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TITLE: Post-ischemic Myocardial Function: No Anesthetic Protection

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Sinclair et al[1] have recently reported that thiopental produced dose-related decreases in creatinine kinase release (protection) after global anoxia in the isolated perfused non-working rat heart (Langendorff model). We selected a very different model namely performance of standard ventricular function curves pre- and again at intervals post-global ischemia (aortic crossclamp) in the open chest dog. Our purpose was to examine the possibilities that 1) anesthetics might ameliorate functional deterioration from global ischemia and 2) there might be qualitative or quantitative differences between clinically relevant anesthetic techniques.

Methods

Dogs were subjected to cannulation which allowed switching from total to right heart bypass, after anesthetization with the study technique (n=24). This was accomplished via vena caval drainage into a reservoir-bubble oxygenator-roller pump-heat exchanger circuit which could be returned either via the femoral artery (total heart bypass) or the left atrium (for right heart bypass). A third cannula drained the right atrium and ventricle for determination of coronary blood flow (CBF) (timed collection). Myocardial oxygen consumption ($M\dot{V}O_2$) was determined as the product of CBF and arterial-coronary venous oxygen content difference. Standard ventricular function curves were determined by placing the animal on right heart bypass, incrementally increasing flow to the left atrium (0.8, 1.2, 1.6, 2.0 and 2.4 l/min/m^2) and measuring resultant left ventricular end diastolic pressures (LVEDP). The heart was paced after SA node crush. Mean arterial pressure was held constant with an aortic snare and an artery-to-venous reservoir shunt. After control ventricular function curves were determined, the animal was placed on total heart bypass, cooled to 28°C, and the aorta crossclamped for 60 minutes. Normal saline at 28°C (pH 7.40) was infused via the aortic root initially (200 ml) and q 15 minutes during the crossclamp. The crossclamp was removed and the animal was rewarmed. Ventricular function curves and $M\dot{V}O_2$'s were determined q ½ hour after crossclamp removal for two hours. Four anesthetic techniques were studied: halothane .43% (½ MAC, n=6), halothane .86% (1 MAC, n=7), pentobarbital 40 mg/kg (n=6), and morphine, 3 mg/kg (n=5).

Results

There were no significant differences in control ventricular function curves between any of the four anesthetics. Even between steady state ½ and 1 MAC halothane, there were no detectable differences in ventricular function (see Fig. 1). The function curves' similarities were confirmed by the $M\dot{V}O_2$ data. After 1 hour crossclamp, ventricular function curves were depressed as expected (Fig. 1). At 2.0 l/min/m^2, LVEDP's averaged 7 ± 1 mmHg for all anesthetics during controls and 11 ± 1 mmHg one hour post-ischemia. The degree of deterioration as measured by both slope and displacement of post-ischemic function curves was not significantly different between any of the anesthetics.

Discussion

In the present study, we could not show any of the four anesthetics to be protective against global ischemic deterioration measured functionally. Our results are at variance with those of Sinclair et al[1]. Their study was of CK release in post-anoxic, isolated clear-liquid perfused, non-working rat hearts. Our study was of ventricular function in working intact dog hearts perfused with blood. Thus barbiturates might affect basal cell maintenance processes, or stabilized membranes re: CK release, but when actual ventricular function is quantitated, the effect cannot be discerned. If this is so, then functional studies would seem more clinically relevant. We found little difference in ventricular function during the control period between ½ and 1 MAC halothane at steady state. We believe that "cardiac depression" seen at these low concentrations is likely due to peripheral effects. We conclude that neither pentobarbital nor morphine nor halothane (½ or 1 MAC) were significantly better with respect to protection of ventricular function following global myocardial ischemia.

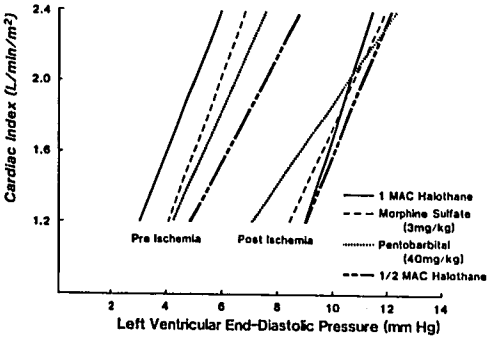

Figure 1: Pre- and post-ischemic ventricular function curves with four different anesthetics.

Reference

1. Sinclair DM, De Moes D, Boink ABTJ, Ruigrok TJC: A protective effect of thiopentone on hypoxic heart muscle. J Mol Cell Cardiol 12:225-227, 1980