STUDIES ON THE TOXIC FFFECTS OF STREPTOLYSIN 'O' : EFFECT ON THE CONTRACTILITY OF ISOLATED AND INTACT MAMMALIAN AND AMPHIBIAN HEART

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Summary: The effect of streptolysin 0 (a streptococcal exotoxin) on the myocardial contractility of isolated and intact mammalian and amphibian heart has been investigated. Streptolysin 0 caused marked reduction or complete caessation of myocardial contractility of mammalian and amphibian heart both *in vivo* and *in vitro*. The effect of submaximal doses of streptolysin 0 on isolated atria was reversible after repeated washings and the myocardial depressant effect of streptolysin 0 was not antagonised by atropine. These observations would suggest that streptolysin 0 is cardiotoxic and may be involved in the causation of myocardial failure associated with acute rheumatic fever in man.

Key words: Streptolysin 0 myocardial contractility

INTRODUCTION

The administration of streptolysin O (a streptococcal exotoxin) to animals is known to result in focal cardiac lesions (3,5). In our earlier studies (4) it was observed that the intrapericardial administration of streptolysin O to rats instantaneously caused reduction in cardiac activity in most and cardiac stand-still in some of them. Besides causing changes in cardiac contractility through morphological cardiac damage, whether streptolysin O can also directly produce functional derangement in cardiac activity is not well known. Therefore it was of interest to investigate the effect of streptolysin O on the contractility of isolated and intact mammalian and amphibian heart.

MATERIALS AND METHODS

(A) **In vitro experiments :** Rabbits and guinea pigs were killed by a blow on the head and the frogs after pithing and their hearts were carefully removed. The atria were cleaned, and mounted in an organ bath containing oxygen saturated Ringer Locke at 35°C. The contractions were recorded kymographically using Starling heart lever with a magnification of ten folds. The atria were allowed to stabilize for 30 min and responses to increasing doses of streptolysin O* were determined.

(B) **In vivo experiments :** In order to measure the contractions of atria and ventricles *in situ* in dogs, cats and rats the animals were anaesthetized with pentobarbitone sodium 35 *mg/kg* intraperitoneally and were ventilated by positive pressure respiration. The chest wall was

*Partially purified reduced lyophilized streptolysin 0 (Burroughs Wellcome, London) dissolved in 0.9 percent saline was used.

opened by a mid-sternal incision and the pericardium was opened longitudinally; pericardial margins were stitched to the sternum, making a cradle for myocardium. The contractions of the atria and ventricles were recorded kymographically. Responses to increasing doses of streptolysin O administered intravenously were determined.

In case of frogs the heart of the pithed animal was perfused by Bulbring's method and the ventricular contractions were recorded kymographically. Streptolysin O was administered in increasing doses along with the perfusion fluid through rubber tubing.

The experiments were concluded when myocardial contractions ceased or no further reduction in myocardial contractility was noted by increasing the dose.

In order to understand the probable mechanism of myocardial depressant action of streptolysin O, its effect on the atropinized heart of cat and frog was also studied.

RESULTS

(A) **In vitro experiments :** The effect of streptolysin O on the rate and force of myocardial contractility of isolated atria of rabbit, guinea pig and frog is shown in Fig. 1. The streptolysin O in doses of 0.8 *U/ml* produced a maximum reduction of 70 percent in the contractile force of isolated rabbit atria, while doses of 0.16 *U/ml* and 0.05 *U/ml* caused complete cessation of atrial contractility in guinea pigs and frogs respectively. The myocardial depressant effect of submaximal doses of streptolysin O was reversible after repeated washings.

The streptolysin O also caused a reduction in the rate of atria but this effect was less marked and had no definite relationship either to the doses of streptolysin 0 or to the magnitude of decrease in the force of atrial contractility (Fig. 1).

(B) **In vivo experiments :** The effect of streptolysin O on the contractility of the mammalian and amphibian heart *in situ* is shown in Fig. 2. Streptolysin O caused appreciable reduction in the contractile force of both the atria and ventricles in rats and dogs. In rats a dose of 9 and 12 *U/kg* caused atrial and ventricular standstill respectively, while in dogs the maximum reduction of 33 and 38 percent in the contractile force of atria and ventricles respectively was achieved by a dose of 4 *U/kg*. In cats, streptolysin O in doses of 1 *U/kg* caused a maximum reduction of 46 percent in the contractile force of the ventricles, the cat atria however, did not show any response; in frogs a maximum reduction of 50% in the myocordial contractility was produced by a dose of 8 *U/kg*. Atropine did not antagonise the myocardial depressant effect of streptolysin O on cat and frog heart *in situ*.

