Effect of Splanchnicotomy on the Adrenaline-Secretory Action of Carbaminoylcholine

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The experiments were performed on dogs anesthetized with Evipan-sodium. The left splanchnic nerves were sectioned two hours prior to observation. Samples of adrenal venous blood from the right as well as from the left adrenal gland were taken through the lumbar route and their adrenaline content was estimated by the BLOOR & BULLEN'S colorimetric method. On receiving carbaminoylcholine, the adrenaline secretion rate of the acutely denervated gland was accelerated, but the rate of increase was almost the same as that of the gland with intact innervation. Thus, it is concluded that the adrenaline-secretory action of carbaminoylcholine is not influenced by splanchnicotomy.

It was found in our previous study a) that carbaminoylcholine was capable of markedly increasing the adrenaline secretion of the adrenal gland. However, the question as to whether the effect of carbaminoylcholine is due to central or peripheral stimulation needs further investigation.

Thus, attempts were made in the present investigation to determine whether the adrenaline-secretory action of carbaminoylcholine is affected by the acute denervation of the adrenal medulla.

METHODS

Dogs weighing 9.1 to 10.1 kg were used. The experiments were carried out under Evipan-sodium anesthesia. The lumbo-adrenal veins in both sides were exposed through the lumbar approach using the method of SATAKE et al.a) The denervation of the left adrenal gland was performed by the section of the splanchnic nerves on the left side two hours before observation. On the right side no nerve section was done. The adrenal venous blood was collected by a small cannula inserted into the exposed lumbo-adrenal vein. The femoral artery was connected with a mercury manometer to register the blood pressure and the saphenous vein was prepared for the intravenous injection.

After an injection of 1 mg per kg of atropine, carbaminoylcholine (Doryl, Merck) in doses of 0.25 mg and 0.4 mg per kg was injected intravenously. The adrenal venous blood from the gland of one side was sampled before the carbaminoylcholine injection as well as during the first and the second sixty-second periods after the start of injection. After a while, atropine was injected again. Then the same dose
of carbaminoylcholine as before was administered, and the adrenal vein blood from the gland of the opposite side was sampled in the same manner as before. The adrenaline content of the blood samples was measured by the colorimetric method of BLOOR & BULLEN, adrenaline (Merck) being taken as the reference standard.

RESULTS AND DISCUSSION

In all animals, whose left splanchnic nerves were sectioned two hours prior to the experiment, a comparison was made between the responsiveness of the adrenal gland with intact innervation to carbaminoylcholine and that of the denervated one. The results of these experiments are summarized in Table 1.

### Table 1.
The Augmented Adrenaline Secretion Causable by Carbaminoylcholine in the Intact and the Acutely Denervated Adrenal Gland

<table>
<thead>
<tr>
<th>No. of animal</th>
<th>Dose of carbaminoylcholine (mg per kg)</th>
<th>Adrenaline secretion rate (µg per kg per minute)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before injection</td>
<td>Intact gland</td>
</tr>
<tr>
<td></td>
<td>0″- 60″</td>
<td>60″-120″</td>
</tr>
<tr>
<td>Dog 1 ♀ 10.1 kg</td>
<td>0.25</td>
<td>0.02</td>
</tr>
<tr>
<td>Dog 2 ♂ 9.1 kg</td>
<td>0.25</td>
<td>0.06</td>
</tr>
<tr>
<td>Dog 3 ♂ 9.8 kg</td>
<td>0.25</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>* Immeasurably small amount of adrenaline in adrenal venous blood.</td>
<td></td>
</tr>
</tbody>
</table>

In Dog 1, carbaminoylcholine in a dose of 0.25 mg per kg was injected twice intravenously. Before the first carbaminoylcholine injection, the adrenaline secretion rate of the right gland with intact innervation was estimated as 0.02 µg per kg per minute. On receiving carbaminoylcholine, the secretion rate showed a slight but definite increase and it was estimated to be 0.06 µg with the blood sample taken in the first sixty-second period after the start of injection. And then the second carbaminoylcholine injection was made. At this time, the rate of adrenaline secretion of the acutely denervated left gland was measured, which was found to have increased only slightly, 0.05 µg being estimated during the first sixty-second period.

