

Title : LOCAL ANESTHETICS AND DILTIAZEM IN CONSCIOUS DOGS.

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INTRODUCTION. Diltiazem (DTZ) is a widely used calcium blocker for the treatment of angina pectoris and it has been successfully proposed to prevent intraoperative myocardial ischemia without deleterious drug-interactions with general anesthetics (1). However, that could be different with local anesthetics since accentuation of the cardiac depressant effects of verapamil by lidocaine (L) and bupivacaine (B) has been demonstrated (2). Thus, the aim of this work was to study the cardiovascular effects of iv DTZ with and without a concomitant infusion of either L or B in conscious dogs.

METHODS. Seven mongrel dogs were chronically instrumented with catheter in aorta for measurement of mean arterial pressure (MAP) and a miniature pressure transducer in the left ventricle (LV) for LV pressure measurement from which LV dP/dt was derived. Heart rate (HR), PR and QT intervals were measured from ECG. Studies were conducted at least 3 weeks after surgery. Each dog received a 40 min infusion of DTZ ($20 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) in 3 randomized circumstances on 3 separate days. So, after the 10th min of DTZ infusion, a simultaneous 30 min infusion of either normal saline (1 ml/min), or L ($60 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), after an iv bolus of 1.5 mg/kg, or B ($15 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), after an iv bolus of 0.4 mg/kg was started. A blood sample was drawn at the end of combined infusion to assay L and B serum levels by HPLC. Means \pm SEM are reported. After ANOVA, the differences between the groups at a given time or in each group as a function of time were estimated by paired t test.

RESULTS. There were no differences in basal values among the 3 groups before any treatment (table 1). As shown on fig 1, at the 10th min of DTZ infusion, MAP decreased, HR increased and PR interval lengthened to the same extent in all groups. These effects remained unchanged at the 40th min of DTZ + Saline infusion. At the 40th min of DTZ + L infusion (Serum L : $3.6 \pm 0.4 \mu\text{g/ml}$), more marked tachycardia and lengthening of PR interval were observed without change in MAP. At the end of DTZ + B infusion (Serum B : $1.3 \pm 0.2 \mu\text{g/ml}$), additional decrease in MAP and lengthening of PR interval were observed without change in HR. In all groups, LV dP/dt remained unchanged and, as shown in fig 2, QT interval remained related to RR interval

DISCUSSION. As previously demonstrated with verapamil (2), L and B enhance the negative dromotropic effect of DTZ. However, in contrast with verapamil, neither AV block, nor myocardial depression appeared with DTZ. Present results might be explained by a common action of DTZ, L and B on calcium and/or sodium channels, and/or by a buffering of the L and B-induced sympathetic stimulation by the adrenergic effect of DTZ (3). Thus, caution should be exercised in practice of regional anesthesia in DTZ-treated patients, and L may have to be preferred to B as a local anesthetic agent.

	DTZ + SALINE	DTZ + L	DTZ + B
MAP (mmHg)	98 \pm 2	100 \pm 5	97 \pm 3
HR (beats/min)	91 \pm 2	91 \pm 3	90 \pm 4
PR interval (ms)	124 \pm 3	121 \pm 3	122 \pm 3
QT interval (ms)	176 \pm 8	180 \pm 6	189 \pm 9
LV dP/dt (mmHg/s)	3079 \pm 51	2943 \pm 20	3000 \pm 22

Table 1. Basal values of measured variables

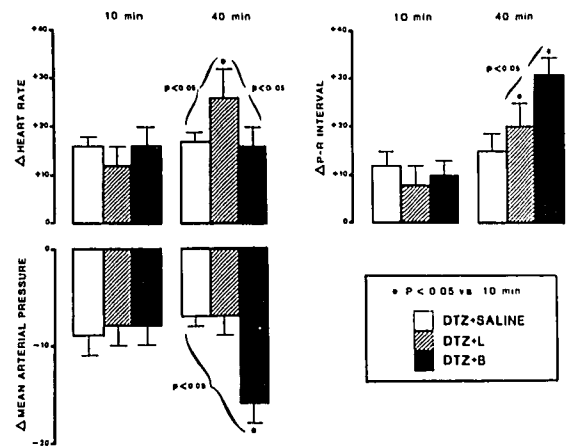


Fig 1. Changes in the cardiovascular variables at the 10th and the 40th of DTZ+Saline, L or B infusions.

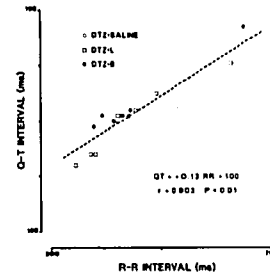


Fig 2. QT int/RR int relation during DTZ + Saline, L or B infusions.

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