K7 Use of the Covino Algorithm in Evaluating the Additive Toxicity of Lidocaine® and Bupivacaine

David M. Benjamin, PhD, Tufts Medical School, 77 Florence Street, Suite 107, Chestnut Hill, MA*

This research project are discuss how to convert bupivacaine blood levels to lidocaine equivalents so that the blood levels of both drugs can be used to assess toxicity in combined lidocaine/bupivacaine toxicity.

The local anesthetics (LAs) lidocaine® and bupivacaine are commonly used together in many surgical and cosmetic procedures. Routes of administration run the full gamut and include: intravenous (IV) lidocaine® as an antiarrhythmic, local infiltration for surgical repair of lacerations and during "face lifts", extensive infiltration for liposuction, and epidural and subarachnoid administration for abdominal and lower extremity surgery. LA administration may be either the sole analgesic employed, or may be combined as an adjunct with general anesthesia. However, local anesthetics are not innocuous and serious central nervous system (CNS) and cardiovascular toxicity can result in seizures, cardiovascular collapse and death. Antiarrhythmic levels of lidocaine® range from 2-5 mcg/ml and toxic effects are well-established in the 6-10 mcg/ml range; however, the same relationship is less well understood for bupivacaine, and evaluation of blood levels for mixed lidocaine®/bupivacaine toxicity is poorly understood as evidenced by the following case report.

Facts of the case: RB was a 60-year-old female in good general health who underwent facial cosmetic surgery and subsequently died from cardiorespiratory collapse. She had been diagnosed with depression and was taking Fluoxetine (Prozac®) and no other medications. The medical examiner's report stated the following: The intubation went smoothly and she was initially stable from a cardiovascular point of view. About five minutes into the anesthesia a local anesthetic consisting of lidocaine, bupivacaine and epinephrine was injected beneath the skin of the face and scalp. She began to demonstrate cardiovascular instability …. Heart rate decreased to the 30s and CPR was begun with return of pulse and blood pressure. She again deteriorated and was transferred by paramedics to the ER…. Her condition gradually deteriorated to anoxic encephalopathy and she was pronounced dead approximately seven hours after the initial cardiovascular collapse. Toxicology anteand postmortem lidocaine® and bupivacaine blood levels were:

Time	Ante-Mortem Blood Concentrations (mcg/ml)		Post-Mortem Blood Concentrations (mcg/ml)	
	Lidocaine®	Bupivacaine	Lidocaine®	Bupivacaine
9:50 a.m.	3.1	0.9		
10:34 a.m.	4.5	2.0		
4:27 p.m.		DEATH		
At autopsy: (46 hours after death)			5.3	3.3

Injection sites were identified as follows: "On the midline upper forehead just below the hairline is a punctuate mark representing a needle puncture. A second punctuate mark is present on the left lower forehead just above the lateral end of the left eyebrow. A third punctuate mark is noted on the left upper lateral cheek just lateral to the lateral angle of the left eye. Fourth and fifth punctures are noted on the lateral aspect of the right eye…. A ½ inch area of subcutaneous hemorrhage is present about the lower of the two puncture marks near the lateral angle of the right eye." The Medical Examiner also offered the following interpretation in his report, "Lidocaine® and bupivacaine levels are within the range previously documented following clinical administration. The actual mechanism of her cardiorespiratory collapse is unknown."

Benjamin G. Covino, MD, PhD, was Professor of Anesthesiology at Harvard Medical School and Vice-President of Astra Pharmaceuticals, (a company that marketed lidocaine® and bupivacaine) from the mid1960s through the 1980s and was an internationally-respected expert in local anesthesia pharmacology and toxicology. Dr. Covino recognized that bupivacaine was four times as potent as lidocaine® and that toxic blood levels of lidocaine® ranged from 6-10 mcg/ml while those of bupivacaine ranged from 1.5-2.5 mcg/ml. Dr. Covino was also the first investigator to convert blood levels of bupivacaine to "lidocaine® equivalents" by multiplying the bupivacaine blood level by four and adding that number to the blood level of lidocaine® to obtain the combined blood level of both local anesthetic agents in "lidocaine® equivalents". Applying the "Covino Algorithm" to the above data, at 9:50 am, a lidocaine® equivalent level of 6.7 and at 10:34 am, a lidocaine® equivalent level of 12.5, well into the toxic cardiodepressant level, and rising. The rapid appearance of bradycardia most likely indicated an initial unintended intravascular administration followed by continuous absorption from the infiltrated region resulting in an additive toxic cardiovascular effect that was further compromised by poor management and hypoxemia, and resulted in the death of a patient.

Lidocaine®, Bupivacaine, Additive Toxicity

 ** Presenting Author*