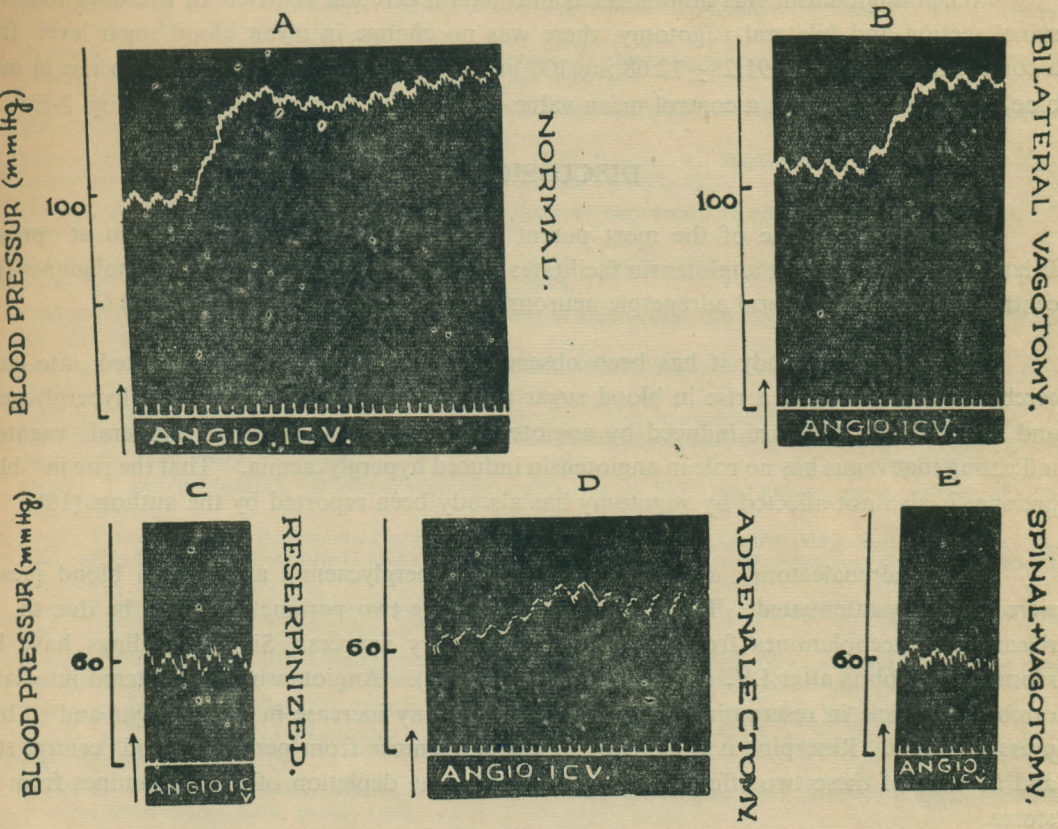

Fig. 2: Showing effects of intracerebroventricular admini stration of angiotensin II (4.0 μg) on blood pressure in dogs under different experimental procedures.

A. Normal dogs
B. Vagotomized dogs
C. Reserpinized dogs
D. Adrenalectomized dogs
E. Spinal section and vagotomized dogs.
Horizontal calibration indicates 30 seconds.

within 60 minutes reaching its normal level within 135 minutes (Table I, Fig. 1). There was an increase in mean blood pressure level to 78.25±8.53 *mg* Hg from a control mean value of 56.73±6.14 mm Hg. (Table I, Fig. 2-D).

There was no change in mean blood sugar level from a control mean value of 89.74±8.36 *mg*/100 *ml* when angiotensin was injected into lateral cerebral ventricle of five dogs 24 hours

after reserpinization (Table I, Fig. 1). There was no change in mean blood pressure level from a control mean value of 62.68±6.26 *mg* Hg (Table I, Fig. 2-C).

When angiotensin was administered into lateral cerebral ventricle of five dogs following spinal section and bilateral vagotomy, there was no change in mean blood sugar level from a control mean value of 91.28±12.68 *mg*/100 *ml* (Table I, Fig. 1). There was no rise in mean blood pressure level from a control mean value of 61.82±8.53 mm Hg (Table I, Fig. 2-E).

DISCUSSION

Angiotensin is one of the most potent vasoconstrictor substances known at present. It has been observed that angiotensin facilitates or promotes the release of catecholamines from central as well as peripheral adrenergic neurons and from the adrenal medulla (4,6).

In the present study it has been observed that angiotensin administered into lateral cerebral ventricle causes a rise in blood sugar and blood pressure levels. The hyperglycaemia and rise in blood pressure induced by angiotensin were not affected by bilateral vagotomy indicating that vagus has no role in angiotensin induced hyperglycaemia. That the rise in blood pressure is also not affected by vagotomy has already been reported by the authors (16).

After adrenalectomy, angiotensin induced hyperglycaemia and rise in blood pressure were markedly attenuated. The small change in these two parameters could be due to the release of catecholamines from other extra-medullary sources. Similar findings have been reported in rabbits after I.V. infusion of angiotensin(2). Angiotensin administered into lateral cerebral ventricle in reserpinized dogs did not show any increase in blood sugar and blood pressure levels. Reserpine is a depletor of catecholamines from peripheral and central stores and absence of these two effects seem to be due to the depletion of catecholamines from its stores.

It is suggested that angiotensin administered into lateral cerebral ventricle stimulates the central sympathetic structures (hypothalemic or medullary neurons) to cause a marked release of catecholamines from peripheral stores specially adrenal medulla. This contention is sustained by the observation in spinal and vagotomized preparations also. The hyperglycaemia and increased blood pressure level in dogs are therefore due to the liberation of catechamines induced by angiotensin.

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