TITLE : LIDOCAINE DOSE-RELATED ALTERATION OF BAROREFLEX CONTROL OF HEART RATE IN CONSCIOUS DOGS.

AUTHORS : A. Edouard, M.D., A. Berdeaux, Pharm.D., J. Langloys, M.D., K. Samii, M.D., Y. Noviant, M.D.

AFFILIATION : Départements d'Anesthesiologie et de Pharmacologie Clinique - Université Paris-Sud Hopital de Bicêtre - 94270 Le Kremlin-Bicêtre - FRANCE.

INTRODUCTION. It has been demonstrated that lidocaine (L)epidural anesthesia-induced hypotension related to the neural blockade might be modulated by autonomic nervous system depending on circulating L plasma levels (LPL) (1). This mechanism might also partly explain the absence of reflex tachycardia through baroreflex alteration. In the present work, we tested this hypothesis by studying the role of L on baroreflex control of heart rate (HR) at two therapeutic LPL in conscious dogs.

METHODS. Seven mongrel dogs were chronically instrumented with catheter in aorta for measurement of systolic, diastolic and mean arterial pressures (respectively SAP, DAP and MAP). A cardiotachometer triggered by ECG provided records of HR. Studies were conducted at least 3 weeks after surgery. A catheter was inserted in a leg vein for the intravenous (iv) injection of drugs. L was infused at either 30 (L30) or 60 mcg/kg/min (L60) during 50 min after a loading iv dose of L (1.5 mg/kg). The 2 rates of infusion were given on a separate week. Arterial blood samples were drawn at 30 min of infusion (T30) to assay LPL in duplicate by the EMIT homogeneous enzyme immunoassay. MAP, HR, heart period (R-R interval) were recorded and baroreflex testing was made by iv bolus of nitroglycerin (NG 10 mcg/kg) and phenylephrine (PHE 5 mcg/kg) in a 1 ml-volume to lower and raise SAP by 20-30 mm Hg. Each R-R interval was plotted as a function of the preceeding SAP. The analysis was performed beat by beat beginning only after the first noticeable change in R-R interval. Baroreflex sensitivity (BRS) was expressed in msec/mm Hg as the slope of the regression line between SAP and R-R interval. The slope was accepted for further analysis only if the correlation coefficient was 0.8 or greater. Average values $\pm$ SEM were reported. All data were compared to control values by paired t-test.

RESULTS are reported in tables I and II. L30 and L60 achieved different LPL at T30 ($p<0.001$). During L30 infusion, MAP, HR, R-R interval and BRS during baroreflex activation (PHE) and deactivation (NG) remained unchanged. During L60 infusion, MAP was slightly increased but HR did not change. The maximal NG-induced hypotension was more marked at T30 than during control without simultaneous change in HR and R-R interval variations. The maximal PHE-induced hypertension was reduced and cardiac slowing was magnified. BRS during baroreflex activation (PHE) was significantly increased. Tremor was observed in four dogs over seven during L60 infusion.

DISCUSSION. This study demonstrates that in contrast with low LPL (1-2 mcg/ml), higher LPL (3-4 mcg/ml) alterate the baroreflex control of HR mainly by increasing the efferent vagal tone. Two mechanisms may be proposed : (i) an enhancement in sympathetic vasoconstrictor activity on baroreceptors areas (2) due to a central adrenergic system activation (3) and responsible of the T30 slight hypertension and tremor (ii) an increase in arterial compliance (4) consistent with a direct vasodilator effect of L and reflected by marked NG-induced hypotension and limitation of PHE-induced hypertension. Thus, depending on LPL, L interacts with baroreflex control of HR and may contribute to the absence of tachycardia in response to the epidural anesthesia-induced hypotension.

		CONTROL	LIDOCAINE T30
Lidocaine Plasma Level (mcg/ml)	L30	-	1.9 ± 0.2
	L60	-	3.3 ± 0.2
Mean Arterial Pressure (mm Hg)	L30	97 ± 5	95 ± 3
	L60	96 ± 2	106 ± 6**
Heart Rate (beats/min)	L30	87 ± 6	95 ± 5
	L60	92 ± 5	93 ± 4
Mean R-R Interval (msec)	L30	708 ± 60	626 ± 37
	L60	662 ± 36	660 ± 33

Table I : Basal values of MAP, HR and R-R interval. Significant change from control : ** $p<0.01$.

		CONTROL		LIDOCAINE T 30	
		N G	PHE	N G	PHE
ΔMAP	L30	-25 ± 1	+24 ± 3	-23 ± 2	+22 ± 3
	L60	-21 ± 2	+31 ± 4	-25 ± 3**	+24 ± 2*
ΔHR	L30	+82 ± 8	-47 ± 5	+90 ± 8	-55 ± 5
	L60	+58 ± 9	-54 ± 3	+63 ± 9	-62 ± 3*
ΔR-R Int	L30	-340 ± 43	+848 ± 41	-290 ± 13	+848 ± 60
	L60	-264 ± 30	+758 ± 61	-265 ± 27	+971 ± 53**
BRS	L30	13.8 ± 1.9	22.7 ± 1.8	12.4 ± 1.5	20.7 ± 3.3
	L60	11.8 ± 1.5	21.8 ± 3.6	11.3 ± 1.9	25.8 ± 3.6**

Table II : BRS and maximal vasoactive drug-induced changes (Δ) in MAP, HR and R-R interval. Significant change from control : * $p<0.05$, ** $p<0.01$.

REFERENCES

1. BONICA JJ, BERGES PU, MORIKAWA K : Circulatory effects of peridural block : I. Effects of level of analgesia and dose of lidocaine. Anesthesiology 33 : 619-625, 1970.

2. SAMPSON SR, MILLS E : Effects of sympathetic stimulation on discharge of carotid sinus baroreceptors. Am. J. Physiol. 218 : 1650-1653, 1970.

3. McWHIRTER WR, SCHMIDT FH, FREDERICKSON EL et al. : Cardiovascular effects of controlled lidocaine overdosage in dogs anesthetized with nitrous oxide. Anesthesiology 39 : 398-404, 1973.

4. RANDALL O, ESLER M, CULP B et al. : Determinants of baroreflex sensitivity in man. J. Lab. Clin. Med. 91 : 514-519, 1978.