A NOTE ON THE EFFECTS OF HAMYCIN ON THE PERFUSED RAT HEART

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The effects of hamycin, a cardiotonic polyene antibiotic, were studied on the perfused heart of the albino rat, a species resistant to the digitalis glycosides. Perfusion with a concentration of 1×10^{-6} g./ml. induced systolic arrest in 15 to 20 min. This was preceded by auriculo-ventricular block and a decrease in the heart rate. Effects on the amplitude of contraction and coronary flow were however variable. Ouabain. 2×10^{-6} g./ml. and propylene glycol, which was the solvent for hamycin, did not have any significant effects on this preparation.

The digitalis-like activity of hamycin, a new antifungal antibiotic, has been reported by Arora (1962), and Arora and Arora (1963). Its effects on the rat heart, a species resistant to the known digitalis glycosides, are described below.

Experimental and Results

Hearts from albino rats were perfused (Langendorff's preparation) with Ringer-Locke solution (NaCl 0·9, KCl 0·042, $CaCl_2$ 0·024, $NaHCO_3$ 0·03, Glucose 0·05 per cent) at 35°. After a stabilisation period of 30 to 45 min. drug perfusion was started. Fourteen experiments were made with hamycin 1×10^{-6} g./ml., four were made with ouabain 2×10^{-6} g./ml. and four with Ringer-Locke solution containing the same amount of

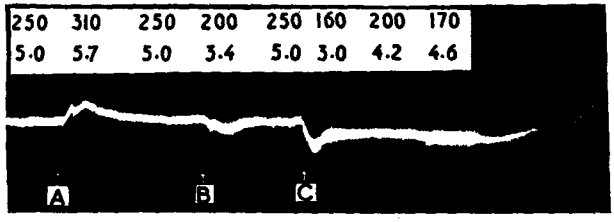

Fig. 1. Perfused rat heart (Langendorff's preparation). Records from above downwards are: heart rate/min.; coronary outflow ml./min. and contractions of the heart. Drugs were injected as follows; A, adrenaline 0·1 μg. B, posterior pituitary extract 0·1 unit; C, start of perfusion with hamycin 1×10^{-6} g./ml.

propylene glycol as in experiments with hamycin. Solutions of hamycin were first made in propylene glycol at 85°, before diluting in physiological solutions. Also, in these experiments, the Ringer-Locke solution used for perfusing the hearts before starting hamycin perfusion contained the same amount of propylene glycol as contained in Ringer-Locke solution with hamycin. Since hamycin induced systolic contracture in 15 to 20 min., experiments with ouabain and propylene glycol were also run for 20 min.

only. Sensitivity of the perfused hearts to adrenaline and posterior pituitary extract was tested in 7 preparations before beginning drug perfusion. Consistent effects on heart rate, coronary flow and tone were obtained with doses of 0·1 μg. of adrenaline and 0·1 unit of posterior pituitary extract, injected into the cannula (Fig. 1). Doses of 0·01 μg. of adrenaline and 0·01 unit of posterior pituitary extract were ineffective.

Hamycin induced complete systolic contracture in 15 to 20 min. in all the 14 experiments but the events preceding this were variable. An initial decrease in the tone occurred in all experiments and was followed by a partial or complete recovery in 7 (Fig. 1). In the other 7 experiments the tone continued to decrease till complete cessation of ventricular activity (Fig. 2). The ventricles then passed gradually into systolic

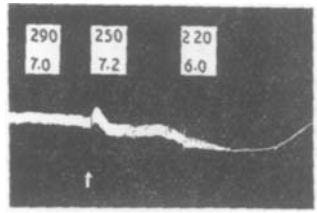

FIG. 2. Perfused rat heart (Langendorff's preparation). Records from above downwards are: heart rate/min.; coronary outflow ml./min. and contractions of the heart. At arrow perfusion with hamycin, 1×10^{-6} g./ml. was started.

contracture. In all but 3 experiments an incomplete auricular-ventricular (a-v) block followed the decrease in tone. The auricles however continued to beat after the ventricles had stopped. An increase in the amplitude of contraction was seen in 9 experiments, occurring either before or after the onset of a-v block; in the remaining 5 experiments both the tone and the amplitude of contraction continued to decrease till the ventricles stopped (Fig. 2). Before the onset of a-v block, a mean decrease of 21·1 per cent $\pm$ 2·19 s.e. was noted in the heart rate but the coronary flow was not consistently effected. Two additional experiments in which a-v block appeared within 1 min. of the onset of perfusion and one more experiment in which the heart rate was not recorded, are not included in these statistics.

Ouabain, 2×10^{-6} g./ml., failed to induce systolic arrest. In 2 of the 4 experiments, a slight increase in the amplitude of contraction and a slight decrease in the heart rate was seen. Coronary flow was not affected significantly.

Control preparations did not show any alteration in the tone, amplitude of contraction, heart rate or coronary flow over the duration of the experiments.

The ability of hamycin to decrease heart rate and induce a-v block and systolic arrest in the rat heart, further confirms its cardiotonic activity. Since the rat heart is resistant to the digitalis glycosides, the interesting possibility of the application of hamycin in digitalis resistant cases would

deserve a consideration if and when a clinical application can be affected.

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