REPLETION OF THE CATECHOLAMINE OF THE HEART AFTER RESERPINE ADMINISTRATION

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A difference has been demonstrated between the total catecholamine contents of the atrium and the ventricle in the dog heart (1) and in the rabbit heart (2): the level being higher in the atrium than in the ventricle.

Moreover, a depletion of catecholamine in various tissues after reserpine injection was reported by many workers (3-6) and several studies (7, 8) have indicated that the heart is capable of taking up noradrenaline from the circulating blood.

Recently, Sakaguchi et al. (9) assayed the adrenaline and noradrenaline content of the rat heart at various times after reserpine administration and observed that the noradrenaline content of the rat heart was usually reduced by 6 hours after reserpine administration, but began to increase 24 hours after the reserpine treatment, and had returned to normal within a month. Other workers (10) showed that maximal depletion of cardiac catecholamine occurred 4 hours after a single dose of reserpine to the rat, and the normal level was not regained until about 10 days after the dose.

However, no experiments were made on the difference between the recovery of the catecholamine contents of the atrium and the ventricle after reserpine administration.

The purpose of the present studies was to obtain information on this point.

METHODS

Male rabbits weighing 2.5-3.0 kg were used in all experiments. Reserpine was dissolved in 20% ascorbic acid and administered subcutaneously, 2.5 mg/kg to one group and 5.0 mg/kg to the other group of animals. Rabbits were placed in a room at 19±2°C, and killed by a blow on the neck 12 hours after reserpine injection in one group and 24 hours in the other group.

Various tissues (atrium, ventricle, spleen, adrenal gland and whole brain) were immediately removed and chilled with ice. Catecholamine determination was carried out by the ethylenediamine condensing method (11) with the noradrenaline fraction of the extraction method of Matsuoka (12), and the contents were calculated as catecholamine in term of microgram (adrenaline and noradrenaline) per 1 g wet weight of tissues.

The catecholamine contents of the atrium and ventricle were calculated as the
averages of the values of 2 rabbits.

Reserpine was supplied from Dainippon Pharmaceutical Co., Ltd.

RESULTS

As controls, two groups of animals were used. One group received 20% ascorbic acid and the other group was untreated. No difference was found between the catecholamine contents of these two groups (Table 1).

1) Changes in catecholamine contents of the rabbit atrium and ventricle after reserpine injection

In untreated animals and in animals which had received 20% ascorbic acid, the catecholamine content of the atrium was higher than that of the ventricle (Table 1).

When a single dose of 2.5 mg/kg of reserpine was administered, the catecholamine content of the atrium decreased very rapidly for 12 hours but then began to increase and 24 hours after the treatment it had returned to the control level. The catecholamine content of the ventricle continued to decrease for 24 hours after administration of reserpine.

On administration of 5.0 mg/kg of reserpine, the catecholamine content of the atrium did not increase after 24 hours, and in both the atrium and the ventricle no significant difference was found in the catecholamine contents after 12 hours and after 24 hours (Fig. 1).

![Graph](image)

**Fig. 1.** Changes in catecholamine contents of the rabbit atrium and ventricle after subcutaneous injection of reserpine.

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2) Change in catecholamine content of the rabbit spleen after reserpine injection

After a dose of 2.5 mg/kg of reserpine, the catecholamine content of the spleen decreased for 12 hours and then began to return to normal. Thus, a significant difference (P<0.05) was shown between the value at 12 hours and that at 24 hours after treatment, though at the latter time the value had not yet reached the control level. Following a dose of 5.0 mg/kg of reserpine, the catecholamine content decreased to the same extent as with 2.5 mg/kg for 12 hours, but after 24 hours a further reduction was observed.
3) Change in catecholamine content of the rabbit adrenal gland after reserpine injection

With a dose of 2.5 mg/kg of reserpine, the catecholamine content of the adrenal gland decreased very markedly until 12 hours after the injection, but in the following 12 hours further reduction was comparatively small.

With a dose of 5.0 mg/kg of reserpine, the change in the catecholamine content was little different from that with 2.5 mg/kg of reserpine.

4) Change in catecholamine content of the rabbit whole brain after reserpine injection

As is evident from Fig. 2, there was no difference between the catecholamine contents of the groups which received 2.5 and 5.0 mg/kg of reserpine as in the case of the adrenal gland, but the degree of depletion was relatively small.

The catecholamine contents of various tissues under different conditions are summarized in Table 1.
TABLE 1. Changes in catecholamine contents of rabbit tissues after subcutaneous injection of reserpine.

