Title: EFFECTS OF CHRONIC NIFEDIPINE ADMINISTRATION IN THE RAT HEART EXPOSED TO ENFLURANE

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Introduction: Previous studies (1) have demonstrated a salutary effect of enflurane administration in the post ischemic recovery period in the isolated rat heart Langendorff model. Those investigators suggested that this effect may be secondary to modulation of calcium transport (2) by protecting the intracellular milieu during ischemic insult and resulting ionic fluxes. In this regard, this same model was used to investigate the combined effects of chronic nifedipine administration to a population of rats who were then exposed to enflurane. The calcium channel blocking properties of chronically administered nifedipine coupled with the protective effects of enflurane were hypothesized to be synergistic, leading to even greater protection from ischemia. Also, the combined inotropic depressive effects were investigated pre- and post-ischemically.

Methods: Four groups of male Sprague-Dawley rats were divided so that two of the groups received parenteral nifedipine, 10ug/kg i.p. b.i.d. for seven days. Group A consisted of controls. Group B consisted of rats pre-treated with nifedipine but receiving no enflurane. Group C consisted of rats who received only enflurane at one MAC, and group D were rats who were pretreated with nifedipine and received one MAC enflurane. Each rat was anesthetized with pentobarbital intraperitonealy and had its heart rapidly excised, mounted upon Langendorff perfusion cannula, then perfused with Krebs Henseleit buffer (KHB) bubbled with 95% O_2 and 5% CO_2 at 37° C. A left ventricular balloon measured peak systolic pressures (PP) while the hearts were paced at 300/min. PP was measured at 10 min and 20 min. Enflurane was bubbled into a separate perfusate reservoir of KHB and administered to groups C and D for 10 minutes between the 10 and 20 min PP recording. Global ischemia was then induced by occlusion of KHB buffer perfusion. Time of ischemic contracture (TIC) was determined as the time to note a 2 mm Hg rise in pressure. Perfusion was then reinstituted with plain KHB for 20 min, at which time PP was again noted as well as the occurence of fibrillation. Coronary flows were also monitored at all times of pressure recordings. Recovery of function was evaluated as a percentage of the 10 min pre-ischemic PP. The data was analyzed by one way ANOVA tests and the prevalence of fibrillation was evaluated by chi square analysis.

Results: PP's and coronary flows were statistically comparable at 10 min in all groups (table 1). PP's at 20 min. were depressed significantly in the enflurane group (B) and the combined nifedipine-enflurane group (D) although the percentage of depression was not significantly different from that of enflurane alone. Recovery percentages were significantly better than control (A, 52%) in the enflurane group (B, 80%) and the nifedipine group (C, 71%). However, recovery percent in the combined treatment group (D, 64%) was insignificantly different than control. TIC's were not significantly different in any group. Coronary flows were not statistically different from control at any time. The percentage of hearts fibrillating after ischemia was significantly less than group A (control) in only the enflurane treated group.

Discussion: We confirmed the findings of other investigators (1) in that enflurane alone allowed for a 80% recovery after ischemia. Chronic nifedipine allowed for a 71% recovery, indicating that it exerts a protective effect from ischemia as defined by reperfusion recovery of peak systolic pressures. Surprisingly, when nifedipine and enflurane were combined, peak pressure recovery was lower after ischemia than with each individually. The administration of enflurane in the rat heart pretreated with nifedipine seems to cause a synergistic inotropic depression after ischemia rather than a synergistic protective effect as hypothesized.

TABLE 1.

PP (torr) ± 1 SEM	N	10'	20'	% Dep 10'-20'/10'	20' Rep	mean % Rec 20'R/10'	T.I.C. (min)
GROUP							
A (control)	10	91±1.7	92±1.8	--	47±4.3	52	13.5±.74
B (enflurane)	10	90±2.8	77±3.3 *	15±2.2	71±3.7	80 *	16.1±.98
C (nifedipine)	7	82±4.9	87±3.8	--	57±3.9	71 *	13.5±.76
D (nif+enf)	8	81±3.9	67±2.0 *	19±2.0	50±5.7	64	14.2±.65

* p less than .05

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