Although streptolysin O caused some reduction in the heart rate of these animals, there was no relationship either with the doses of streptolysin O or with the magnitude of reduction in the myocardial contractility.

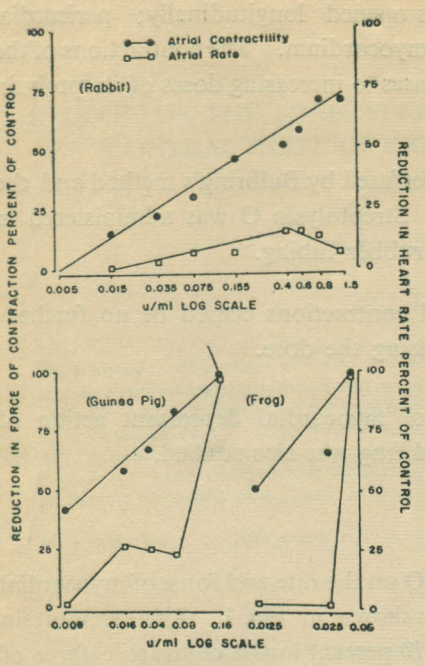

Fig. 1 : Shows the effect of streptolysin 0 on the rate and force of myocardial contractility of isolated atria of rabbit, guinea pig and frog.

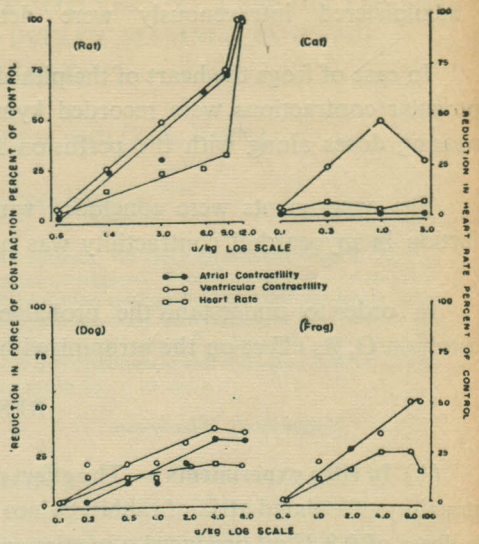

Fig. 2 : Shows the effect of streptolysin 0 on the heart rate and myocardial contractility of atria and vehtricle of rat, cat and dog and ventricle of frog *in vivo*.

DISCUSSION

The findings of the present study revealed that small doses of streptolysin O cause reduction in the contractility of isolated and intact mammalian and amphibian heart. These findings lend support to our earlier observations (4) and are consistent with the observations of other workers that streptolysin O decreases the contractility of rabbit heart *in vivo* (5) and hearts of rabbit, guinea pig and rat *in vitro* (6).

In the present study an interesting observation has been that the increasing doses of streptolysin O caused increasing depression of frog atria *in vitro* and intact heart *in situ*, These findings , are at variance with those of Cantoni and Bernhiemer (1,2), who have reported that the isolated frog heart does not respond to initial administration of streptolysin O irrespective of the doses used and have suggested that initial contact may sensitize the organ so that after washing, subsequent application of even a smaller concentration of streptolysin O produces marked myocardial depression.

The mechanism of myocardial deprassant effect of streptolysin O is not well understood. Reitz *et al.*(7) have suggested that streptolysin O produces this effect by release of acetylcholine. Since in the present study the myocardial depressant effect of streptolysin O on cat and frog

heart *in situ* was not blocked by atropine, it does not seem to be due to cholinergic stimulation. Streptolysin O may be exerting a quinidine like effect on the myocardium; this suggestion shall be consistent with the reversible nature of the effect. The decrease in the myocardial contractility produced by streptolysin O in animals would suggest that the streptolysin O may be involved in the causation of myocardial failure associated with acute rheumatic fever in man.

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