

Title: IS ETIDOCAINE MORE CARDIOTOXIC THAN LIDOCAINE?

Authors: H.O. Morishima, M.D., Ph.D., H. Pedersen, M.D., M. Finster, M.D., H.S. Feldman, B. Sc., and B.G. Covino, Ph.D., M.D.

Affiliation: Departments of Anesthesiology, Obstetrics and Gynecology, College of Physicians and Surgeons of Columbia University, New York, N.Y. 10032, and Department of Anaesthesia, Harvard Medical School, Boston, MA, 02115

Introduction. It is generally assumed that the cardiovascular symptoms of local anesthetic toxicity are elicited by doses and blood levels significantly higher than those provoking convulsions. This was found to be true when lidocaine was administered by constant intravenous infusion to adult, newborn or fetal sheep.¹ However, recently reported incidents of cardiac arrest occurring shortly after the onset of convulsions in patients who received inadvertent intravascular injections of etidocaine or bupivacaine have suggested the possibility that these newer agents may be more cardiotoxic.² The present study was undertaken to determine toxicity thresholds for etidocaine in the sheep model and to compare them with data previously obtained for lidocaine.

Methods. Etidocaine hydrochloride was administered intravenously by constant infusion (0.5 mg/kg/min) into 9 nonpregnant adults, 9 newborn and 9 fetal sheep. Arterial blood pressure, heart rate, respiratory movements and fetal EEG were monitored continuously. No respiratory or cardiovascular support was provided. Arterial blood samples were withdrawn at the onset of each toxic manifestation which appeared in the following sequence: convulsions, hypotension, respiratory arrest, circulatory collapse. All samples were analyzed for pH, blood gases and etidocaine concentrations using a gas chromatographic technique.

Results. In the adult, convulsions occurred following a significantly smaller dose of etidocaine than that given to the newborn (2.21 ± 0.23 vs 5.71 ± 0.46 mg/kg) (mean ± SE). The same was true for circulatory collapse: 9.36 ± 1.42 vs 13.47 ± 1.31 mg/kg. The highest dosage was necessary to produce convulsions (15.56 ± 5.36 mg/kg) and circulatory collapse (82.70 ± 24.10 mg/kg) in the fetus. In contrast, blood concentrations associated with these toxic manifestations were similar in the adult and the newborn (convulsions: 3.92 ± 0.46 vs 3.21 ± 0.27 µg/ml; circulatory collapse: 6.63 ± 0.92 vs 8.05 ± 0.90 µg/ml). Fetuses convulsed at

significantly lower blood levels (1.41 ± 0.31 µg/ml) and developed circulatory collapse at levels similar to those in other age groups (10.99 ± 2.13 µg/ml). Comparison of the dosage and blood concentrations associated with the onset of convulsions (CNS) and circulatory collapse (CC), expressed as CC/CNS ratios, for etidocaine and lidocaine is displayed in the table below (values are mean ± SE):

	Dosage Ratio (CC/CNS)		Blood concentration Ratio (CC/CNS)	
	Etidocaine	Lidocaine*	Etidocaine	Lidocaine
Adult	4.44 ± 0.85	7.13 ± 1.13	1.72 ± 0.23§	3.52 ± 0.26
Newborn	2.36 ± 0.16§	3.82 ± 0.26	2.48 ± 0.10§	3.59 ± 0.33
Fetus	6.06 ± 1.24	11.40 ± 3.30	9.08 ± 1.44	5.61 ± 1.77

* Calculated from previously published data

§ Significantly different from lidocaine

A significantly lower dosage ratio for etidocaine was noted in the newborn while the etidocaine blood concentration ratios were significantly lower in the adult and the newborn.

Conclusions:

1. The newborn is no more sensitive to etidocaine than is the adult. The larger dose requirement in the newborn is probably related to greater volume of distribution.

2. The high dose requirement by the fetus is undoubtedly due to the placental transfer of the drug into the mother.

3. In the absence of respiratory and circulatory support, etidocaine appears to be more cardiotoxic than lidocaine.

References:

1. Morishima HO, Pedersen H, Finster M, et al: Toxicity of lidocaine in adult, newborn and fetal sheep. *Anesthesiology* 55:57-61, 1981

2. Albright GA: Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. *Anesthesiology* 51:285-287, 1979