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Apparent differences between the effects of hyoscine *in vivo* and *in vitro* on the responses of chicken oesophagus to nerve stimulation

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Summary

1. In chickens anaesthetized with sodium pentobarbitone, stimulation of a vagus nerve produced contractions in the muscles in the pre-crop oesophagus which were only partly antagonized by hyoscine.

2. The effect of hyoscine in an isolated preparation of chicken oesophagus responding to nerve stimulation was shown previously to be similar to that now found in the *in vivo* preparation.

Introduction

Hyoscine only partly antagonizes the longitudinal contraction in the chicken isolated oesophagus produced by stimulation of the extrinsic parasympathetic nerves, a residual contraction of the preparation being demonstrable in the presence of the drug at a concentration which antagonizes acetylcholine more than 250 times. In decerebrate preparations of chickens, however, hyoscine seemed to abolish the response to stimulation of a vagus nerve as detected with an intra-oesophageal balloon (Hassan, 1969). An explanation for this apparent difference in effectiveness of hyoscine *in vitro* and *in vivo* has been sought here.

Methods

Six cockerels (Brown Leghorn), body weight $2{\cdot}18 \pm 0{\cdot}11$ kg (mean $\pm$S.E.M.), were anaesthetized with sodium pentobarbitone, 35 mg/kg. The anaesthetic was dissolved in 0·9% w/v aqueous NaCl just before injection into an ischiatic vein. A small balloon tied on polyethylene tubing was introduced into the pre-crop oesophagus from the mouth and connected to a Greer manometer which monitored changes in intra-oesophageal pressure on a Devices pen recorder. The balloons were made from fine rubber finger stalls and were filled with air at a pressure equivalent to about 2 cm H_2O. Calibrations on the polyethylene tubing marked the position of the balloon in the oesophagus. In five experiments the oesophagus was secured to a bar just proximal to the crop, and a thread from the middle of the pre-crop oesophagus attached to an isotonic displacement meter which exerted a load of 2·5 g. The isotonic displacement meter was calibrated and produced a linear record of the longitudinal contractions on a second channel of the Devices pen recorder. The right vagus nerve was cut high in the neck and the distal end put on bipolar platinum electrodes in a pool of liquid paraffin. The nerve was stimulated with square wave pulses (1 ms, 25 Hz, 5 V) for 10 s at 5 min intervals,

the stimuli being monitored. A glass cannula was tied in an ischiatic vein for the administration of hyoscine hydrobromide.

Results

In the first experiment a balloon was positioned in the middle of the pre-crop oesophagus and the peripheral end of the right vagus nerve put on stimulating electrodes. Stimulation of the nerve produced a brisk rise in intra-oesophageal

