Title: ENHANCED MYOCARDIAL DEPRESSION FROM BUPIVACAINE IN DIABETIC RATS

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Introduction. Sudden cardiovascular collapse after the administration of bupivacaine (BUPIV) has been reported. This may be due, in part, to BUPIV's cardiotoxicity (1-2). Diabetes is associated with depression of myocardial function (3-4). We hypothesized that BUPIV would induce more severe alterations in contractile performance in hearts of diabetic animals than in nondiabetic animals. We compared the direct effects of BUPIV on the diabetic rat myocardium using an isolated perfused (Langendorff) heart preparation.

Method. Male Sprague-Dawley rats weighing 200-250g were randomly divided into four groups, control (C), control with BUPIV (CB), diabetic (D) and diabetic with BUPIV (DB). The diabetic group received a single injection of streptozotocin (55 mg/kg, iv) in the tail vein. Age-matched control rats received vehicle alone (0.01M citrate buffer in saline). The diabetic state was verified by plasma glucose levels exceeding 300mg/dl in blood samples obtained just before anesthetizing the animals (vide infra).

12 weeks after induction of diabetes, hearts were excised under ether anesthesia following administration of heparin (1 unit/g, iv), arrested by plunging them into iced perfusion media, mounted and perfused at 75cmH_2O pressure with a modified Krebs-Hensleit bicarbonate solution aerated with 95% O2 and 5% CO2.

Contractile activity was sensed with a Grass FT .03 force transducer attached at the cardiac apex. Contractile force potentials were differentiated electronically to yield ΔForce/Δtime (dF/dt) and expressed as percent of the value obtained immediately prior to adding BUPIV. The atrial and ventricular electrocardiograms (ECG) were recorded from surface electrodes. Coronary blood flow was determined by measuring the total effluent over a 1-min period.

After an 1hr equilibration period hearts were exposed to BUPIV 3.0mcg/ml, which was added to the perfusate reservoir containing oxygenated medium.

All results (dF/dt, heart rate [HR] and coronary blood flow [CF]) were expressed in terms of the percent of the 60 min value±SEM. Statistical analysis was accomplished utilizing student's unpaired t-test for group mean data. A p value of <0.05 was taken as indicating statistical significance.

Results. BUPIV did not decrease myocardial contractility in control animals (C vs. CB). However, BUPIV decreased contractility significantly in diabetic animals (CB vs. DB and D vs. DB) at nearly all time periods (Fig). BUPIV decreased HR and CF significantly and similarly in control and diabetic animals.

Discussion. Although 3mcg/ml BUPIV has already been shown to be toxic to the isolated guineapig heart (1), our results suggest that this dose of BUPIV does not decrease contractility of the isolated rat heart from normal animals. On the other hand, 3mcg/ml BUPIV caused a significant decrease in contractility in the 12 week diabetic heart. These results demonstrate that the presence of a diabetic state appears to enhance the sensitivity of the heart to the myocardial depressant effect of BUPIV. If these results are confirmed at other time intervals in the diabetic state, they indicate yet another risk of anesthesia care imposed by diabetes mellitus.

References.

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