A NOTE ON THE ACTION OF GALLAMINE ON ISOLATED RABBIT AURICLES

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The action of gallamine triethiodide on the effects of methacholine and acetylcholine on isolated spontaneously beating rabbit auricles in oxygenated mammalian Ringer's solution at 30° has been investigated. Gallamine blocked the effects of both drugs. The effects of gallamine were similar to those of atropine, but gallamine was weaker and was more readily removed by washing.

When gallamine triethiodide is administered to anaesthetised human subjects, with the exception of those who have been given cyclopropane, it causes tachycardia (Doughty and Wylie, 1951). The mechanism by which it produces this effect is disputed. Riker and Wescoe (1951) and Wein (1951) suggested that the tachycardia was due to an atropine-like action, but Della Bella, Rognoni and Gopal (1961) state that gallamine has no atropine-like action on the heart. Since there was some doubt regarding the mechanism by which gallamine causes tachycardia, this subject has been reinvestigated.

Methods

Hearts were removed from two-month-old rabbits, which had been killed by stunning and by bleeding from the carotid arteries. After dissection and cleaning, unseparated right and left auricles were suspended in 50 ml. oxygenated mammalian Ringer's solution at a temperature of 30° in a constant-temperature organ bath. The auricular contractions were recorded using a Starling heart lever on smoked paper. In each experiment

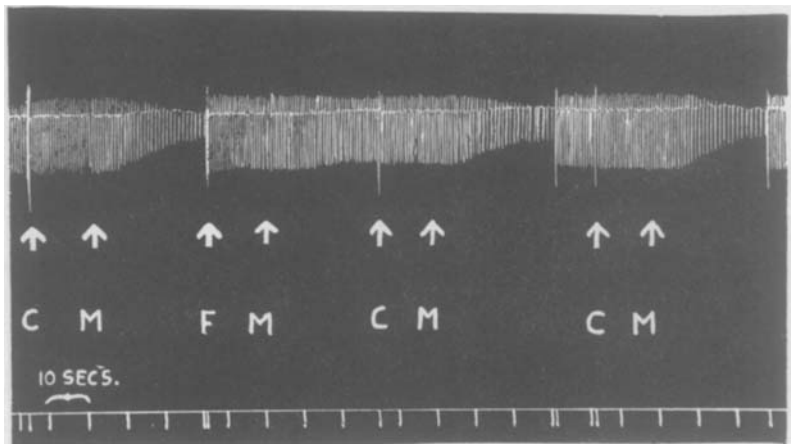

Fig. 1. Isolated spontaneously beating rabbit auricles in oxygenated mammalian Ringer solution at 30°. At M. methacholine chloride 10·0 μg. was added to the bath. At F, gallamine triethiodide 480·0 μg. in 0·6 ml. distilled water was added. At C, 0·6 ml. distilled water was added. Between additions of distilled water or gallamine, and methacholine, there was an interval of 2 min. Between additions of methacholine, there was a 5 min. interval.

the drug being investigated or a control, consisting of a volume of distilled water equal to that containing the drug, was added to bath 2 min. before the addition of acetylcholine or methacholine. Normal contractions of the auricles were recorded for 15 sec. Acetylcholine 20 μg. or methacholine 10 μg. was then added and the effect was recorded for 30 sec. Between each addition of acetylcholine or methacholine there was a 5 min. interval.

Results

Gallamine triethiodide, 480 μg., blocked the effect of 10 μg. methacholine (Fig. 1). A similar effect was seen with acetylcholine.

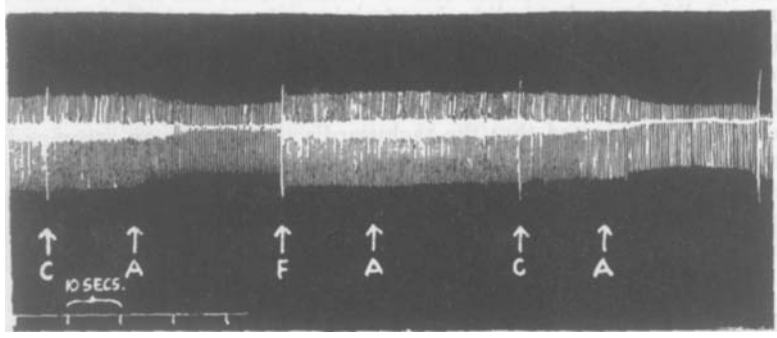

FIG. 2. Isolated spontaneously beating rabbit auricles in oxygenated mammalian Ringer solution at 30°. At A, acetylcholine chloride 20·0 μg. was added to the bath. At F, 480·0 μg. gallamine triethiodide in 0·6 ml. was added. At C, 0·6 ml. distilled water was added. Time intervals as in Fig. 1.