<table>
<thead>
<tr>
<th>Treatment (mg/kg s.c.)</th>
<th>Spleen</th>
<th>Brain</th>
<th>Atrium</th>
<th>Ventricle</th>
<th>Adrenal gland</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1.405 ± 0.620*</td>
<td>0.466 ± 0.191</td>
<td>1.263 ± 0.525</td>
<td>0.664 ± 0.204</td>
<td>421.0 ± 151.0</td>
</tr>
<tr>
<td>V.C 200 24hr</td>
<td>1.640 ± 0.934</td>
<td>0.568</td>
<td>1.174 ± 0.685</td>
<td>0.456 ± 0.248</td>
<td>368.0 ± 136.5</td>
</tr>
<tr>
<td>Res. 2.5 12hr</td>
<td>0.613 ± 0.238</td>
<td>0.274 ± 0.253</td>
<td>0.443 ± 0.147</td>
<td>0.247 ± 0.062</td>
<td>62.3 ± 42.4</td>
</tr>
<tr>
<td>Res. 2.5 24hr</td>
<td>0.709 ± 0.173</td>
<td>0.215 ± 0.086</td>
<td>0.727 ± 0.238</td>
<td>0.327 ± 0.108</td>
<td>60.9 ± 46.2</td>
</tr>
<tr>
<td>Res. 5.0 12hr</td>
<td>0.546 ± 0.207</td>
<td>0.236 ± 0.271</td>
<td>0.434 ± 0.206</td>
<td>0.260 ± 0.271</td>
<td>81.7 ± 70.3</td>
</tr>
<tr>
<td>Res. 5.0 24hr</td>
<td>0.382 ± 0.199</td>
<td>0.139</td>
<td>0.259 ± 0.248</td>
<td>0.270 ± 0.206</td>
<td>17.4 ± 17.6</td>
</tr>
</tbody>
</table>

Values are expressed as μg/g of catecholamine (adrenaline and noradrenaline).

* : Standard deviation.

Reserpine was dissolved in 20% ascorbic acid solution.

DISCUSSION

The depleting action of reserpine on the catecholamine stores is very large (3-6), and 90% depletion of rat heart occurred 4 hours after a single dose of reserpine (10).

When a dose of 5.0 mg/kg of reserpine was injected, the catecholamine contents of the ventricle, adrenal gland and whole brain decreased continuously for 24 hours. However in the spleen and atrium, with a dose of 2.5 mg/kg of reserpine there was a significant difference between the values after 12 hours and after 24 hours, especially in the atrium where the content after 24 hours had returned to the control value.

Thus, in reserpine treated rabbits, although there is no difference in the rate of decrease in the catecholamine contents of the atrium and ventricle, the rate of restoration of the level to normal is higher in the atrium.

Various reports (1, 2) indicate that in normal animals, the catecholamine content of the atrium is higher than that of the ventricle, and that of the right atrium is highest. In the present experiments it was also found that the catecholamine content of the atrium was significantly higher than that of the ventricle.

These findings on the atrium, namely the higher concentration and quicker restoration of the catecholamine content to normal than that of the ventricle after depletion by reserpine, suggest the important role of noradrenaline in the autonomic innervation of this part of the heart. According to Bhagat (10), administration of noradrenaline after various periods to reserpine treated rats showed that after 24 hours the uptake of exogenous noradrenaline by the rat heart began to increase, and administration of DOPA or dopamine to adrenalectomized reserpine-treated rats enhanced the replenishment of the cardiac stores of catecholamines.

From the present experiments, it is uncertain whether the replacement of the catecholamine of the atrium after reserpine treatment was due to uptake of catecholamine from the circulating blood or to its synthesis in the atrium from precursors. The first step in the restoration of the cardiac catecholamine may occur in the atrium.
It is also of interest that after reserpine treatment the catecholamine content of
the spleen is restored more quickly than that of other tissues, but the significance of
this is unknown.

SUMMARY

The changes in the catecholamine contents of various tissues of rabbits after
subcutaneous reserpine injection were determined.

The catecholamine concentration was higher in the atrium than in the ventricle
and the restoration to the normal level after reserpine treatment was quicker in the
atrium. In the spleen a restoration of the level was also observed, but the degree of
restoration was rather small. In other tissues, namely whole brain and adrenal gland,
the catecholamine content decreased continuously for 24 hours after reserpine treatment,
as in the case of the ventricle.

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