Effect of Tetramethylammonium and Potassium Chloride on Adrenal 17-Hydroxycorticosteroid Secretion in Unanesthetized Dogs

By Tatuzi Suzuki, Sennosuke Ohukuzi, Hideo Matsui and Kensaku Otsuka

From the Department of Physiology, Nagasaki University
School of Medicine, Nagasaki

(Received for publication, August 20, 1965)

Adrenal 17-hydroxycorticosteroid (17-OHCS) secretion was followed after injection of tetramethylammonium or potassium chloride. In unanesthetized dogs the adrenal venous blood was collected by a modification of the method of Satake and his co-workers and was analyzed for 17-OHCS by the method of Nelson and Samuels. The 17-OHCS secretion rate before injection was 0.03-0.29 μg/kg/min. After injection of tetramethylammonium it increased markedly in all of 3 dogs and attained to 1.10-1.43 μg/kg/min. After injection of potassium chloride it increased definitely in 2 of 3 dogs and attained to 1.14-1.73 μg/kg/min.

In our previous study1 the effect of eserine and atropine on adrenal 17-hydroxycorticosteroid (17-OHCS) secretion rate in unanesthetized dogs was evaluated directly. A marked increase in 17-OHCS secretion was observed after i.v. injection of eserine or atropine. In the present study effect of two ganglionic stimulating agents, tetramethylammonium (TMA) and potassium chloride (KCl), on adrenal 17-OHCS secretion was evaluated directly in unanesthetized dogs.

METHODS

Six mongrel dogs, 12 to 15 kg in weight, were used in experiments. The adrenal venous blood collection was performed by using a modification of the method of Satake, Sugawara and Watanabe,2 as was done in our previous studies.1,3-7 The dorsal spinal roots of the 11th thoracic to the 3rd lumbar spinal cord segments, in which the sensory nerve fibers from the lumbar region run, were cut under sodium pentobarbital (25 mg/kg, i.v.) anesthesia. Experiments were carried out several weeks after spinal root section. On the day before experiment the lumbo-adrenal vein was exposed by the lumbar approach without opening the abdominal cavity. Small side branches of the lumbo-adrenal vein were doubly...
ligated and cut. Adrenal vein cannulation was made at the site just lateral to the adrenal gland. A small rubber tube was connected with the cannula. For directing the adrenal blood flow to the exterior through the cannula and the rubber tube, a silk thread was placed around the adrenal vein between the adrenal gland and the vena cava, the thread being pulled gently at the time of adrenal venous blood collection. Heparin sodium was used for preventing blood coagulation. About 18 hr after the adrenal vein cannulation the actual experiment was started.

For the estimation of pre-injection secretion rates adrenal venous blood was collected twice with a 20-min interval. Then TMA or KCl was injected. Tetramethylammonium bromide (Merck) was injected i.v. as 0.4% solution in a dose of 1.0 mg/kg body-wt. in 15 sec KCl was injected i.v. as 10% solution in a dose of 30 mg/kg in 30 sec. At 5, 10, 20, 40, 60 and 90 min after injection of TMA or KCl the adrenal venous blood samples were taken. Adrenal venous plasma was analyzed for 17-OHCS by the method of Nelson and Samuels.8

RESULTS AND DISCUSSION

Just before end of TMA injection, deep and fast respiration was observed, which lasted for about 45 sec. In experiments of KCl injection respiration became deeper and faster at the end of injection. However it returned soon to its pre-injection rate and depth.

Adrenal 17-OHCS secretion rate before and after injection of TMA or KCl are presented in Table I. The pre-injection secretion rates of 17-OHCS were 0.03-0.29 µg/kg/min. After injection of TMA the 17-OHCS secretion rate increased markedly without exception, the maximal secretion rate being 1.10-1.43 µg/kg/min. At 40 min after injection of TMA the secretion rate resumed the pre-injection secretion rate. In our previous study it was found that the adrenal 17-OHCS secretion rate increased after injection of eserine and it resumed the pre-injection value after 60-90 min. An elevated level of the adrenal 17-OHCS secretion rate

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Body-wt. kg and sex</th>
<th>Injection</th>
<th>Adrenal 17-OHCS secretion rate µg/kg/min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Min before injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>1</td>
<td>15.4 ♀</td>
<td>TMA</td>
<td>0.14</td>
</tr>
<tr>
<td>2</td>
<td>13.9 ♀</td>
<td>&quot;</td>
<td>0.05</td>
</tr>
<tr>
<td>3</td>
<td>12.9 ♀</td>
<td>&quot;</td>
<td>0.05</td>
</tr>
<tr>
<td>4</td>
<td>14.0 ♀</td>
<td>KCl</td>
<td>0.13</td>
</tr>
<tr>
<td>5</td>
<td>12.3 ♀</td>
<td>&quot;</td>
<td>0.21</td>
</tr>
<tr>
<td>6</td>
<td>12.1 ♀</td>
<td>&quot;</td>
<td>0.06</td>
</tr>
</tbody>
</table>
produced by injection of atropine persisted for more than 1.5-2 hr. The duration of increased 17-OHCS secretion after TMA injection was thus rather short in comparison with that observed after eserine or atropine injection. After injection of KCl a marked increase in the 17-OHCS secretion was observed in 2 dogs (dogs 4 and 6). The maximal secretion rate (1.14 and 1.73 μg/kg/min) was observed at 5 min after injection. The secretion rate returned to its pre-injection rate at 10 or 20 min after injection. In dog 6 it increased again and the second peak of the 17-OHCS secretion rate was observed at 60 min after injection. In dog 5, however, only a slight increase in the secretion rate was observed at 20 min after injection.

From these experiments it is concluded that TMA and KCl may induce a marked increase in adrenal 17-OHCS secretion in unanesthetized dogs.

It is well established that TMA⁹ or KCl¹⁰ produces a marked increase in adrenal medullary secretion. It is, however, not probable that adrenal cortical hormone secretion in response to TMA or KCl is mediated by adrenal medullary hormones, since these have no consistent effect at least in the dog on the pituitary-adrenocortical activity.

References