Effect of Hexamethonium on the Adrenaline-Secretory Response of the Adrenal Gland to Carbaminoylcholine

By

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It was demonstrated that the augmentation of adrenaline secretion of the adrenal gland causable by acetylcholine was greatly reduced by hexamethonium.\(^1\)

Carbaminoylcholine was proved to produce an increase in the adrenaline secretion of the adrenal gland.\(^2\) Moreover, Yamashita et al.\(^3\) found that the adrenaline-secretory action of carbaminoylcholine was in its potency several times as strong as that of acetylcholine.

The present study was attempted to know whether the effect of carbaminoylcholine on the adrenaline secretion is reduced by hexamethonium.

EXPERIMENTAL

Methods

The experiments were performed in eight dogs, weighing between 8.0 and 17.5 kg., under Evipan-sodium anesthesia. In all experiments, the greater and lesser splanchnic nerves were cut on the left side through the lumbar route before the start of experiments. In order to collect the adrenal venous blood, a small cannula was inserted into the left adrenal vein according to the technique described by Satake et al.\(^4\) All the chemicals were injected intravenously into the saphenous vein.

For the purpose of suppressing the muscarine-like action of carbaminoylcholine, atropine sulfate was given in a dose of 1 mg. per kg. of body weight, as was done in experiments of Yamashita et al.\(^5\) and Suzuki et al.\(^6\) After the control adrenal venous blood samples were collected, carbaminoylcholine chloride (Doryl, Merck) in a dose of 0.4 mg. per kg. was injected intravenously in 15 seconds. During the first and the second 60-second period after the start of carbaminoylcholine injection, the adrenal venous blood collections were made. After about half an hour, hexa-
methonium (Bistrium bromide, Squibb) in doses of 0.75 mg., 0.50 mg., or 0.25 mg. per kg. was injected intravenously. Again, after collecting control blood sample, carbaminolcholine in the same dose as before was injected and the collections of the adrenal venous blood were performed. The adrenaline content of the adrenal venous blood samples was estimated colorimetrically by the arseno-molybdic acid method of Bloor and Bullen. Adrenaline (Merck) was used as the reference standard.

Results

The data are summarized in Table I

Hexamethonium in a dose of 0.75 mg. per kg. was injected in 4 dogs.

In Exp. 1, the adrenaline secretion rate before the first carbaminoylcholine injection was immeasurably small. By the injection, the rate of adrenaline secretion was increased remarkably and was estimated at 0.43 μg. per kg. of body weight per minute in the first 60-second period.

**Table I**

<table>
<thead>
<tr>
<th>No. of experiment</th>
<th>Body weight and sex</th>
<th>Dose of hexamethonium (mg.) per kg.</th>
<th>Adrenaline secretion rate (μg.) per kg. per minute</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before hexamethonium</td>
<td>After carbaminoylcholine (sec.)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Before carbaminoylcholine</td>
<td>0-10</td>
</tr>
<tr>
<td>1</td>
<td>8.0 kg. ♂</td>
<td>0.75</td>
<td>*</td>
</tr>
<tr>
<td>2</td>
<td>8.6 kg. ♂</td>
<td>0.75</td>
<td>0.01</td>
</tr>
<tr>
<td>3</td>
<td>9.7 kg. ♂</td>
<td>0.75</td>
<td>0.01</td>
</tr>
<tr>
<td>4</td>
<td>10.8 kg. ♂</td>
<td>0.75</td>
<td>0.01</td>
</tr>
<tr>
<td>5</td>
<td>10.5 kg. ♀</td>
<td>0.50</td>
<td>0.01</td>
</tr>
<tr>
<td>6</td>
<td>12.5 kg. ♂</td>
<td>0.50</td>
<td>0.01</td>
</tr>
<tr>
<td>7</td>
<td>10.9 kg. ♀</td>
<td>0.25</td>
<td>0.04</td>
</tr>
<tr>
<td>8</td>
<td>17.5 kg. ♀</td>
<td>0.25</td>
<td>*</td>
</tr>
</tbody>
</table>

* Immeasurably small adrenaline content of the adrenal venous blood.

In the next 60-second period it was 0.02 μg. After the application of hexamethonium the rate of adrenaline secretion was 0.01 μg. By the second carbaminoylcholine injection the secretion rate was not increased. It was 0.01 μg. and immeasurably small rate in the first and the second 60-second period, respectively.

Similar results were obtained in Exp. 2. The adrenaline secretion
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rate before the first carbaminoylcholine injection was 0.01 µg. per kg. per minute. After carbaminoylcholine injection, it was increased remarkably and reached 0.41 µg. in the first 60-second period. In the next 60-second period it was 0.03 µg. After hexamethonium the secretion rate was 0.01 µg. In the first and the second 60-second period after the second carbaminoylcholine injection it was 0.02 µg. and 0.01 µg., respectively.

In Exp. 3, the pre-injection control secretion rate of adrenaline was 0.01 µg. per kg. per minute. After the first carbaminoylcholine injection, the adrenaline secretion rate was increased markedly and reached 0.35 µg. in the first 60-second period. In the second 60-second period it was 0.08 µg. After hexamethonium the adrenaline secretion rate was too small to be estimated. The secretion rate after the second carbaminoylcholine injection was 0.02 µg. in the first as well as in the second 60-second period.

