Title: EFFECTS OF HALOTHANE ON POTASSIUM-INDUCED CONTRACTURES IN RABBIT PAPILLARY MUSCLES

Authors: T.B. Kloosterboer, M.D., M.R. Lauer M.S., B.F. Rusy, M.D.

Affiliation: Departments of Anesthesiology and Physiology, University of Wisconsin Medical School, Madison, Wisconsin, 53792

Introduction. The in vitro exposure of cardiac muscle to superfusates containing very high concentrations of potassium (K) and low concentrations of sodium (Na) causes the development of a reversible contracture (CT). The CT is believed to be the consequence of a K-induced depolarization of the muscle cell membrane resulting in the influx of calcium (Ca) and activation of the contractile apparatus[1]. This model allows one to study the effects of potent negative inotropic agents, such as halothane (H), on the events important in coupling excitation to contraction in cardiac muscle. The purpose of the present experiments is to examine the ability of H to prevent the development of K-induced CTs in cardiac muscle, to reverse CTs that have already developed, and to alter the activity of the membrane-bound Na/Ca exchange system.

Methods. Papillary muscles of less than 1 mm in diameter were removed from the right ventricle of New Zealand white rabbits sacrificed by a blow to the head. One end of the muscle was secured with silk suture to a stationary post in a tissue bath. The other end of the muscle was likewise attached to the rigid free arm of a force transducer. The resting tension applied to the papillary muscle was adjusted to one gram using a worm gear-driven micrometer. The preparation was superfused with oxygenated Tyrode solution at pH 7.3 and a temperature of 37°C. Contractions were produced by electrically stimulating the tissue at 12/min. Sustained, reversible CTs were produced by switching to an isotonic superfusate containing 140 mM K and 18 mM Na. H-containing solutions were produced using a calibrated Draeger vaporizer. H concentrations are expressed as vaporizer setting.

Results. In 8 muscles, the developed force (DF) was (mean ± sem) 285 ± 25 mg; the DF in the presence of 1% H was 96 ± 11 mg; the magnitude of high K CTs was 503 ± 51 mg; and the magnitude of high K CTs in 1% H-treated preparations was 97 ± 18 mg. Figure 1 shows the effects of exposing a papillary muscle to the high K superfusate (HK). Note that within minutes of returning to the normal Tyrode (NT) solution, the muscle resting tension returns to the control level and normal contractions ensue. Figure 2 shows an example of a preparation exposed to a high K superfusate bubbled with 1% H (HK+H) after pretreatment with H-containing normal Tyrode solution (NT+H). The addition of H dramatically decreases the magnitude of the CT. Figure 3 illustrates the typical effects of 1% H on the the level of an already developed CT. In 5 experiments, there was no detectable reduction in the magnitude of the high level of resting tension upon switching to the HK+H superfusate. Moreover, upon switching from HK+H to NT+H, the resting tension relaxation proceeds unimpeded.

Discussion. The results show that a concentration of H that dramatically inhibits the development of a K-induced CT has no detectable effect on the magnitude of a CT that has already developed. This result is consistent with a suggestion that the negative inotropic effect of H is due primarily to the inhibition of Ca influx, possibly by way of the slow inward current. Additionally, upon return to a normal superfusate, relaxation of the CT, a consequence of the Na/Ca exchange system, is not inhibited by the presence of H in the superfusate. This latter result suggests that halothane does not inhibit the Na/Ca co-transport system.

References.

1. Chapman RA: Excitation-contraction coupling in cardiac muscle. Prog Biophys Molec Biol 35:1-52, 1979

FIGURE 1

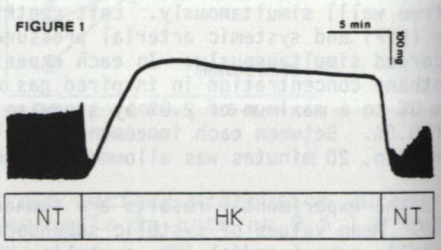


FIGURE 2

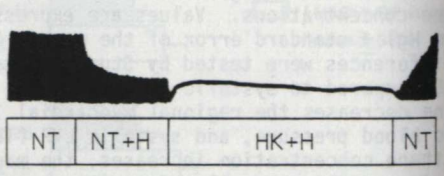


FIGURE 3