ACTION OF ACETYLCHOLINE ON THE ATROPINISED FROG HEART DURING THE WINTER MONTHS

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Summary : During the winter months, high doses of acetylcholine produced positive inotropic action without any chronotropic action on the perfused atropinised frog heart, in 5 out of 24 preparations. In the remaining preparations acetylcholine failed to produce any action and positive inotropic effect of acetylcholine on these preparations was noticed if they were perfused with the medium containing excess of calcium. However, the rate remained unchanged. The positive inotropic action was blocked by the local anaesthetic amethocaine and thus may be due to increased penetration of calcium into the cardiac cell.

Key words : acetylcholine atropine calcium frog heart

INTRODUCTION

High doses of acetylcholine produce positive inotropic and positive chronotropic actio on the atropinised frog heart (7,9). We have however, now observed that during the winte months (January to March) acetylcholine either produces no action or only positive inotrop action on the perfused atropinised frog heart. This phenomenon has been studied in detail an is being reported now.

MATERIALS AND METHODS

The heart of the common Indian frog Rana tigrina was perfused through inferior ven cava by the method of Bulbring as described by Burn (1). 10^{-6} *gm/ml* of atropine sulphate wa added to the perfusion medium. High calcium Ringer contained three times the usual amount o calcium chloride i.e. it was prepared by adding 0.34 *gm/litre* of calcium chloride to the amph bian Ringar described by Burn (loc-cit). The contractions were recorded on the smoked drur with a simple lever.

RESULTS AND DISCUSSION

1-64 /*µg* of acetylcholine were injected into the cannula in geometrical progression. 1, & 4 *µg* of acetylcholine failed to produce any action in all the preparations. 8, 16 and 32 µ of acetylcholine when injected into the perfusion fluid produced increase in the amplitude in out of 24 preparations (Fig. 1-B). In two preparations there was also increase in the tone (Fi 1-C). But the rate was not changed. The effect was dose dependent. When the same dos

were repeated on the same preparation the responses showed tachyphylaxis but were qualitatively reproducible (Fig. 1-B). Higher doses (64 & 100 μg) produced depression of the atropinised frog

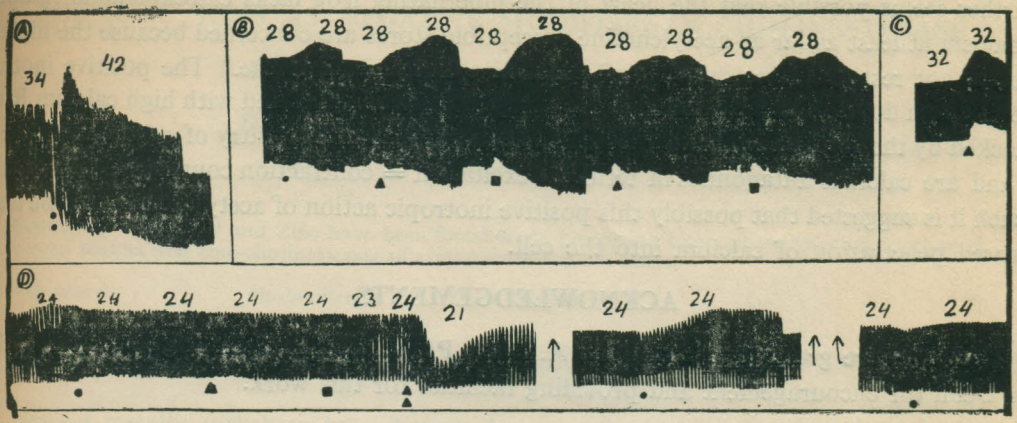

Fig. 1 : Effect of acetylcholine (Ach) on the atropinised perfused frog heart. Figures at the top are heart rate/minute.

Panel A shows effect of acetylcholine during the summer months (August) Panels B, C & D show the effect of Ach. during the winter months (January-March).

At ↑ perfusion with high calcium Ringer was started.

At ↑ ↑ amethocaine (500 μg) injected into the cannula.

●Ach 8 μ, ▲Ach 16 μ, ■Ach 32 μ, ▲Ach 64 μ

●Ach 100 μ

heart (Fig. 1-D). In the remaining preparations doses of 8-32 /μg of acetylcholine failed to produce any action (Fig-1-D). In these preparations if perfusion was switched over to high calcium Ringer, 8, 16 and 32 μg of acetylcholine when injected into the perfusion medium caused increase in the amplitude (Fig. 1-D), but still there was no change in the rate. Local anaesthetics block the positive inotropic action of low doses of acetylcholine on the frog heart perfused with high calcium Ringer (7,8). Thus, the action of these comparatively high doses of acetylcholine on the atropinised frog heart perfused with high calcium Ringer was studied 10 minutes after injecting amethociane (500 μg) into the cannula. The increase in the amplitude caused by acetylcholine was completely blocked by amethocaine (Fig. 1-D).

During hibernation catecholamines are depleted from the frog heart (6) and it is well known that the stores of catecholamines in the depleted organs can be replenished by catecholamine infusion (2). Thus, the action of acetylcholine was studied after noradrenaline infusion (30 μg of noradrenaline was infused in 20 minutes). It has been reported that the sympathetic nerve endings of the frog heart contain adranaline rather noradranaline (3). So, the action of acetylcholine on the atropinised heart of Rana tigrina was also studied after adrenaline infusion (30 μg of adrenaline was infused in 20 minutes). Adrenaline or noradrenaline infusion failed to modify the action of acetylcholine.

High doses of acetylcholine fail to produce the usual nicotinic action i.e. positive inotropic and chronotropic actions on the atropinised frog heart during winter months. This may be due

to the fact that the catecholamine stores are depleted in the heart of the hibernating frog (6). It further seems possible that the heart of the hibernating frog lacks catecholamine reuptake mechanism at least as far as acetylcholine susceptible stores are concerned because the nicotinic action is not restored after infusion of adranaline and noradrenaline. The positive inotropic action of high doses of acetylcholine on the atropinised hearts perfused with high calcium Ringer is blocked by the local anaesthetic. Local anaesthetics prevent the entry of calcium into the cell (4), and are calcium antagonists in terms of excitation = contraction coupling of the heart (5). As such it is suggested that possibly this positive inotropic action of acetylcholine may be due to increased penetration of calcium into the cell.

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