PHARMACOLOGY

THE EFFECT OF PAPAVERINE AND DIBAZOL* ON THE RATE OF THE
CORONARY CIRCULATION

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The drugs used in the treatment of angina pectoris exert different effects on the coronary vessels. In this
respect their comparative experimental evaluation is of great interest. We began the study of the drugs used in
the treatment of coronary insufficiency with an investigation of papaverine and dibazol.

The effect of papaverine on the coronary vessels was studied experimentally at first on the isolated heart
[5, 7, 10], and later on the heart-lung preparation [8] and on the heart in situ [3, 4, 9]. However, no detailed
investigation of the effect of papaverine on the coronary vessels of the intact animals has yet been made.

Despite the clinical use of dibazol there is insufficient experimental confirmation of its effect on the coro-
nary vessels. The references in the literature to this problem are confined to the work of D. S. Paskov [2], who
showed that dibazol causes slight dilatation of the lumens of the coronary vessels of the isolated human heart. Gen-
erally speaking no investigation of the effect of dibazol on the coronary vessels has been carried out in the intact
animal. Similarly no study has been made of the combined effect of papaverine and dibazol on the rate of the
venous blood flow. Nevertheless a combination of the two drugs is often used in clinical practice.

EXPERIMENTAL METHOD

In this work we used a method which permitted determination of the rate of flow of a volume of blood from
the coronary sinus. The experiments were performed on cats under nembutal anesthesia (40 mg/kg). With the
application of artificial respiration to the animals, the thorax was opened and a polythene catheter introduced
into the coronary sinus through the right auricle, after which heparin was injected (1500 units/kg body weight
of the animal). The blood from the coronary sinus passed along the polythene catheter into a measuring tube
and caused a small float to rise, the movement of which was recorded mechanically on the smoked drum of a
kymograph. The volume of blood flowing from the coronary sinus in 15 min was measured periodically. A de-
tailed account of the method was given in the paper by N. V. Kaverina [1].

The size of the blood flow was estimated in ml/min per 100 g weight of the heart. Normally the mean
volume of blood flowing from the coronary sinus of the cat amounted to 43 ml/min per 100 g weight of the heart
(results of 35 experiments) with a mean square deviation of 13.8. This value of the rate of the blood flow in the
heart corresponds approximately to the figures obtained by Gregg in experiments on dogs.

The blood pressure in the carotid artery was recorded. The tested drugs were injected intravenously.

* Dibazol is 2-benzyl-benzimidazol hydrochloride — Publisher's note.
EXPERIMENTAL RESULTS

Experiments with Papaverine

The character of the effect of papaverine on the rate of the coronary blood flow may be judged from Fig. 1: in an effective dose (2 mg/kg) papaverine causes a marked increase in the rate of the blood flow from the coronary sinus.

**Table 1**

The Effect of Papaverine and Dibazol on the Rate of the Coronary Blood Flow

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose in mg/kg</th>
<th>No. of expts.</th>
<th>Maximum increase in rate of coronary blood flow in %</th>
<th>Duration of action in minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papaverine</td>
<td>0.5</td>
<td>10</td>
<td>28</td>
<td>10 &amp; 70</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0.5</td>
<td>44</td>
<td>26 &amp; 55</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.5</td>
<td>72</td>
<td>38 &amp; 116</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.5</td>
<td>114</td>
<td></td>
</tr>
<tr>
<td>Dibazol</td>
<td>3</td>
<td>5</td>
<td>18</td>
<td>10 &amp; 24</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>6</td>
<td>30</td>
<td>15 &amp; 43</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>5</td>
<td>39</td>
<td>33 &amp; 60</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>1</td>
<td>10</td>
<td>--</td>
</tr>
</tbody>
</table>

The summarized results of the series of experiments with papaverine are shown in Table 1. With increase in the dose of papaverine the strength and duration of its action increased. In a dose of 0.5 mg/kg papaverine causes maximum increase in the rate of the coronary blood flow by 28% for 10 min; in a dose of 4 mg/kg, in spite of a sharp fall in blood pressure, it increases the rate of the blood flow by 114% and its action lasts 1.5 hrs.

**Fig. 1.** The effect of papaverine on the rate of the blood flow from the coronary sinus. Interpretation of the curves (from above downwards): arterial pressure, blood flow from the coronary sinus, stimulation marker, time marker (5 sec). The figures indicate rate of flow of blood in ml/min per 100 g weight of the heart. The figures below the line of the time marker indicate the length of time after the injection of the drug that determination of the rate of the blood flow was made.

The characteristic feature of the reaction of the coronary vessels to papaverine in different animals is its great variability. In a dose of 0.5 mg/kg papaverine causes an increase of 10-70% in the rate of the coronary