A STUDY OF THE EFFECTS OF GALLAMINE ON CHOLINERGIC RECEPTORS

R.A. DHUME, M.G. GOGATE, J.F. MASCARENHAS AND M.R. VARDE

Department of Physiology, Goa Medical College, Bambolim, Goa.

Summary: In Cats and Rana Tigrina gallamine when administered in the recommended dose of 1 *mg/kg* of body weight to restrain animals, has significant vagal blocking effects on the heart and the stomach. The receptors blocked by this drug are of cholinergic nature. No blocking action was noted on the urinary bladder in cats but an increase in excitability was observed instead.

Key words: frog cat gallamine cholinergic receptors cardiac muscle smooth muscle of stomach detrusor muscle

INTRODUCTION

Restraining conscious animals with gallamine has been a method of choice in the study of visceral responses induced on central nervous stimulation. Segura (7) reported cardiac abnormalities on stimulation of the forebrain of conscious toads restrained with gallamine and claimed that the efferent impulses bringing about cardiac abnormalities were mediated through the vagi. Dhume *et al.* (2) recorded increase in the basal heart rates in Rana Tigrina under gallamine. This was presumably due to vagal blockade resulting from gallamine as the latter is known to block the vagus (4,6).

The aim of the present work was to assess the action of gallamine on visceral effects such as cardiac muscle, smooth muscle of gastro-intestinal tract and detrusor muscle of bladder, in Rana Tigrina and cats restrained with gallamine by using a dose just enough to paralyse skeletal muscles.

MATERIALS AND METHODS

Rana Tigrina: 22 frogs of either sex weighing between 300 to 400 *gms*, were anaesthetised by immersion in 25% of urethane until the corneal reflex was sluggish. The experiments were performed on 9 frogs during summer (atm. temp. 25°-32.5°C), 8 frogs during monsoon (atm. temp. 24°-29.5°C) and 5 frogs during winter (atm. temp. 20°-31.6°C). Anterior abdominal vein was cannulated for injection of the drug. The chest was opened and both the vagosympathetic trunks were prepared for stimulation. The heart was exposed for direct recording of its contractions. The stomach was separated at pyloric and, taking care not to damage the mesenteric vascular arches and was connected to a simple lever for recording purpose. The sciatic nerve was exposed in the thigh for stimulation and the tendon of gastrocnemius muscle was connected to an isotonic lever for recording muscle twitches. The stimuli (4-8 volts for

vagus and 0.5 to 2 volts for the sciatic nerve, 25-30 cps of frequency) were delivered from "Techno Electronic stimulator". After recording the effect of stimulation of vagus and sciatic nerve with a threshold stimulus, gallamine was injected in the dose of 0.1-0.2 *mg* mixed with 1 *ml* of 0.65% of saline. After an interval of 15 min the stimuli were repeated and the records of contraction of the heart stomach and the mucle were obtained.

In 4 frogs effect of acetylcholine on the heart was assessed before and after the administration of gallamine.

Cats: Ten cats weighing between 2.5 to 3.5 *kgs* were anaesthetised with pentobarbitone sodium (30 *mg/kg* i.p.). The trachea was cannulated for artificial ventilation. The gastrocnemius muscle twitches were recorded with the help of an isotonic lever. The systemic femoral arterial pressure was recorded on kymograph with mercury manometer. The electrocardiograms were recorded with lead I on dynograph (Beckman). The femoral vein was cannulated for injection of the drug. The urethra was exposed by supra public incision, a polythene tube was inserted through the cut urethra and connected to the mercury manometer for recording cystometrograms. The right peripheral ends of sciatic, pelvic and vagus nerves were prepared for stimulation with parameters of 2-8 volts, 25 cycles per second of frequency.

