EFFECT OF CENTRALLY ADMINISTERED ANGIOTENSIN ON URINE OUTPUT IN DOGS

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Summary: The effect of angiotensin II was studied on urine volume, urine sodium and potassium in mongrel dogs. Intracerebro-ventricular (icv) administration of angiotensin (100.0 μg) caused significant increase in urine volume without significant change in urine sodium and potassium level. Similar effect is also obtained in denervated dogs. The effect of intracerebroventricularly administered angiotensin is possibly due to the decrease in secretion of the Antidiuretic hormone (ADH) from posterior lobe of pituitary gland.

Key words: Angiotensin vagotomy spinal section polyuria

INTRODUCTION

It has been generally accepted that the pressor effects of angiotensin are the result of the direct action of the polypeptide on the vascular smooth muscle (6). Studies by Benelli et al. (2) and Feldberg et al. (7) have suggested that angiotensin may facilitate or promote the release of catecholamines from central and peripheral adrenergic neurones and adrenal medulla. Walter et al. (14) and Smookler et al. (13) concluded that angiotensin II administered into perfused lateral ventricle of the anaesthetized cat produced marked pressor response of central origin. Angiotensin has been shown to have a direct renal action (5). Angiotensin has been shown to have a direct renal action (5).

In view of the reported relationship of angiotensin with hypertension and its involvement in the control of sodium balance by aldosterone secretion (9) it was thought to investigate the effect of intracerebroventricular administration of angiotensin on urine volume, urine sodium and potassium in dogs.
**MATERIAL AND METHODS**

Male and female dogs, weighing 8-12 kg were used in the present study. They were anaesthetized with 10% chloralose solution (80-100 mg/kg) in normal saline and administered intravenously. The standard dose of angiotensin II (Hypertensin-Ciba) used was 100 μg in 0.2 ml normal saline administered by intracerebroventricular route after any surgical procedure. Intravenous infusion of normal saline was made (10 drops/min) through a polythene catheter into femoral vein throughout the experiment. Cannulation of lateral cerebral ventricle was done according to the technique of Bhargava and Tangri (4). A constant ventilation of lungs was maintained by intubation of the trachea and connecting it to a respirator. The spinal cord was transected at C2 level and bilateral vagotomy (denervation) was done according to the technique of Singh et al. (12). B.P. dropped to the level of 60±10 mm Hg at the time of spinal transection which again returned to the level of 100±10 mm Hg at the time of icv administration. In all the dogs both ureters were cannulated and urine samples were collected in measuring cylinders with the help of polythene catheter inserted in ureters. The urine volume was measured at 15 min interval for 120 min and its sodium and potassium contents were estimated with the help of flame photometer. In five control experiments, the effect of this infusion on urine volume, urine sodium and potassium was observed and it was found that constant infusion caused a steady flow of urine after 60 min of starting the infusion.

**RESULTS**

*Effect of intracerebroventricular administration of angiotensin II :*

In twelve normal anaesthetized dogs administration of angiotensin produced a significant increase in urine volume without significant change in urine sodium and potassium. The maximum effect was observed in 45 min followed by a gradual return to the basal level within 180 min (Table I). Repeated ICV administration of angiotensin at 180 min interval produced similar type of response 0.2 ml of vehicle solution alone did not cause any significant change in urine volume, urine sodium and potassium.

*Effect of intracerebroventricular administration of angiotensin/ following spinal section and bilateral vagotomy :*

Angiotensin again caused a significant increase in urine volume without significant change in urine sodium and potassium in twelve dogs (Table I).
Angiotensin is one of the most potent vasoconstrictor known at present. It has been observed that angiotensin facilitates or promotes the release of catecholamines from central as well as peripheral adrenergic neurones and from adrenal medulla (7,10). Ganten et al. (8) reported that angiotensin is endogenous to brain and that brain contains renin, renin substrate, angiotensin converting enzyme and angiotensin II. Besides most tissue contain enzymes catabolizing angiotensin. Barthwal et al. (1) showed that angiotensin is present in brain stem specially in hypothalamus of dog's brain.

