Effect of Aminophylline on the SA Node of the Dog Heart in situ

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CHIBA, S. and HASHIMOTO, K. Effect of Aminophylline on the SA Node of the Dog Heart in situ. Tohoku J. exp. Med., 1973, 109 (2), 203-204 — The perfusion of the sinus node artery in 9 dogs in situ was performed. The selective injection of aminophylline into the sinus node artery induced a positive chronotropic response. The positive chronotropic response to aminophylline was suppressed not only by propranolol but also by tetrodotoxin. It is suggested that the positive chronotropic action of aminophylline is partially due to catecholamine release from adrenergic nerve terminals by excitation of local nerve fibers. ———aminophylline; SA node; propranolol; tetrodotoxin

In 1968, Westfall and Fleming studied the chronotropic response to aminophylline in heart-lung preparation on dogs, pretreated with reserpine for one or three days. They showed that chronotropic effects of aminophylline were significantly suppressed by pretreatment with reserpine or treatment with propranolol. In this study, we examined effects of aminophylline on the SA nodal pacemaker activity, using a direct perfusion method of the canine sinus node artery in situ (Hashimoto et al. 1967).

In nine mongrel dogs, which were anesthetized with sodium pentobarbital, tracheotomized for artificial respiration and vagotomized, the chest was opened through the 4th right intercostal space and the heart was kept in its original position by making a pericardial cradle. The sinus node artery was cannulated and perfused under constant pressure at 100 mm Hg.

When aminophylline at doses from 30 to 300 μg into the sinus node artery was injected, a positive chronotropic response was usually observed as shown in Fig. 1 and Table 1. Successive administration of aminophylline caused repetitively similar acceleration responses. The solvent, ethylenediamine dihydrochloride, induced a slight negative chronotropic response at a dose of 100 μg. The positive chronotropic response to aminophylline was completely suppressed after 3 μg of propranolol. Tetrodotoxin, 1 μg, which is enough to block transmitter release caused by nerve excitation (Hashimoto and

Fig. 1. Responses of the SA node to increasing doses of aminophylline. Upper and lower curves represent the systemic blood pressure (SBP) and heart rate (HR), respectively.

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### Table 1. Chronotropic responses of the SA node to aminophylline (mean±S.E.)

<table>
<thead>
<tr>
<th>Dose (µg)</th>
<th>No. of dogs</th>
<th>Initial heart rate (beats/min)</th>
<th>Positive chronotropic effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Per cent increase (%)</td>
</tr>
<tr>
<td>30</td>
<td>5</td>
<td>145±4.4</td>
<td>5.6±1.8</td>
</tr>
<tr>
<td>100</td>
<td>8</td>
<td>144±4.7</td>
<td>16.5±3.5</td>
</tr>
<tr>
<td>300</td>
<td>9</td>
<td>141±8.0</td>
<td>27.3±4.8</td>
</tr>
</tbody>
</table>

![Fig. 2. Inhibition of the positive chronotropic response to 100 µg of aminophylline (A) and facilitation of that to 1 µg of tyramine (T) by 1 µg of tetrodotoxin (TTX).](image)

Chiba, 1969), suppressed a positive chronotropic response to aminophylline, although positive chronotropic responses not only to norepinephrine but also to tyramine were not blocked by tetrodotoxin. Fig. 2 shows that indirect action of 1 µg of tyramine is not inhibited by 1 µg of tetrodotoxin, while that of 100 µg of aminophylline is significantly suppressed by tetrodotoxin. Recently, we demonstrated that caffeine injected into the sinus node artery induced double peaked positive chronotropic responses, i.e., rapidly induced initial acceleration followed by slowly induced but long-lasting one (Chiba et al. 1972). The initial positive response to caffeine was hardly suppressed by either propranolol or tetrodotoxin, although long-lasting acceleration was effectively suppressed by either of them which was very similar to the response to aminophylline.

It is suggested that the positive chronotropic response to aminophylline is partially due to catecholamine release by excitation of terminal adrenergic nerve fiber.

### References


