Title : SYMPATHETIC TONE BLOCKADE ENHANCES BUPIVACAINE CARDIOTOXICITY IN ANESTHETIZED DOGS.

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Introduction. Bupivacaine (B) cardiotoxicity seemed to be related to a direct impairment of cardiac electrophysiology and to a decrease of myocardial contractility. However the influence of autonomous nervous system (ANS) in the mechanisms of this cardiotoxicity had never been specified. Thus, the aim of this study was to specify if direct cardiac effects of B could be enhanced or compensated by interactions with the ANS.

Methods. 21 mongrel dogs (13.7 ± 2.1kg) were anesthetized using IV pentobarbital 40mg/kg, intubated and maintained on controlled ventilation and constant temperature. In addition of ECG lead II, a bipolar catheter (USCI 6F) was passed through a femoral vein, under fluoroscopy, up to the right ventricle to record His-bundle electrogram. The controlateral femoral vein was canulated and used for drugs injection. Mean aortic pressure (MAP) was registered through a 5F femoral artery catheter. All data were recorded on a GOULD ES 1000 polygraph at paper speed of 100mm/sec. The electrophysiologic data were measured (msec) : sinus cycle length (R-R), QRS complex duration (QRS), atria-His and His-ventricle intervals (AH, HV). The animals were allocated in 3 groups of 7 dogs, all of them receiving B 4mg/kg IV over 10 sec. Group I was control group, Group II received atropine sulfate 0.2mg/kg IV 10 min prior to B injection. Group III received propranolol 0.2mg/kg IV 15 min prior to B injection. All data were measured 5 min prior to B injection (baseline) and then every 1 min untill 5 min. Data were reported as percentage of change from baseline ± SEM. Comparison between groups was performed using ANOVA test. Differences were considered significant if $p < .05$.

Results. In each of the 3 groups, at the end of B injection, one dog died by serious ventricular disturbances. These dogs were excluded from the study. In group I,II,III the maximum percentages of variation were respectively : RR : +28.4 ± 6.6, +22.8 ± 3.4, +36.3 ± 7 - AH : fig 1 - HV : fig 2 - QRS : +96.8 ± 18.3, +107.1 ± 25.6, +116.9 ± 25 - MAP : fig 3. The only significant difference was found with regard to AH ($p < .01$) and MAP ($p < .05$) between Group III and the other groups.

Conclusions/discussion. 1 - In all groups, the main effect of B was an impairment in infranode conduction, especially by a blocking of fast inward current INa (1). 2 - Cholinergic nervous system does not seem to be implicated in the cardiotoxicity of B because group II never showed any modification taking comparison with group I. 3 - B cardiotoxicity is enhanced in group III. It reveals by the mean of a greater MAP decrease and a greater lengthning of AH interval. As previously reported, modifications of AH and MAP obtained in Group III were far more important than those expected with propranolol alone (2). Moreover beta-blockers unmask the calcium antagonism of most of cardiac drugs which inhibits INa (2). This fact confirms that, using high doses, B also inhibits the calcium channels (3). Then, sympathetic tone should relatively protect from the cardiotoxicity of B. Conversely, this toxicity should be enhanced in patients presenting a failing sympathetic nervous system (beta-blockers, thoracic epidural anesthesia...).

References. 1 - Clarkson CW, Hondeghem LM: ANESTHESIOLOGY 62 : 396-405, 1985.
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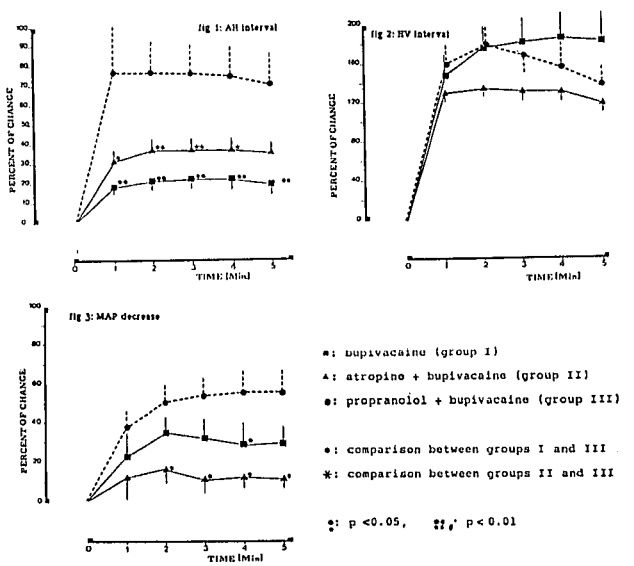

The results are expressed as per cent changes of the control values, each point represents the mean ± SEM.