Title HEMODYNAMIC EFFECTS OF DIAZEPAM-BUPIVACAINE INTERACTION IN CONSCIOUS DOGS

Authors Jean-Louis GERARD, MD, Jacques DURANTEAU, MD, Riaz AHMAD, MD, Alain EDOUARD, MD, and Alain BERDEAUX, MD, Ph D

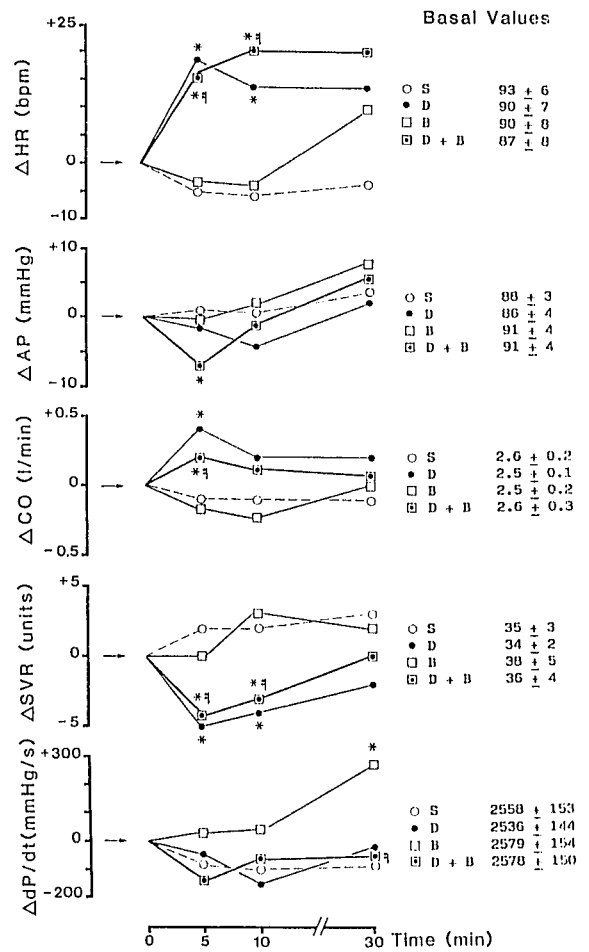
Affiliation Départements d'Anesthésiologie et de Pharmacologie, Université de Paris-Sud, Hôpital de Bicêtre, 94275 Kremlin-Bicêtre cedex, FRANCE

INTRODUCTION. Controversies exist concerning the cardiovascular effects of diazepam (D) and bupivacaine (B) concurrent administration. Indeed, both cardioprotective (1) and cardiotoxic (2) effects of diazepam have been reported. Since all previous studies have been performed at toxic bupivacaine serum levels (BSL), our goal was to investigate this issue when diazepam and bupivacaine were present only at therapeutic levels.

METHODS. Six mongrel dogs were anesthetized and chronically instrumented with : an intraaortic catheter for measurement of mean arterial pressure (AP), a miniature pressure transducer in the left ventricle (LV) for LV pressure measurement from which myocardial contractile force (LV dP/dt) was derived, and an electromagnetic flow probe around the ascending aorta for recording of mean cardiac output (CO). Systemic vascular resistance (SVR) was calculated as AP/CO. PR and QT intervals were measured and heart rate (HR) and RR interval recorded from the EKG. Studies were conducted at least 3 weeks after surgery. Each dog received 4 treatments in a random order at weekly intervals : (1) saline (S), 1 ml/min for 30 min; (2) diazepam, 0.2 mg/kg iv bolus; (3) bupivacaine, 0.4 mg/kg iv bolus followed by 15 μg/kg/min for 30 min; and (4) D + B : diazepam as in (2) followed by bupivacaine as in (3). Blood was sampled at 5 and 30 min of infusion in all treatment groups to measure arterial blood gases (ABG) and in groups (3) and (4) to assay BSL (HPLC method). Comparison of data was performed by ANOVA for repeated measures. Means $\pm$ SEM are reported. $P < 0.05$ was considered significant. QT-RR relations were tested by linear regression.

RESULTS. Mean BSL remained stable in the same range in all groups at 1.3 ± 0.5 μg/ml. The primary effect of diazepam was to induce early vasodilation, SVR decreased at 5 min, with concomitant increases in HR and CO. AP and LV dP/dt remained unchanged. In contrast bupivacaine induced a delayed (30 min) increase in HR and LV dP/dt, without changes in AP and CO. The combined effect of D + B included a decreased SVR and increased HR and CO, occuring at 5-10 min. However the increase in HR was sustained throughout the experiment. Unlike bupivacaine alone, the tachycardia was not accompanied by any increase in myocardial contractility. The slopes of QT-RR relations were the same and ABG were unchanged in the 4 treatments groups throughout the study.

DISCUSSION. Our study demonstrates that in conscious dogs, bupivacaine and diazepam at therapeutic BSL do not cause the severe dysrhythmic effects previously reported with these drugs at toxic levels in anesthetized rats (2). Bupivacaine alone exerts a mild sympathomimetic effect (3); the addition of diazepam, by blunting this effect may decrease the margin of safety during bupivacaine administration. This may particularly relevant during epidural administration of bupivacaine when the sympathetic response is important with respect to counteracting vasodilation. Also caution should be exercised when administering sedation during regional anesthesia in patients with impaired cardiac function.



Hemodynamic changes during S, D, B and D+B treatments
*** P < 0.05 vs. saline (S)**
‡ P < 0.05 vs. bupivacaine (B)

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