Title: BUPIVACAINE CARDIOTOXICITY IN NORMAL AND ACIDOTIC RABBITS

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Introduction: Controversy persists over the cardiac toxicity of bupivacaine relative to other local anesthetics if accidentally administered intravenously. In lightly anesthetized dogs cardiac toxicity of bupivacaine and lidocaine following intravenous injection was proportional to their potencies as local anesthetics.[1] In sheep, however, bupivacaine was clearly more cardiotoxic than lidocaine.[2,3] This study examines the cardiac effects of intravenous administration of convulsant doses of lidocaine and bupivacaine in unanesthetized rabbits. To simulate the acidosis and hypoxia associated with the inadequate ventilation that may occur during seizures, we also studied unanesthetized rabbits with preinduced acidosis and hypoxia.

Methods: In 23 "nonacidotic" rabbits, catheters were placed in femoral arteries and veins during halothane-oxygen anesthesia. After recovery from preparatory surgery, 10 rabbits ("low dose" group) were randomly assigned to receive lidocaine, 5.7 mg/kg, or bupivacaine, 2.1 mg/kg, IV over 10 sec. These doses are equivalent (on a mg/kg basis) to those administered epidurally (or accidentally, intravascularly) during cesarean delivery. The other 13 rabbits were given twice these doses ("high dose" group). Continuous EKG and femoral arterial pressure tracings were analyzed for cardiovascular changes and arrhythmias. Ten "acidotic" rabbits had similar surgery and recovery periods. However, prior to local anesthetic injection, they breathed an air-nitrogen-carbon dioxide mixture that produced a stable pH of 7.17±0.02 (SD) and a lowered P_aO_2 by 10-20 torr. Rabbits then received lidocaine, 5.7 mg/kg, or bupivacaine, 2.1 mg/kg, as described earlier. Continuous EKG and blood pressure tracings were analyzed.

Results: Twenty-two "nonacidotic" rabbits had clinical evidence of local anesthetic-induced seizures. These seizures did not produce acidosis or significant hypoxia. Nine of ten animals with preinduced acidosis seized. No deaths, significant hemodynamic changes, or serious arrhythmias occurred after intravenous injections of either low- or high-dose lidocaine. In contrast, bupivacaine injection produced serious rhythm abnormalities in all rabbits, particularly wide QRS complex bradycardia and tachycardia, A-V conduction block, and electromechanical dissociation (table). These arrhythmias were frequently associated with significant hemodynamic changes (greater than 50% decrease in mean arterial pressure). Furthermore, 4 of 5 acidotic rabbits given low-dose bupivacaine and 2 of 7 nonacidotic rabbits given high-dose bupivacaine died within 3 min.

Discussion: Cardiovascular collapse and death have been reported following accidental intravenous injection of bupivacaine during attempted regional anesthesia.[4] Moore has postulated that ineffective resuscitation, not bupivacaine-induced cardiac toxicity, is the cause of this cardiovascular collapse.[5] We have shown that rapid intravenous injection of clinically equivalent doses of bupivacaine, but not lidocaine, produces serious cardiac arrhythmias and death in normoxic, nonacidotic rabbits. Acidosis further exacerbates the cardiotoxic effects of bupivacaine. These results are in contrast to previous studies in lightly anesthetized dogs,[1] and in agreement with previous studies in sheep.[2,3]

References:

1. Liu P, Feldman HS, Covino BM, et al: Acute cardiovascular toxicity of intravenous amide local anesthetics in anesthetized ventilated dogs. Anesth Analg 61:317-322, 1982

2. Kotelko DM, Shnider SM, Dailey PA, et al: Bupivacaine-induced cardiac arrhythmias in sheep. Anesthesiology 60:10-18 1984

3. Thigpen JW, Kotelko DM, Shnider SM, et al: Bupivacaine cardiotoxicity in hypoxic-acidotic sheep. Anesthesiology 59:A204, 1983

4. Albright GA: Cardiac toxicity following regional anesthesia with etidocaine or bupivacaine. Anesthesiology 51:285-287, 1979

5. Moore DC: Administer oxygen first in the treatment of local anesthetic-induced convulsions. Anesthesiology 53:346-347, 1980

ARRHYTHMIAS IN RABBITS AFTER IV ADMINISTRATION OF LOCAL ANESTHETICS (Percent)

	LIDOCAINE			BUPIVACAINE		
	LD	HD	Acid.	LD	HD	Acid.
n =	5	6	5	5	7	5
Sinus tach/SVT	0	33	60	40	14	0
Sinus bradycardia	0	50	0	20	28	0
Wide QRS complex rhythym	0	0	0	40	14	0
bradycardia	0	0	0	60	100	100
tachycardia	0	0	0	0	42	0
AV block	0	0	0	0	72	0
EM dissociation	0	0	0	0	14	20
Death	0	0	0	0	28	80

LD = low dose: HD = high dose: Acid. = acidotic.