THE EFFECT OF PROPRANOLOL ON THE STRESS AND SHAY ULCERATIONS IN RATS

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Received for publication January 14, 1969

As reviewed by Ahlquist (1), adrenergic beta-receptor blocking agents have various action on the several organs in vivo and in vitro. Concerning the gastric physiology, these agents showed the inhibition of gastric secretion and motility in experimental animals (2, 3). However, Rosoff and Goldman (4) described that propranolol resulted in a marked increase in the number and severity of ulceration in fasted rats immobilized for

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8 hours. We also studied the effect of the agent on the stress ulceration in rats and found strong preventive effect on the ulcer contrary to the above authors. In addition, we confirmed the preventive effect of the agent on Shay ulceration. Donryu strain male rats, 200-250 g were used in the following experiments. Stress ulcer formation—As described previously (3), the animals were placed in the stress cage and immersed into water bath (23°C) for 7 hours to the level of xiphoid. At the end of the stress, the animals were killed by a blow, and the stomach was removed, inflated with 1% formalin solution and placed into 1% formalin solution for 5 minutes. Thereafter the stomach was cut open along the greater curvature and examined for lesions macroscopically. The ulcer index was calculated as the sum of the length of each lesion in the stomach. Shay ulcer formation—The animals were deprived of food for 48 hours in the individual cage prior to the experiment. Under ether anesthesia, the abdomen was incised and the junction between the pylorus and duodenum was ligated, as described by Shay et al. (6). Sixteen hours later, the animals were killed by a blow and the gastric contents were analysed. Acidity was determined by 0.1 N NaOH using phenolphthalein and Topfer’s reagent as an indicator. Peptic activity was determined by modified Bock’s method using albumin substrate (7).

The gastric ulceration in the forestomach was examined macroscopically and the ulcer index was determined as a sum of the diameter of each lesion. Perforation of the stomach was considered as 50 in ulcer index. Propranolol hydrochloride was dissolved in 0.9% saline solution and administered subcutaneously 30 minutes before the ulceration. As shown in Table 1, propranolol, 1 mg/kg, had no effect on the stress ulceration but at 10 mg/kg, the ulceration was significantly prevented. With the increase of the dose, the preventive ratio increased. By the way, it was found that the stomach of the animals subjected to the agent retained a plenty of ingested food compared with that of a control group. Hence, it was confirmed that propranolol has a relatively strong inhibitory action on the gastric emptying. On the other hand, propranolol also inhibited sig-

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of animals</th>
<th>Dose (mg/kg)</th>
<th>Incidence of ulceration (%)</th>
<th>Ulcer index (mean±S.E.)</th>
<th>Inhibition ratio of ulceration (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>20</td>
<td>–</td>
<td>100</td>
<td>24.0±2.3</td>
<td>2.5</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>1</td>
<td>100</td>
<td>23.4±4.7</td>
<td>39.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>10</td>
<td>100</td>
<td>14.5±2.1</td>
<td>60.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Propranolol (s.c.)</td>
<td>12</td>
<td>20</td>
<td>83.3</td>
<td>7.6±2.6</td>
<td>2.9±1.1</td>
<td>96.3</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>50</td>
<td>63.6</td>
<td>0.9±0.6</td>
<td>80.8</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Level of significance was calculated using student’s t-test.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of animals (mg/kg)</th>
<th>Dose (mg/kg)</th>
<th>Volume (ml)</th>
<th>Acidity Free (mEq/L)</th>
<th>Total (mEq/L)</th>
<th>Peptic activity (μg/ml)</th>
<th>Ulcer index (mean±S.E.)</th>
<th>Incidence of perforation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>9</td>
<td>–</td>
<td>9.7±0.7</td>
<td>22.2±11.7</td>
<td>64.4±11.3</td>
<td>268</td>
<td>39.4±11.4</td>
<td>44.4</td>
</tr>
<tr>
<td>Propranolol (s.c.)</td>
<td>10</td>
<td>20</td>
<td>7.6±0.7</td>
<td>35.4±7.0</td>
<td>67.9±4.2</td>
<td>248</td>
<td>20.0±7.0</td>
<td>20.0</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>50</td>
<td>7.7±0.5</td>
<td>48.9±4.4</td>
<td>81.9±5.0</td>
<td>206</td>
<td>9.3±5.3**</td>
<td>10.0</td>
</tr>
</tbody>
</table>

*P<0.05 **P<0.01

Peptic activity was expressed as the content of tyrosin released from albumin substrate after 30 minutes incubation with the gastric juice.
significantly the ulceration by pylorus ligation (Table 2). Propranolol 20, 50 mg/kg slightly reduced the secretory volume and peptic activity but increased the acidity. From these results, we confirmed that propranolol has a strong anti-ulcer property, probably because of the inhibition of gastric motility and peptic activity. However, we cannot neglect the participation of the essential effect of propranolol as a beta-receptor blocking agent on the blood vessels of the stomach. Now, we are studying the effect of other beta-blocking agents on the gastric ulceration.

REFERENCES


MECHANICAL RESPONSE OF GUINEA PIG TAENIA COLI IN HIGH-K/Na-DEFICIENT MEDIUM UNDER ANOXIA

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Received for publication January 23, 1969

For investigation of the properties of smooth muscle contraction hypertonically added 40 mm K medium has been used as a routine in this laboratory. Others have used isotonic high K/Na deficient medium for the same purpose.

The distinct difference existing between the mechanical response of guinea pig taenia coli in hyper-40 K medium and that in iso-152 K medium has been reported earlier. The response in hyper-40 K medium consisted of a phasic and a tonic phase (1). The tonic response in hyper-40 K medium at a steady level was very much higher than that in iso-152 K medium (2). The tissue calcium in hyper-40 K medium increased considerably above control levels while that in iso-152 K medium decreased sharply below control levels (2). The 46Ca uptake of the fraction which did not exchange within 4 minutes in hyper-40 K medium was also considerably above control while that in iso-152 K medium was not above control (2).

The tonic response in hyper-40 K medium has been found to be abolished by factors suppressing sodium transport mechanism or aerobic breakdown of carbohydrates (3), but the nature of this response in iso-152 K medium has not been studied. This small contraction was therefore investigated.

Strips of taenia coli isolated from white male guinea pigs were suspended in an organ bath containing Tyrode solution of the following composition (mm): NaCl 136.8, KCl 2.7, CaCl2 2.5, MgCl2 1.0, NaH2PO4 0.4, NaHCO3 11.9 and glucose 5.5, saturated with 95% O2 and 5% CO2 mixture at 37°C. Iso-152 K medium was prepared by substituting all sodium ions of normal Tyrode solution by potassium ions. Hyper-40 K medium was prepared by the addition of KCl crystals to normal Tyrode solution to give a final concentration of 42.7 mm K. Tension changes were recorded isometrically with mechanoelectro-transducer.

日本語

* A student from Ceylon on a scholarship granted by the Ministry of Education, Japan.
This work was partly supported by a research grant from the Ministry of Education, Japan.