Effects of Rhomotoxin on Cat Papillary Muscle

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Summary: Clinical experience has demonstrated that rhomotoxin, isolated from the fruits of Rhododendron molle G. Don, has antihypertensive and antiarrhythmic effects. In the present work, its direct actions on cat papillary muscle were as follows:

1. Rhomotoxin 2.7 μM increased contractility and automaticity induced by adrenaline, but exerted no influence on excitability and functional refractory period.

2. Rhomotoxin 27.1 μM shortened functional refractory period, decreased excitability and contractility accompanied by the appearance of spontaneous automaticity.

It is suggested that the above effects of rhomotoxin might be due to the change in resting potential of the myocardial cell as a result of altered transmembrane sodium movement.

Key words: rhomotoxin, cat papillary muscle

Balima, the fruit of Rhododendron molle G. Don, has long been used as an analgesic in the treatment of traumatic injuries in Chinese folk medicine. Its active principle, rhomotoxin (mol. wt. 368), first isolated by the Department of Pharmacy, the First Teaching Hospital, Wuhan Medical College, was later identified as the same substance as Rhodojaponin. Animal experiment has demonstrated that it could reduce the blood pressure and the heart rate, inhibit carotid pressor reflex as well as myocardial contractility. Clinically, rhomotoxin has been used in the treatment of severe hypertension and supraventricular tachycardia successfully.

In the present paper, the effects of rhomotoxin on the contractility, excitability, refractory period and automaticity of cat papillary muscle were studied in order to assess its direct activity on heart.

METHODS AND RESULTS

Cats weighing 1.5—2.5 kg were anesthetized with urethan (1 g/I.P.). Right ventricular papillary muscle dissected out from the heart was perfused with Tryode's solution aerated with 95% O₂ and CO₂ (pH 7.3—7.4). After an equilibration period of 1 h, the contractility, automaticity, excitability and refractory period of papillary muscle were determined by the same method as employed in our previous work. 5 papillary muscles were used in each determination.

Cumulative concentration-response curve of rhomotoxin on isometric contraction of papillary muscle was obtained first (fig.1). As seen from the curve, both bath concentrations of 2.7 μM of
rhomotoxin which increased the force of contraction by 80% (low concentration) and of 27.1 µM which induced toxic reaction (high concentration) were chosen for the following experiments respectively.

1. Contractility

Rhomotoxin 2.7 µM showed positive inotropic effect on papillary muscle within 1 min and reached its maximum at 10—15 min (fig.2), but on the contrary high concentration (27.1 µM) decreased the force of contraction and evoked arrhythmia.

2. Excitability

Excitability of papillary muscle was expressed by intensity—duration curve. Shifting of the curve denotes change in excitability. As shown in fig.3, after addition of rhomotoxin 2.7 µM, there was no significant change in excitability ($P>0.05$), while at high concentration (27.1 µM) the curve was shifted to the right, indicating lowering of excitability.

3. Functional refractory period (FRP)

FRP of cat papillary muscle was determined by paired-impulse technique. The minimal interval in ms between two pulses required to induce a visible response (a distinct increase in the force of contraction followed by a small secondary twitch) is known as the FRP of papillary muscle. The FRP of control was $254 \pm 4$ ms. Rhomotoxin 2.7 µM altered the FRP of papillary muscle from $254 \pm 4$ ms to $240 \pm 8$ ms ($P>0.05$), while 27.1 µM shortened it from $254 \pm 4$ ms to $210 \pm 15$ ms ($P<0.05$). Thus, it indicates that FRP was not influenced by low concentration but was reduced by high concentration of rhomotoxin (fig.4).

4. Automaticity