Title: THE PROTECTIVE EFFECT OF TERBUTALINE ON BUPIVACAINE-INDUCED CARDIOTOXICITY

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Introduction: Terbutaline is a β agonist drug used to inhibit uterine contraction. Intravascular injection of bupivacaine, a long-acting amide anesthetic used in laboring patients, has been associated with cardiovascular collapse in the pregnant patient.(1) In spite of its cardiotoxicity, bupivacaine is still a widely used local anesthetic in both non-pregnant and pregnant patients. The purpose of this study was to determine if terbutaline had a protective or toxic effect in rats exposed to intravenous bupivacaine.

Methods: Seventy-two adult male Sprague-Dawley rats weighing approximately 300g were randomly divided into four groups. The rats were anesthetized with 40-60 mg/kg of intraperitoneal pentobarbital. A femoral vein was cannulated, and femoral venous blood gases were measured. A preliminary dose response experiment showed that bupivacaine 4.5mg/kg and 5.0mg/kg when injected intravenously resulted in 25% and 50% fatalities respectively. Based on these studies, 4.5mg/kg and 5.0mg/kg bupivacaine 0.5% solution was chosen for intravenous injection. Rats in Group I and II received pretreatment with either normal saline or terbutaline 40µg/kg in equal volume over two minutes. One minute following pretreatment, all rats in Groups I and II received 4.5mg/kg of 0.5% bupivacaine over 10 seconds. The same protocol for rats in Groups III and IV was followed except that bupivacaine 5mg/kg was used. The experiments were performed between 9:00 and 12 noon to avoid diurnal variations. Respirations, heart rate, and rhythm were monitored throughout the experiment. The rats were not ventilated or oxygenated to mimic the usual clinical situation of bupivacaine-induced cardiotoxicity (BCT). Rats were classified as survivors or fatalities at three minutes following the administration of IV bupivacaine. The rats that maintained adequate ventilation, rhythm, and heart rate were classified as survivors. The rats that developed apnea, cyanosis, and agonal rhythm with no cardiac impulse were classified as fatalities.

Results: There was no significant difference in fatalities in the low dose bupivacaine groups. (groups I and II) However, three of twenty-four (12.5%) rats died in the terbutaline treated group compared to nine out of twenty-four (37.5%) rats in the high dose bupivacaine groups (groups III and IV) ($p<.05$, Chi-square, Fisher's exact test). There were no significant differences in the blood gases, weights, or pentobarbital doses between the groups (ANOVA). All of the rats developed apnea at 8-10 seconds following the injection of bupivacaine. The rats that did not survive remained apneic, became cyanotic and developed agonal cardiac rhythm and cardiac arrest.

Table I.

Group	n	Bupivacaine mg/kg	Pretreatment	Fatal/ survivors	(%)
I	12	4.5	saline	4/11*	36.0%**
II	12	4.5	terbutaline	5/12	41.6%
III	24	5.0	saline	9/24	37.5%#
IV	24	5.0	terbutaline	3/24	12.5%

* one rat died after nembutal dose ** not significant # $p<.05$

Discussion: Recently, this rat model was used to identify the toxicity of epinephrine and phenylephrine in regard to BCT(2). Bupivacaine, at high blood concentrations is known to increase systemic and pulmonary vascular resistance, and possibly cause coronary vasoconstriction. Unlike the α effects of epinephrine and phenylephrine, the β (vasodilation) effect of terbutaline may play a role in the reduction of vascular resistance that possibly contributes to protection from BCT. The results of this study suggest that terbutaline does not contribute to BCT and at best, decreases the risk of BCT. Further studies that reflect the situation in pregnant women are needed.

Reference: 1. Albright GA: Clinical aspects of bupivacaine toxicity presentation to the Food and Drug Administration, October 4, 1983.
2. Kambam J, Kinney W, et al: Epinephrine and phenylephrine increase cardiorespiratory toxicity of intravenously administered bupivacaine in rats. Anesth-Analg, 1990.(in press)

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TITLE: EPIDURAL CATHETER ASPIRATE

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Introduction: The presence of glucose (G) in the epidural catheter aspirate is used to differentiate CSF from local anesthetics (LA). Occasionally we have detected G in aspirates obtained from patients who received uneventful lumbar epidural anesthesia (LEA). In this study we assessed the frequency of positive aspirates for G from lumbar catheters. To elucidate the source of G, we analyzed aspirate samples for prealbumin, a protein which composes 5-7% of the CSF proteins, but is found only in trace amounts in the serum or transudate fluid[1].

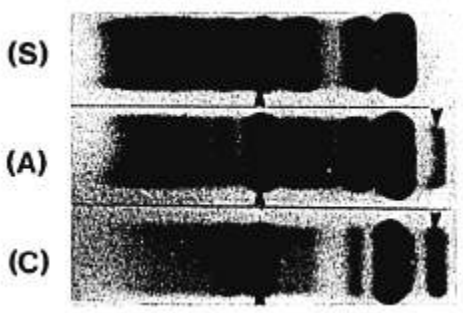
Methods: The protocol was approved by the review board and informed consent obtained. Aspirates were collected from 26 parturients undergoing uneventful LEA for labor analgesia (n = 12) or cesarean section (CS, n=14). The catheter was aspirated before and after the initial LA dose, and every 30 minutes thereafter. The aspirate was tested for G using glucose oxidase test paper. Following forty-fold concentration, four G positive aspirates were subjected to agarose-gel immunoelectrophoresis for prealbumin. Serial dilutions of blood in normal saline and LA were tested for G. Biuret test was used to measure total protein concentration in the aspirate.

Results: Aspirates from ten CS (0.3 - 0.6 ml) and four labor patients (0.2 - 0.4 ml) tested positive for G. Patient's blood diluted > 1:100 tested negative for G. At 1:100 dilution, blood samples appeared bloody. No aspirate was visibly blood stained to this extent. No patient showed evidence of dural puncture. Aspirates contained negligible total protein concentrations. The LA tested negative for G. A prealbumin electrophoresis band was readily detectable in two aspirates (Fig).

Discussion: Our findings show that the testing for G in epidural catheter aspirate can be misleading. The source of G in epidural aspirate is unclear; however, the prealbumin band seen in some but not in all G positive aspirates indicates CSF leakage into the epidural space as one possible source. The aspirate is not an exudate because it contained no protein. The CSF may enter the epidural space via the arachnoid villi protruding into the epidural space.[2]

References:
1. Gavin R: N Z Med J 64:280, 1965
2. Reisner LS: Anesthesiology 44: 451, 1976

FIGURE: Electrophoresis patterns of serum (S), aspirate (A) and CSF (C)



Legend: Upward arrows - transferrin; Downward arrows - prealbumin.