In Exp. 4, the adrenaline secretion rate before carbaminoylcholine was 0.01 µg. per kg. per minute. On receiving carbaminoylcholine it was accelerated remarkably and reached 0.65 µg. in the first 60-second period. Then it decreased to 0.03 µg. After hexamethonium the adrenaline secretion rate was 0.06 µg. After the second carbaminoylcholine injection the adrenaline secretion rate was estimated at 0.09 µg. and 0.03 µg. in the first and the second 60-second period, respectively.

In Exps. 5 and 6, hexamethonium in a dose of 0.50 mg. per kg. was applied.

In Exp. 5, the rate of adrenaline secretion was increased by the first carbaminoylcholine injection from 0.01 µg. to 0.32 µg. per kg. per minute in the first 60-second period. In the next 60-second period it was measured as 0.06 µg. After hexamethonium injection, the secretion rate was immeasurably small. After the second carbaminoylcholine injection the rate of adrenaline secretion was 0.06 µg. and 0.02 µg. in the first and the second 60-second period, respectively.

The results of Exp. 6 were almost the same as those of Exp. 5. The adrenaline secretion rate before the first carbaminoylcholine injection was 0.01 µg. per kg. per minute. On receiving carbaminoylcholine the adrenaline secretion rate increased. It was measured as 0.32 µg. and 0.03 µg. in the first and the second 60-second period, respectively. After hexamethonium the secretion rate was immeasurably small. Then carbaminoylcholine was injected again. The adrenaline secretion rate was measured as 0.06 µg. and 0.01 µg. in the first and the second 60-second period.

In Exps. 7 and 8, hexamethonium was given in a dose of 0.25 mg. per kg.

In Exp. 7, the adrenaline secretion rate before the first carbaminoylcholine injection was 0.04 µg. per kg. per minute. It was augmented by
carbaminoylcholine and was measured as 0.57 µg. and 0.09 µg. in the first and the second 60-second period, respectively. The rate of adrenaline secretion after hexamethonium was 0.02 µg. Carbaminoylcholine was injected again. The adrenaline secretion rate was increased. It was 0.24 µg. and 0.03 µg. in the first and the second 60-second period, respectively.

In Exp. 8, the rate of adrenaline secretion was immeasurably small before the first carbaminoylcholine injection. After the injection it increased and reached 0.35 µg. per kg. per minute in the first 60-second. In the 60-second period it was 0.05 µg. After hexamethonium the secretion rate was 0.02 µg. After the second carbaminoylcholine injection it increased, 0.16 µg. and 0.04 µg. being measured in the first and the second 60-second period, respectively.

**DISCUSSION**

In Exps. 1–4, hexamethonium was injected in a dose of 0.75 mg. per kg. Before the application of hexamethonium, the adrenaline secretion was increased by carbaminoylcholine, the maximum being estimated at 0.35–65 µg. during the first 60-second period. After hexamethonium a definite increase in the adrenaline secretion rate was not produced by the carbaminoylcholine injection. It was measured as 0.01–0.09 µg. in the first 60-second period. Calculating the ratio of the latter to the former in each case, it is 7:100 on the average. This indicates that hexamethonium, given in a dose of 0.75 mg. per kg., suppresses definitely the augmented adrenaline secretion causable by 0.4 mg. carbaminoylcholine per kg.

In Exps. 5 and 6, in which hexamethonium was given in a dose of 0.5 mg. per kg., the mean ratio is calculated as 19:100. In these cases the suppressive effect of hexamethonium on the adrenaline-secretory action of carbaminoylcholine was clearly demonstrated.

In Exps. 7 and 8, in which 0.25 mg. hexamethonium per kg. was given. The adrenaline secretion rate was increased definitely by carbaminoylcholine even after hexamethonium application, indicating that this dose of hexamethonium is not large enough for preventing the augmented adrenaline secretion causable by carbaminoylcholine.

Almost the same results were obtained in the acetylcholine-experiments of Yamashita. In his experiments it was demonstrated that hexamethonium, given in doses of 0.50–1.0 mg. per kg., was capable of suppressing the augmented adrenaline secretion causable by 2.0 mg. acetylcholine per kg., whereas 0.25 mg. hexamethonium per kg. did not suppress it.
SUMMARY

Experiments were performed in eight dogs under Evipan-sodium anesthesia. The adrenal venous blood was collected by the cannula inserted into the adrenal vein according to the method of Satake et al. and was estimated for adrenaline by use of the arseno-molybdic acid method of Bloor and Bullen.

By the injection of carbaminoylcholine in a dose of 0.4 mg. per kg. the adrenaline secretion rate of the adrenal gland was markedly increased and was estimated at 0.32–0.65 μg. per kg. per minute in the first 60-second period after the start of injection.

Hexamethonium in doses of 0.50–0.75 mg. per kg. was applied and this was followed by the injection of carbaminoylcholine in the same dose as before. At this time, the augmentation of adrenaline secretion was small, 0.01–0.09 μg. being estimated there.

Thus, it may be concluded with definiteness that hexamethonium is capable of reducing the augmented adrenaline secretion of the adrenal gland causable by carbaminoylcholine.

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References