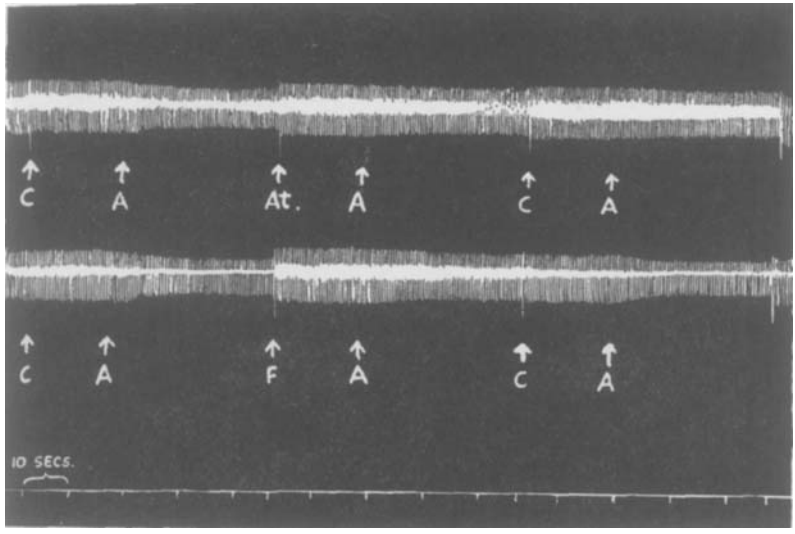

FIG. 3. Isolated spontaneously beating rabbit auricles in oxygenated mammalian Ringer solution at 30°. At A 20·0 μg. acetylcholine was added to the bath. At F, gallamine triethiodide 240·0 μg. in 0·3 ml. distilled water was added. At C, 0·3 ml. distilled water was added. At "At." 0·6 μg. atropine in 0·3 ml. distilled water was added. The time intervals as Fig. 1.

Gallamine triethiodide, 480 μg., completely blocked the effect of 20 μg. acetylcholine (Fig. 2). The effects of gallamine and atropine were compared using the same pair of auricles. Gallamine produced a qualitatively similar effect to that of atropine. However, two differences were noted. The effect of gallamine was very weak compared with that of atropine

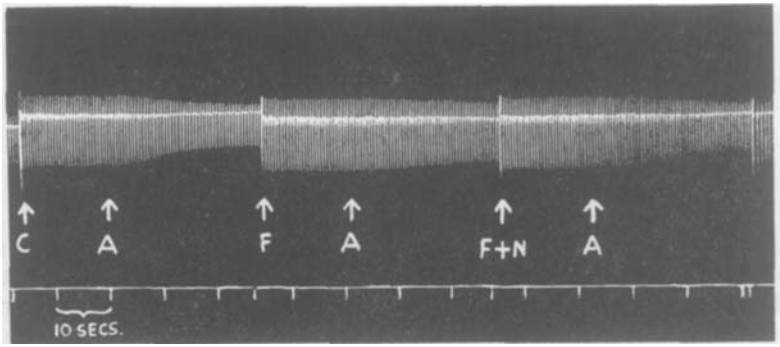

FIG. 4. Isolated spontaneously beating rabbit auricles in oxygenated mammalian Ringer solution at 30°. At A 20·0 μg. acetylcholine was added to the bath. At F, 320·0 μg. gallamine triethiodide in 1·0 ml. distilled water was added. At F + N, gallamine 320·0 μg. and neostigmine methylsulphate, 300·0 μg. in 1·0 ml. of distilled water was added to the bath. Time intervals as Fig. 1.

and also was readily reversed by washing whereas that of atropine persisted (Fig. 3). Neostigmine methylsulphate 300 μg. prevented 320 μg. gallamine from blocking the effect of 20 μg. acetylcholine (Fig. 4).

DISCUSSION

Since methacholine has predominantly muscarine-like actions, it would appear that gallamine has a similar action on the heart to that of atropine, differing only from the latter by being weaker and being more readily reversible by washing. Mushin, Wein, Mason and Langston (1949) reported that gallamine does not have a significant effect on the blood pressure. It therefore appears that gallamine causes tachycardia by blocking the muscarine-like effects on the heart of acetylcholine, which is liberated from the post-ganglionic endings of the vagus nerve. This confirms the findings of Wein (1951) and of Riker and Wescoe (1951). Doughty and Wylie (1951) reported that the tachycardia could be reversed by administering neostigmine methylsulphate to their patients. This effect has been seen experimentally.

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