Tolerance of Human and Rat Atrial Muscle to Hypothermia and Anoxia

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The advent of open-heart surgery has made available for the first time "fresh" bits of human heart muscle which can be used to study the protective effect of hypothermia on the recovery of contractility of muscle subjected to anoxic stress.

There are a number of reports in the literature which demonstrate the tolerance of man and experimental animals to anoxia and varying degrees of hypothermia.1-11 These investigations utilized survival of the patient or experimental animal as a measure of the protective effect of hypothermia against anoxic stress, and this effect is undoubtedly most important. However, since the vital property of heart muscle is contractility, it was felt that a simple method for quantitative evaluation of this property under conditions of hypothermia and anoxia in vitro might be of value. No work has been reported utilizing human cardiac muscle for this type of investigation. Parallel studies were carried out using rat atria for comparative purposes.

Methods

Adult albino rats were anesthetized with ether and their hearts rapidly excised and placed in 50 ml. of Krebs solution at room temperature.12 The solution was oxygenated constantly with a mixture of 95 per cent oxygen and 5 per cent carbon dioxide.

The left atrium was excised and suspended in the muscle chamber13 by means of a lucite rod with a silver wire hook at its inferior end and silver chloride wire electrodes embedded in the rod and projecting from the inferior end of the rod. Loops of fine silk thread attached to either end of the atrium were then attached to the hook on the lucite rod and a muscle hook which was suspended from a Phipps-Bird heart lever by means of a cotton thread.

Stimulation of the muscle by the silver chloride electrode was accomplished with a square wave stimulator. Voltage was set at about 10 per cent above threshold with a duration of stimulus of 1 msec. for the rat atria and 3 msec. for the human tissue. Frequency of stimulation was 1/sec. An ink-writing pen recorded the muscle contractions on a kymograph.

The muscle chamber was mounted in a constant temperature bath. A no. 21 gauge needle inserted into the bottom of the muscle chamber afforded the outlet for the various gas mixtures to be bubbled through the Krebs' solution.

Stimulation was maintained throughout the equilibrium, anoxic, and recovery phases of each run.

Human atrial tissue* was obtained mainly from the right atrial appendage prior to cardiac bypass and immediately immersed in oxygenated Krebs' solution at room temperature. The strips were prepared by dissecting out intact muscle bundles and mounting them in the muscle chamber in the same manner as were the rat atria.

An anoxic environment was provided by bubbling 95 per cent nitrogen and 5 per cent carbon dioxide through the Krebs' solution. After each period of anoxia, one hour of recovery with the oxygen and carbon dioxide gas mixture was allowed.

Thirty-six rat atria and 27 human cardiac muscle strips were studied. Measurement of muscle contraction was made after the equilibrium period and after a steady state was established in the recovery period. The equilibrium contraction height was called 100 per cent, and the recovery height was expressed as a percentage of the equilibrium height.

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Results

The results are summarized in figures 1, 2, 3, and 4 and show that hypothermia of 25 and 31 C. has a pronounced protective effect on strips of atrial muscle which have been subjected to varying periods of anoxia. Hypothermia of 33 and 35 C. is shown to provide intermediate protection, as demonstrated by the degree of recovery after anoxic stress, compared to the marked reduction in contractile recovery following anoxia at 37 C.

Comparison of the results of rat atrial strips and human atrial strips (figs. 1, 2, 3, and 4)
HYPOTHERMIA AND ANOXIA demonstrates the similarity of the two in response to anoxia and hypothermia. There is a suggestion, however, that the human atrium tolerated anoxia better than the rat atria. The numbers presented here, however, are too few to confirm this impression.

The patterns of contraction of human atrial muscle, when subjected to 31 and 37°C, are shown in figure 5. It is noted that at 31°C, in an anoxic atmosphere, the muscle continues to react but with a greatly reduced contraction height, and there is complete recovery on restoration of the aerobic environment. In contrast, at 37°C, the muscle shows no response to stimulation under anoxic conditions, and the recovery of muscle contractility is very poor. This is probably due to a more rapid utilization of conserved energy at 37°C than at 31°C.

Discussion

Much of what is known of human cardiac physiology has been learned from animal experiments. However, recent work by Sleator and deGubareff14 has demonstrated multiple action potential spikes from isolated single human cardiac muscle fibers following a single stimulus. This type of reaction has not been observed under similar conditions with isolated cardiac muscle fibers from animals. This observation gave added impetus to the present work, in which an effort was made to determine whether human heart muscle differed in its reaction to anoxic stress from that of the experimental animal.

The data presented here not only demonstrate the definite protective effect of hypothermia on the recovery of contractility of cardiac muscle subjected to anoxia, but they also provide a quantitative measure and set limits of time and temperature when subjecting cardiac muscle to anoxia.

This work substantiates the impressions gained by other observers of the safety and protective effect of hypothermia when heart muscle is subjected to anoxia. Hypothermia, then, is a very valuable adjunct in the preparation of a patient for cardiac surgical procedures of relatively short duration, such as the repair of interatrial septal defects of the

Summary

Evidence is presented which strongly suggests the preservation of contractility of human atrial muscle when hypothermia of 25 to 31°C is used during anoxia. Parallel studies were carried out on albino rat atria which gave results similar to that of the human tissue. This report adds further evidence
that hypothermia is valuable in open-heart surgery when anoxic arrest is indicated for the repair of cardiac malformations.

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