A similar experiment was further performed in this dog with carbaminoylcholine in a dose of 0.4 mg per kg. The pre-injection secretion rate of the right gland was immeasurably small. The secretion rate in the first and the second sixty-second period after carbaminoylcholine was 0.48 µg and 0.10 µg per kg per minute, respectively. After the injection of carbaminoylcholine in the same dose, a considerable increase in the adrenaline secretion rate of the left gland was found. It increased from 0.02 µg to 0.50 µg in the first sixty-second period. During the second sixty-second
period somewhat increased secretion rate was still found and it was 0.10 \( \mu g \).

In Dog 2, on receiving carbaminoylcholine in a dose of 0.25 mg per kg, the adrenaline secretion rate of the gland with intact innervation increased from 0.06 \( \mu g \) per kg per minute of the pre-injection rate to 0.51 \( \mu g \) in the first sixty-second period after injection. And then its rate returned to 0.05 \( \mu g \) in the second sixty-second period. The secretion rate of the acutely denervated gland was also considerably augmented by the injection of carbaminoylcholine in the same dose as before and was estimated to be 0.29 \( \mu g \) and 0.09 \( \mu g \) in the first and the second sixty-second period, respectively.

After the injection of carbaminoylcholine in a dose of 0.4 mg per kg, the adrenaline secretion rate of the intact gland increased from 0.09 \( \mu g \) per kg per minute, 1.5 \( \mu g \) being reached in the first sixty-second period. Then it decreased to 0.05 \( \mu g \) in the second sixty-second period. The secretion rate of the acutely denervated gland was also markedly augmented by the injection of 0.4 mg per kg of carbaminoylcholine. During the first sixty-second period after injection it was estimated as 0.95 \( \mu g \). The secretion rate was estimated to be 0.05 \( \mu g \) in the second sixty-second period.

A similar results to Dog 2 were obtained in Dog 3.

The basal rate of adrenaline secretion of the intact gland was 0.02 \( \mu g \) per kg per minute. After injection of 0.25 mg carbaminoylcholine per kg, it was accelerated and reached 0.44 \( \mu g \) in the first sixty-second period. Carbaminoylcholine in the same dose as before was again injected. By the injection, an acceleration in the adrenaline secretion of the acutely denervated gland was elicited. 0.34 \( \mu g \) being estimated in the first sixty-second period. After injection of carbaminoylcholine in a dose of 0.4 mg per kg, a remarkably increased secretion rate was observed in the intact gland. It was estimated to be 1.4 \( \mu g \) and 0.26 \( \mu g \) per kg per minute in the first and the second sixty-second period against 0.04 \( \mu g \) before injection. The adrenaline secretion rate of the acutely denervated gland was increased enormously after injection of carbaminoylcholine in the same dose and it reached 1.3 \( \mu g \) in the first sixty-second period. The pre-injection rate in this case was 0.02 \( \mu g \).

In Dogs 2 and 3, when carbaminoylcholine was injected in a dose of 0.25 mg per kg, the maximum value of the adrenaline secretion of the intact gland was 0.31—0.44 \( \mu g \) per kg per minute, which was estimated with the blood sample taken in the first sixty-second period after the start of injection, and that of the acutely denervated gland was 0.29—0.34 \( \mu g \). Calculating the ratio of the latter to the former in each case, it was 81 : 100 on the average. In the cases in which carbaminoylcholine was given in a dose of 0.4 mg per kg, the adrenaline secretion rate was increased markedly by carbaminoylcholine in the intact as well as in the acutely denervated glands. The mean ratio of the latter to the former was calculated as 78 : 100 on the average.

Dog 1, which did not respond so much to 0.25 mg carbaminoylcholine per kg, gave a definite response at a dose of 0.4 mg per kg. The ratio in this case was 103 : 100.

Thus, there was no significant difference in the responsiveness of the intact and the acutely denervated adrenal glands to carbaminoylcholine. It can be concluded that carbaminoylcholine acts directly on the adrenal medulla to liberate adrenaline.

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REFERENCES