RESULTS

In frogs, gallamine (0.1 to 0.2 *mg* given i.v) produced vagal blocking effect at both the effector sites, namely, the heart and the stomach, in all the experiments performed (Fig. 1). This dose

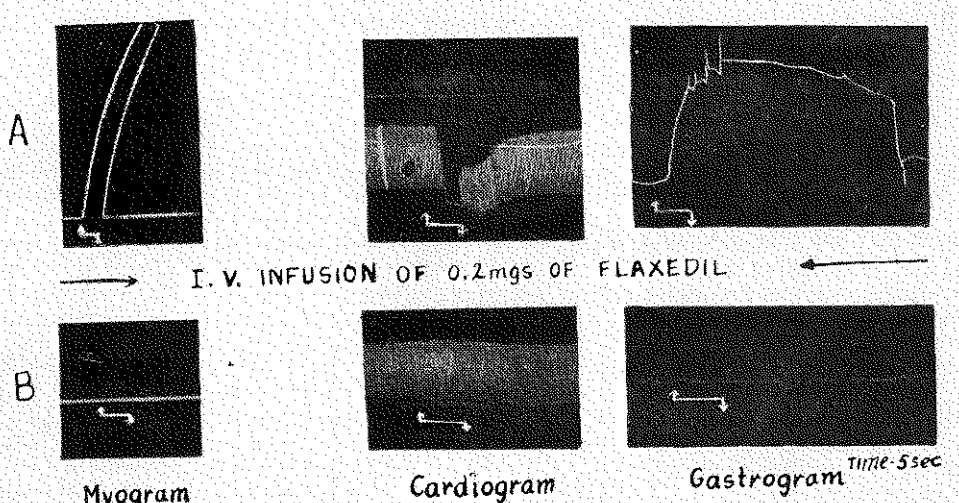

Fig. 1: Left hand panels depict the effects of sciatic nerve stimulation on Frog's gastrocnemius muscle. Middle panels depict the effects of right vagus nerve stimulation on Frog's cardiogram. Right handed panels depict the effects of right vagus nerve stimulation on Frog's gastrogram.

A. Before gallamine B. After gallamine

effectively blocked skeletal muscles.

The action of acetylcholine on the heart was studied in 4 frogs during different seasons of the year. The inhibitory action of acetylcholine on the heart was also blocked by gallamine (Fig. 2).

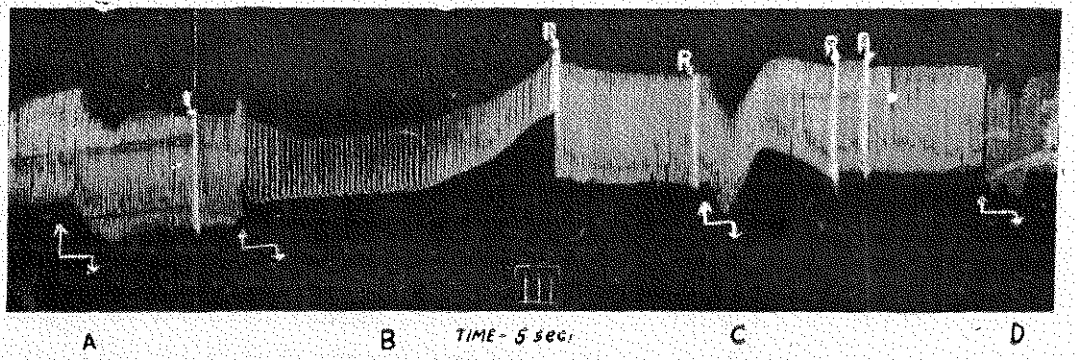

Fig. 2: Effects of acetylcholine of frog's cardiac muscle before and after flaxedil.

A—I.V. Injection of 1 *ml* of 0.65% Nacl.
B—I.V. Injection of acetylcholine (0.5 *mg* in 1 *ml* of saline)
C—I.V. Gallamine (0.2 *mg* in 1 *ml* of saline)
D—I.V. Injection of acetylcholine (0.5 *mg* in 1 *ml* of saline)
R—Rest periods lasting for 5 min.

In cats, the dose of gallamine, (1 *mg/kg.* i v) which was enough to block the skeletal muscles also produced vagal blocking effects. The same dose of gallamine did not block urinary bladder activity induced by pelvic nerve stimulation but brought about an increase in excitability instead (Fig. 3).