In present study, intracerebroventricularly (ICV) administered angiotensin caused a significant increase in urine volume (P > 0.05) without significant change in urine sodium and potassium. The possibility of the effect being mediated by nervous involvement mainly by stimulation of sympathetic nerves of kidney is also ruled out by the fact that sympathetic stimulation causes a profound decrease in urine volume and electrolyte excretion (10). Repeated ICV administration of angiotensin at 180 min interval resulted in a similar type of response. This indicates that phenomenon of tachyphylaxis is not a complicating factor under these experimental conditions. The persistence of effect in spinal section and vagotomized (denervated) dogs indicates that nervous connections do not play any role in angiotensin induced polyuria (P > 0.001).

**TABLE I**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Normal 12 dogs</th>
<th>Denervated 12 dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>U.V. (ml)</td>
<td>U. Na+ (meq/L)</td>
</tr>
<tr>
<td>Initial</td>
<td>3.4 ± 0.38</td>
<td>108 ± 8.2</td>
</tr>
<tr>
<td>15</td>
<td>4.2 ± 0.44</td>
<td>112 ± 10.6</td>
</tr>
<tr>
<td>30</td>
<td>4.8 ± 0.53</td>
<td>110 ± 8.8</td>
</tr>
<tr>
<td>45</td>
<td>5.8 ± 0.62*</td>
<td>109 ± 7.5</td>
</tr>
<tr>
<td>60</td>
<td>5.6 ± 0.33**</td>
<td>104 ± 8.7</td>
</tr>
<tr>
<td>75</td>
<td>4.8 ± 0.44</td>
<td>114 ± 8.4</td>
</tr>
<tr>
<td>90</td>
<td>4.6 ± 0.33</td>
<td>110 ± 8.4</td>
</tr>
<tr>
<td>105</td>
<td>4.0 ± 0.42</td>
<td>112 ± 9.2</td>
</tr>
<tr>
<td>120</td>
<td>3.6 ± 0.33</td>
<td>110 ± 6.8</td>
</tr>
<tr>
<td>180</td>
<td>3.4 ± 0.36</td>
<td>106 ± 7.5</td>
</tr>
</tbody>
</table>

*P > 0.05  **P > 0.001

**DISCUSSION**

Angiotensin is one of the most potent vasoconstrictor known at present. It has been observed that angiotensin facilitates or promotes the release of catecholamines from central as well as peripheral adrenergic neurones and from adrenal medulla (7,10). Ganten et al. (8) reported that angiotensin is endogenous to brain and that brain contains renin, renin substrate, angiotensin converting enzyme and angiotensin II. Besides most tissue contain enzymes catabolizing angiotensin. Barthwal et al. (1) showed that angiotensin is present in brain stem specially in hypothalamus of dog’s brain.

In present study, intracerebroventricularly (ICV) administered angiotensin caused a significant increase in urine volume (P > 0.05) without significant change in urine sodium and potassium. The possibility of the effect being mediated by nervous involvement mainly by stimulation of sympathetic nerves of kidney is also ruled out by the fact that sympathetic stimulation causes a profound decrease in urine volume and electrolyte excretion (10). Repeated ICV administration of angiotensin at 180 min interval resulted in a similar type of response. This indicates that phenomenon of tachyphylaxis is not a complicating factor under these experimental conditions. The persistence of effect in spinal section and vagotomized (denervated) dogs indicates that nervous connections do not play any role in angiotensin induced polyuria (P > 0.001).
It is suggested that ICV angiotensin inhibits the hypothalamic neurones which are responsible for secretion of antidiuretic hormone from posterior lobe of pituitary gland. This decrease in secretion of ADH causes polyuria in dogs. It is speculated that the receptors site for the action of angiotensin lies in the brain although the precise area of brain responsive to angiotensin could not be localized. The receptors of ADH release appears to lie in the paraventricular nuclei and angiotensin diffuses out of ventricular system and comes in contact with its receptors of nuclei known to be associated with ADH secretion (11). Our finding does not support the finding of Mouw et al. (11) who observed a significant release of ADH when angiotensin was perfused in the ventricular system.

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REFERENCES