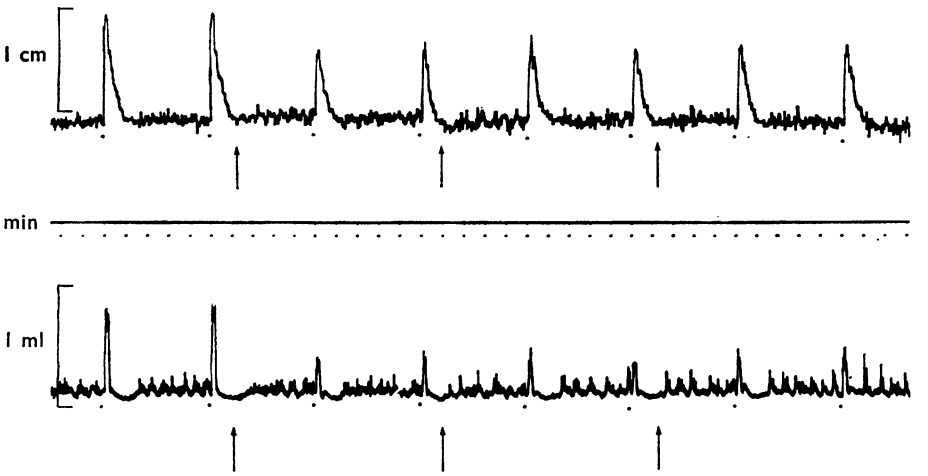

FIG. 1. Cockerel, pentobarbitone anaesthesia. The effect of hyoscine on contractions in the pre-crop oesophagus produced by nerve stimulation. From above downwards: isotonic longitudinal contractions (cm), time (min) and reductions in volume of an intra-luminal balloon (ml). At the dots the right vagus nerve was stimulated for 10 s (1 ms, 25 Hz, 5 V); the arrows mark the intravenous injection of hyoscine at doses of 0·456, 4·56 and 45·6 μmol/kg, respectively.

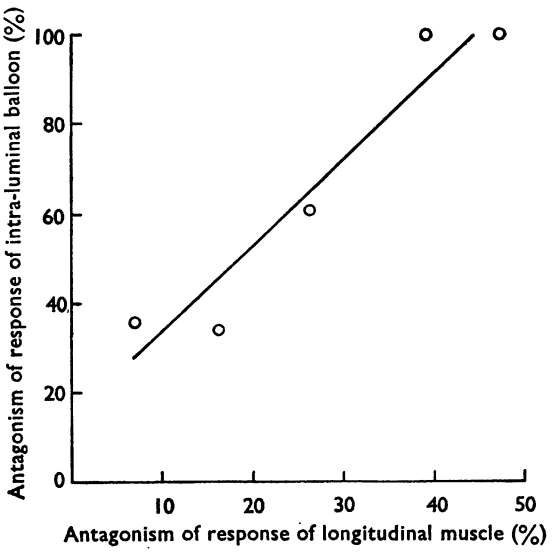

FIG. 2. Antagonism by hyoscine of the contractions in the pre-crop oesophagus produced by 10 s vagal stimulation (1 ms, 25 Hz, 5 V). Ordinates, antagonism of the increase in intra-oesophageal pressure (%); abscissae, antagonism of longitudinal contraction (%). The circles depict the effect of hyoscine (4·56 μmol/kg) in five cockerels anaesthetized with pento-barbitone. The calculated regression line is significant at the 5% level.

pressure which was abolished after intravenous administration of hyoscine hydrobromide (0·456 μmol/kg, 0·2 mg/kg). No response was demonstrable when the period of vagal stimulation was extended to 30 s or the balloon inflated further with 4 ml air. When the skin was incised to expose the oesophagus, however, a longitudinal contraction in the muscle was observed when the nerve was stimulated although the balloon did not register a response. In further experiments both longitudinal contractions and intra-oesophageal pressure were recorded.

A typical experiment is shown in Fig. 1. Hyoscine (0·456 μmol/kg) partly antagonized nerve stimulation producing longitudinal contractions and increases in intra-luminal pressure in the pre-crop oesophagus, the residual responses not being further antagonized by increasing doses of the drug. The results from all five preparations in which hyoscine (0·456 μmol/kg) antagonized the longitudinal contractions and increases in intra-oesophageal pressure produced by nerve stimulation are depicted in Figure 2. In these preparations no further antagonism of the responses was produced when the dose of hyoscine was increased 10 or 50 fold. The antagonism of the increase in intra-oesophageal pressure exhibited considerable variation and seemed complete in two preparations in which the longitudinal contractions were only partly antagonized by hyoscine.

Discussion

The hyoscine-resistant longitudinal contractions in the oesophagus were not an artifact of the isolated preparation as they were always shown in the anaesthetized chickens. In three preparations hyoscine abolished the increase in intra-oesophageal pressure produced by nerve stimulation but in three other preparations it did not do so. Clearly the intra-luminal balloon was insensitive to the hyoscine-resistant contractions in the oesophagus, and this would seem to account for Hassan's inability to demonstrate them *in vivo* with this method.

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REFERENCE

HASSAN, T. (1969). A hyoscine-resistant contraction of isolated chicken oesophagus in response to stimulation of parasympathetic nerves. *Br. J. Pharmac.*, **36**, 268–275.

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