DISCUSSION

Gallamine is known to be a reversible muscle relaxant. It blocks the action of acetylcholine on the motor end plate. It is also known to exhibit an atropine-like vagal blocking action presumably at the peripheral level resulting frequently in sinus tachycardia and occasionally hypertension (4,6). As regards its central effects both excitatory and inibitory actions of gallamine are reported at various synaptic levels (3,5). In fact it was considered unwise to assume that the results obtained on animals paralysed with gallamine are without any effects on the central nervous system (1). Our results are at variance with those obtained by Segura (7) who claimed that in toads the cardiac abnormalities produced by foerebrain stimulation in gallamine treated preparations were mediated through vagi. The discrepancy could be explained by presuming that the receptor in toads might not be of cholinergic nature. As a matter of fact, Singh (8) has presented evidence that in amphibians the transmitter susbtances released by the vagus are subject to seasonal variations and reported various

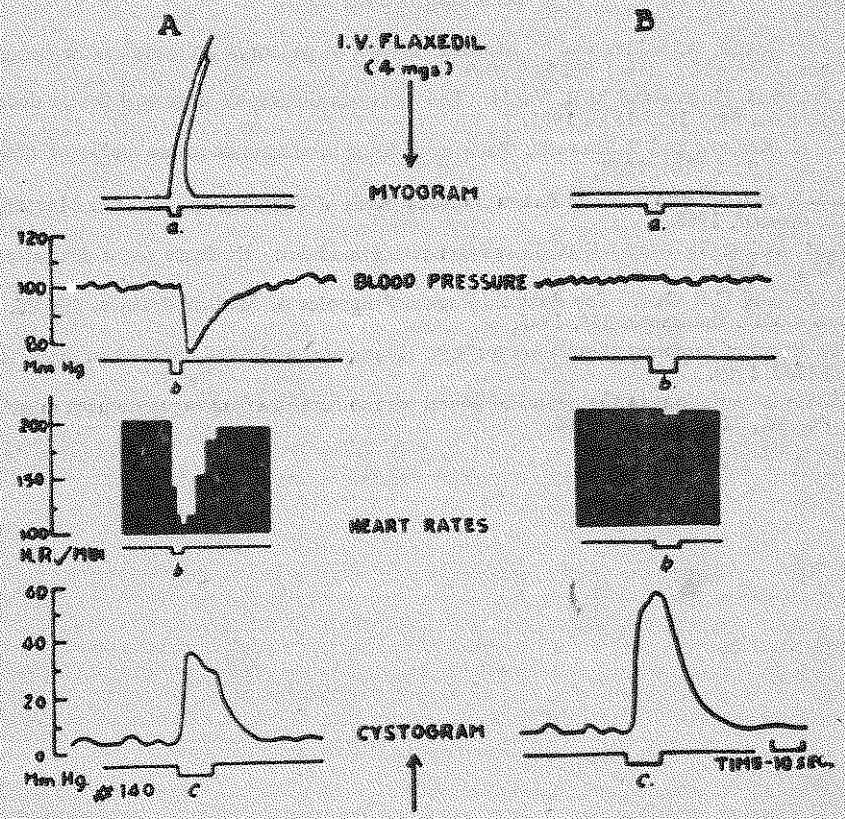

Fig. 3: Effects of gallamine on Cat's myogram, blood pressure, heart rates and cystometrograms.
A—Before gallamine B.—After gallamine
a—Stimulation of peripheral end of sciatic nerve
b—Stimulation of peripheral end of vagus nerve
c—Stimulation of peripheral end of pelvic nerve

chemical transmitters like 5-hydroxytryptamine, adrenaline, and substance P. Furthermore the present results on amphibians as well as on mammals like cats have shown that the blocking effects of gallamine are not limited to the myoneural apparatus but also to other cholinergic sites like heart and stomach.

The action of the gallamine on the urinary bladder was found to be more complex. No blocking effects were observed on stimulation of cut peripheral pelvic nerve in any of the experiments. It is thus seen that the dose of gallamine administered as a skeletal muscle relaxant does not effectively block the cholinergic receptors of urinary bladder.

This study indicates that the untoward effects of gallamine on cholinergic receptors situated at various sites should be taken into account while assessing the results of experiments performed in animals restrained with gallamine.

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